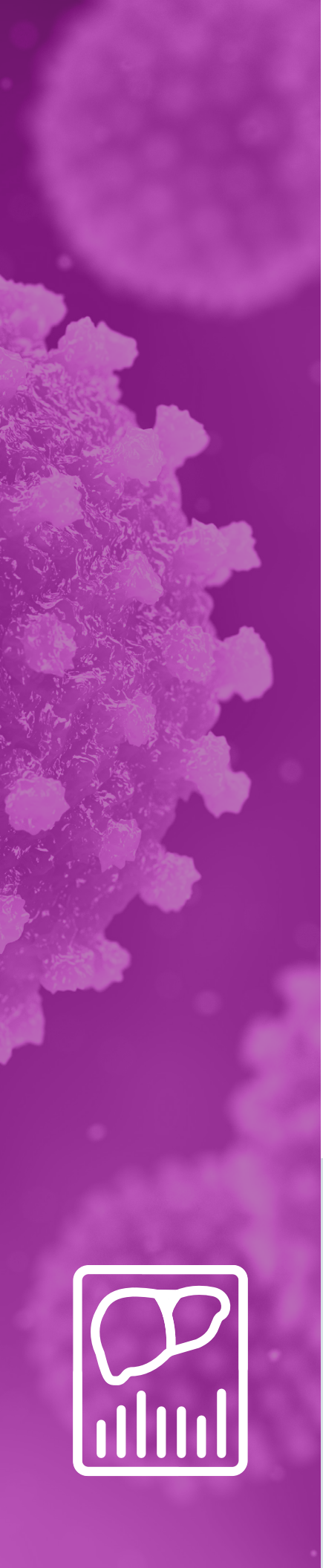

VIRAL HEPATITIS SURVEILLANCE AND CASE MANAGEMENT

GUIDANCE FOR STATE, TERRITORIAL, AND LOCAL HEALTH DEPARTMENTS

Published August 2021

DIVISION OF VIRAL HEPATITIS

Centers for Disease Control and Prevention
National Center for HIV/AIDS, Viral Hepatitis, STD, and TB Prevention

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Terms, Abbreviations, and Acronyms

Gender-neutral terminology will be used throughout for pregnant people, people of childbearing age with childbearing potential, and gestational parents. These terms are used to describe people who are pregnant, have the potential to become pregnant, or have physically given birth, to be inclusive of all gender identities.

AASLD	American Association for the Study of Liver Diseases
ACIP	Advisory Committee on Immunization Practices
ACOG	American College of Obstetrics and Gynecologists
ALT	alanine aminotransferase
Anti-HAV IgG	immunoglobulin class G antibody to hepatitis A virus
Anti-HAV IgM	immunoglobulin class M antibody to hepatitis A virus
Anti-HBc IgM	immunoglobulin class M antibody to hepatitis B core antigen
Anti-HBe	hepatitis B envelope antibody
Anti-HBs	hepatitis B surface antibody
Anti-HCV	hepatitis C virus antibody
CDC	US Centers for Disease Control and Prevention
CFR	Code of Federal Regulations
CLIA	Clinical Laboratory Improvement Amendments
CMS	Centers for Medicare and Medicaid Services
CSELS	Center for Surveillance, Epidemiology, and Laboratory Services
CSTE	Council of State and Territorial Epidemiologists
DAA	direct-acting antiviral agents
DIS	disease investigation specialists
DNA	deoxyribonucleic acid
DVH	Division of Viral Hepatitis
DTAC	Disease Transmission Advisory Committee
EHR	electronic health record
ELR	electronic laboratory reporting
EMR	electronic medical record
FDA	US Food and Drug Administration
ICD-10	International Statistical Classification of Diseases and Related Health Problems, Tenth Revision
IDU	injection drug use
IDSA	Infectious Diseases Society of America
HAI	health care-associated infections
HAV	hepatitis A virus
HBeAg	hepatitis B envelope antigen
HBIG	hepatitis B immunoglobulin
HBV	hepatitis B virus

HBsAg	hepatitis B surface antigen
HCV	hepatitis C virus
HD	health department
HL7	Health Level Seven
LGBTQ+	lesbian, gay, bisexual, transgender, and queer plus
MAT	medication-assisted treatment for opioid use disorder
MMWR	Morbidity and Mortality Weekly Report
MOUD	medication for opioid use disorder
MSM	men who have sex with men
NASTAD	National Alliance of State and Territorial AIDS Directors
NAT	nucleic acid test
NBS	NEDSS-Base System
NEDSS	National Electronic Disease Surveillance System
NETSS	National Electronic Telecommunications System for Surveillance
NNC	Nationally Notifiable Condition
NNDSS	National Notifiable Diseases Surveillance System
NCHHSTP	National Center for HIV/AIDS, Viral Hepatitis, Sexually Transmitted Disease, and Tuberculosis Prevention
NHANES	National Health and Nutrition Examination Survey
OB/GYN	Obstetrics and gynecology
OMB	Office of Management and Budget
OPTN	Organ Procurement and Transplantation Network
PCR	polymerase chain reaction
PHBPP	Perinatal Hepatitis B Prevention Program
PHS	Public Health Services
PII	personally identifiable information
PreP	pre-exposure prophylaxis
PWID	people who inject drugs
PWUD	people who use drugs
PVST	post-vaccination serologic testing
TA	technical assistance
RNA	ribonucleic acid
S/c	signal-to-cutoff
SSP	syringe services programs
STI	sexually transmitted infection
SUD	substance use disorder
TA	technical assistance
Total anti-HAV	total antibody to hepatitis A virus
Total anti-HBc	total antibody to hepatitis B core antigen

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Executive Summary

Since the 2005 edition of the *Guidelines for Viral Hepatitis Surveillance and Case Management*, the epidemiology of viral hepatitis in the United States has changed substantially. Decreases in hepatitis A incidence that occurred following release of the hepatitis A vaccine in the late 1990s ended in 2016, when large person-to-person outbreaks of hepatitis A began being reported primarily among people who use drugs (PWUD) and people experiencing homelessness. Decreases in acute hepatitis B incidence that occurred after release of the hepatitis B vaccine in the 1980s ceased in 2010. Also in 2010, decreases in acute hepatitis C incidence that were first observed in the 1990s began to reverse. Rates of acute hepatitis C have most notably increased among people 20–49 years of age, American Indian/Alaska Native people, and non-Hispanic White people. The shift in acute hepatitis B and hepatitis C incidence is most evident in jurisdictions disproportionately affected by the opioid crisis.

Chronic hepatitis B prevalence has remained relatively stable at an estimated 0.28% during 2011–2016, representing approximately 862,000 people[1]. Prevalence was disproportionately highest among people of Asian/Pacific Islander descent and people born outside of the United States[1]. Chronic hepatitis C prevalence was estimated to be 1.0% during 2013–2016, representing approximately 2.4 million people[2]. Recent declines in hepatitis C-related mortality have been observed and are encouraging[3]; these declines are likely attributable to the availability of highly effective curative therapy with direct-acting antiviral agents coupled with updated testing recommendations.

Viral hepatitis testing recommendations have expanded since 2005, and major advances in information systems and laboratory testing have allowed jurisdictions to conduct more comprehensive viral hepatitis surveillance. In addition, availability of a hepatitis B vaccine and curative hepatitis C therapies have enabled national, state, and local public health agencies to design and implement strategies to eliminate these infections. Monitoring elimination efforts will require development of person-level databases to

- track incidence, prevalence, and mortality through maintenance of surveillance data and matching with secondary data sources;
- detect test conversions that indicate acute infection, resolution, reactivation (for hepatitis B), and re-infections (for hepatitis C); and
- identify people who have been treated or need linkage to health care services.

This document contains the following:

- revised Centers for Disease Control and Prevention (CDC)/Council of State and Territorial Epidemiologists (CSTE) case definitions for hepatitis A, acute hepatitis B, chronic hepatitis B, perinatal hepatitis B, acute hepatitis C, and chronic hepatitis C;
- new CDC/CSTE case definition for perinatal hepatitis C and guidance for hepatitis C during pregnancy and perinatal hepatitis C surveillance and case management;
- data notification mechanisms to CDC including using Health Level Seven (HL7) case notification; and
- updated guidance on reporting, ascertainment, investigation, and classification.

1. General Viral Hepatitis Surveillance Guidance

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1.1. Background

Public health surveillance is the foundation upon which public health programs are designed to prevent and control diseases. Viral hepatitis infections under surveillance by the CDC include hepatitis A, hepatitis B (acute, chronic, and perinatal), and hepatitis C (acute, chronic, and perinatal). The core component of the national viral hepatitis surveillance system is voluntary notification of cases by state, local, and territorial health departments (HDs) to CDC's National Notifiable Diseases Surveillance System (NNDSS).

Each state and territory mandates the conditions and diseases that should be reported to HDs when identified by laboratories, health care providers, and health care facilities. Personal identifiable information (PII) is collected to enable HDs to identify cases for follow-up and to implement prevention and control measures.

HDs then notify CDC of cases of conditions that are included on the Nationally Notifiable Condition (NNC) list. The NNC list is established through a collaboration between CSTE and CDC and is based on conditions for which there is mandatory reporting to HDs, laboratory tests approved by the US Food and Drug Administration (FDA), and established CDC/CSTE case definitions. Case notifications do not include PII as CDC lacks the authority to receive that information and does not conduct follow-up or intervention activities on cases.

As new reports of viral hepatitis infection are received, HDs report information to CDC, including diagnosis, event dates (e.g., illness onset date), and demographic data (e.g., state/territory, county, sex, age, race, and ethnicity). Additional information collected through NNDSS includes clinical features, laboratory test results, and risk behaviors or exposures potentially associated with infection. This information is needed to confirm the diagnosis, determine a source of infection, identify others at risk for infection, and inform prevention measures.

National surveillance for viral hepatitis is based on case definitions developed and approved by CSTE in collaboration with CDC, which can be found on the CDC NNDSS website[4]. Viral hepatitis infections are required to meet specific age, clinical, laboratory, and epidemiologic linkage criteria before being classified as a case. Newly reported cases of hepatitis A, acute hepatitis B, perinatal hepatitis B, acute hepatitis C, and perinatal hepatitis C are considered incident cases. Newly reported cases meeting the chronic hepatitis B and hepatitis C case definitions may reflect prevalent infections. However, because not all viral hepatitis infections are diagnosed or transmitted to NNDSS, CDC traditionally relies on data sources outside of NNDSS to estimate prevalence, including the National Health and Nutrition Examination Survey (NHANES), Centers for Medicare and Medicaid Services (CMS), insurance claims data, hospital discharge data, commercial laboratory data, and pharmacy data. Section 5.4 describes supplemental data sources that can be helpful in improving the understanding of viral hepatitis epidemiology.

Data from NHANES are used to estimate the prevalence of viral hepatitis among non-institutionalized civilian residents of the United States. Because NHANES does not include or may underrepresent some populations who might have a higher prevalence of viral hepatitis (e.g., people experiencing homelessness, people who are incarcerated, certain racial/ethnic minority populations), prevalence estimates obtained from NHANES underestimate the true prevalence in the United States. In recent years, mortality data from the National Vital Statistics System (NVSS) were added to annual viral hepatitis surveillance summaries.

1.2. Goals of Viral Hepatitis Surveillance

The overarching goals of viral hepatitis surveillance are to inform and evaluate the impact of prevention, control, and progress toward elimination. Viral hepatitis surveillance data help jurisdictions

- describe trends in new infections and disease burden;
- detect and monitor outbreaks and guide intervention efforts;
- identify populations at risk for acquiring infection (e.g., people who inject drugs (PWID), justice-involved people, and people experiencing homelessness);
- identify risk behaviors and exposures associated with infection (e.g., non-injection and injection drug use);
- identify people who require linkage to counseling, medical follow-up and treatment, and hepatitis A and hepatitis B vaccination, as appropriate;
- describe outcomes associated with infection (e.g., hospitalizations, cancer, and mortality);
- identify contacts of newly diagnosed infected people requiring referral to counseling and/or immunoprophylaxis, and hepatitis A and hepatitis B vaccination, as appropriate;
- provide information to develop and monitor viral hepatitis care continua to assess impact of viral hepatitis elimination activities; and
- support the design, development, implementation, and evaluation of evidence-based screening, vaccination, and treatment programs and policies.

To achieve surveillance goals, the viral hepatitis surveillance system, like all public health surveillance systems, should optimize the attributes, as described in the Principles of Epidemiology in Public Health Practice[5].

Simple: The structure and operational process of the surveillance system should be as simple as possible while meeting the objectives.

Flexible: The system should be adaptable to changing information needs, operating conditions, case definitions, and technology with little additional time, personnel, or allocated funds.

Data quality: The completeness and validity of the data in the surveillance system should be assessed at routine intervals.

Acceptability: People and organizations targeted for the system, as case patients and data users, should be willing to participate in the surveillance system.

Sensitivity: The sensitivity of a surveillance system describes the ability to detect infections and may also refer to the ability to detect outbreaks.

Positive predictive value: Positive predictive value is the fraction of reported cases that actually have the health-related event under surveillance.

Representativeness: The cases included in the system should accurately reflect infections in the underlying population.

Timeliness: Timeliness reflects the availability of data rapidly enough to take appropriate public health action.

Stability: Stability refers to the reliability of data collection and management of surveillance data and availability of those data.

The ideal viral hepatitis surveillance system should include the spectrum of disease from infection to cure or death, be standardized across jurisdictions, informed by jurisdictions, used for public health action, and conducted comprehensively across all jurisdictions and for all viral hepatitis conditions. While not all surveillance systems can meet every criterion, additional investments are expected to result in improvements to viral hepatitis surveillance.

1.3. CDC/CSTE Surveillance Case Definitions

Viral hepatitis surveillance case definitions are developed by CSTE in collaboration with CDC programs. These case definitions are proposed in CSTE's Position Statements, which provide uniform criteria for case ascertainment, case classification, and national notification to CDC[6]. Changes in case definitions might be needed when there are major clinical advances and changes in laboratory and/or surveillance methodologies. Trends in the number and rate of newly reported cases can be affected by changes in the case definition. CSTE leads the position statement development process[6]. References to CSTE position statements, current and historical case definitions, and historical time line for implementation of each nationally notifiable condition are found on the CDC NNDSS website[4]. The national notification criteria and print criteria for hepatitis A, hepatitis B, and hepatitis C case statuses, based on the current CSTE Position Statements, are summarized in Table 1-1.

Table 1-1. National notification and print criteria for hepatitis A, hepatitis B, and hepatitis C

Condition	National Notification Criteria*	Print Criteria†
Hepatitis A	Confirmed	Confirmed
Acute hepatitis B	Confirmed	Confirmed
Chronic hepatitis B	Confirmed and probable	Confirmed
Perinatal hepatitis B	Confirmed	Confirmed
Acute hepatitis C	Confirmed and probable	Confirmed and probable
Chronic hepatitis C	Confirmed and probable	Confirmed and probable
Perinatal hepatitis C	Confirmed	Confirmed

*The transmission of conditions from health departments to the Centers for Disease Control and Prevention (CDC)'s National Notifiable Diseases Surveillance System (NNDSS).

†The standards upon which CDC can publish cases, as determined by the Council of State and Territorial Epidemiologists (CSTE) and CDC and listed in CSTE Position Statements.

1.4. Reporting of Viral Hepatitis Conditions to the HD

Jurisdictions establish mandatory reporting requirements that specify which conditions must be reported to the HD, what attributes of the condition should be included in the report, and the timeline for reporting. Thus, reporting requirements vary by jurisdiction. Reporting sources usually include laboratories, health care facilities, and health care providers. Vital records and medical records can provide additional information on reported cases. Section 5.4 describes how various data sources can be used for viral hepatitis surveillance. The following are the viral hepatitis conditions that are currently recommended by CSTE to be reportable to the HD:

- Hepatitis A
- Acute hepatitis B
- Chronic hepatitis B
- Perinatal hepatitis B
- Hepatitis B during pregnancy
- Acute hepatitis C
- Chronic hepatitis C
- Perinatal hepatitis C

While not nationally notifiable, hepatitis C during pregnancy is a condition of public health concern and has ramifications for surveillance. Jurisdictions might also receive negative laboratory results and liver functions tests to improve the accuracy of case ascertainment and classification, examine trends in screening, monitor care continua, and calculate overall disease prevalence. However, the utility of these data is dependent on the jurisdiction's ability to store and process high volumes of data, as well as the jurisdiction's legal authority for receiving negative laboratory results. In most cases, negative laboratory results are used only if they are linked to a positive result. Negative laboratory results can be used to identify cases that are classifiable as acute due to test conversion, false-positive test results, cases that have cleared infection, and hepatitis B reactivations and hepatitis C re-infections. Recommended reportable laboratory results for each viral hepatitis condition are found in Sections 2.5 (hepatitis A), 3.4 (hepatitis B), and 4.4 (hepatitis C).

Most HDs have already established strategies to inform laboratories, health care facilities, and health care providers about reporting requirements. Direct outreach to major reporting sources is effective and allows the reporting facilities to ask questions about reporting suspected cases. It is important for viral hepatitis surveillance staff to collaborate with other surveillance staff in the HD to assure that automated systems for capturing electronic laboratory data are accurate and consistent, and that reporting sources receive information about how to report viral hepatitis cases.

In some jurisdictions, programs such as syringe services programs (SSPs) and substance use disorder (SUD) treatment facilities might not have a clear means to report case information. Identifying information needed to create a case and ensure deduplication in the surveillance system might not be obtainable on cases from SSPs, because collection of identifying information can be a barrier to people receiving services. Further, under 42 Code of Federal Regulations (CFR) Part 2[7], patient records created by federally funded programs for the treatment of SUD are protected; this regulatory prohibition on sharing information without consent of the client does not include an exemption for public health. To address these potential barriers, HD surveillance staff should collaborate with these facilities to discuss options that will allow for timely and accurate reporting while ensuring patient confidentiality and compliance with federal law.

To ensure complete reporting of perinatal hepatitis B and hepatitis C cases, HDs should work with birthing facilities to allow reporting of all live births from a gestational parent living with hepatitis B or hepatitis C. Birthing facilities should be provided with a brief, standardized reporting form and written directions about when and how to submit information to the appropriate HD.

1.5. Submission of Notifiable Conditions to CDC

HDs can transmit many case reports for viral hepatitis infections to CDC using standard NNDSS event codes; however, CSTE determines which conditions are notifiable to CDC[8]. The term "notifiable" indicates that CSTE recommends state and territorial HDs transmit these conditions to NNDSS[9]. Table 1-2 lists the nine viral hepatitis conditions that can be transmitted to NNDSS and the corresponding NNDSS event codes. While hepatitis D and hepatitis E are not nationally notifiable infectious conditions[9], NNDSS event codes are available for jurisdictions in which they are reportable conditions.

Table 1-2. Viral hepatitis conditions with corresponding National Notifiable Diseases Surveillance System (NNDSS) event codes and national notification criteria

Condition	NNDSS Event Code	National Notification Criteria
Hepatitis A, acute	10110	Yes
Hepatitis B, acute	10100	Yes
Hepatitis B, perinatal	10104	Yes
Hepatitis B, chronic	10105	Yes
Hepatitis C, acute	10101	Yes
Hepatitis C, perinatal	50248	Yes
Hepatitis C, chronic	10106	Yes
Hepatitis D, acute*	10102	No
Hepatitis E, acute	10103	No

*Hepatitis D is considered a coinfection or superinfection that can only occur in the presence of hepatitis B virus infection.

Each week, state and territorial HDs transmit case reports of viral hepatitis conditions to NNDSS. The CDC Division of Viral Hepatitis (DVH) developed and provided case report forms that contain data elements necessary for case ascertainment, case classification, case investigation, and national notification. The latest case report form can be found on the CDC DVH website[10]. Jurisdictions might opt to collect additional variables to aid in case ascertainment, investigation, characterization, and program evaluation. The CDC case report form was developed based on recommendations from CSTE and serves as a guide for surveillance notification. All viral hepatitis cases must be transmitted electronically to NNDSS. See Section 1.8 for information on data transmission mechanisms for viral hepatitis case notifications to NNDSS.

1.6. Data Elements for Jurisdictional Reporting and National Notification

For viral hepatitis cases that are nationally notifiable to CDC, the following data elements are requested for transmission to NNDSS:

Core standardized data elements: For surveillance data to be useful at the national level, all case reports of notifiable viral hepatitis conditions should be transmitted to NNDSS with a set of core standardized data elements as listed in the current CDC viral hepatitis case report form[10]. Core elements contain information needed to classify and characterize cases. As jurisdictions transition to HL7 case notification under the NNDSS Modernization Initiative, data elements collected should follow the specifications in the message mapping guides[11].

Unique patient identifiers: Using unique identifiers allows jurisdictions to facilitate patient follow-up and link surveillance data with health care data. Patient names and other PII (e.g., date of birth and social security number) are typically stored in the surveillance database maintained by each jurisdiction. Most PII is not transmitted to NNDSS. Policies for ensuring patient privacy and security of data should be in place for any system maintaining patient information. When any type of database is established, the confidentiality of individual identifying information should be ensured according to applicable laws and regulations. See Section 1.11 for guidelines regarding security and confidentiality. CDC uses state- or territory-generated case-level unique identifiers to discuss individual cases with jurisdictions.

Morbidity and Mortality Weekly Report (MMWR) week and year: Jurisdictions assign MMWR week and MMWR year in accordance with NNDSS guidance. Guidance is found on the CDC NNDSS website.

Data elements from laboratory reports: Electronic reporting can improve timeliness and completeness of data. State and territory rules and regulations for laboratory reporting of viral hepatitis infection markers should include requirements to promptly report available test results to public health authorities, including the patient's contact information and health care provider.

Reports of positive test results should also include results for other laboratory markers (including those that are non-positive, negative, or undetectable) relevant to the condition or case classification evaluated on a patient at the same time, including serum alanine aminotransferase (ALT) levels, total bilirubin results, and pregnancy status, if available.

Negative test results, though not reportable in every jurisdiction, are useful for detecting test conversions, ruling out other conditions causing the same clinical presentation, and detecting resolved or cleared infections. Laboratory reports usually contain demographic information (e.g., name, date of birth, sex, address at time of report, current address, and phone number). This information can be used to locate the patient to obtain information that might not be available on the laboratory report (e.g., race, ethnicity, country of birth, and relevant risk history) and provide linkage to care and follow-up, as indicated.

Obtaining relevant risk history on acute cases: People with acute infection should be investigated to determine relevant risk history. The exposure period for ascertaining risk is 15–50 days for hepatitis A, 60–150 days for acute hepatitis B, and 14–182 days for acute hepatitis C prior to the symptom onset date. If the symptom onset date is unknown, the date that the patient first tested positive for the infection can be used as a proxy. Table 1-3 lists the epidemiologic risk behaviors or exposures and groups at risk for hepatitis A, hepatitis B, and hepatitis C as described in the most recent CSTE Position Statements and CDC resource pages for health professionals[12-14]. People >18 years of age are recommended to receive HCV testing, regardless of risk behaviors or exposures[15].

Table 1-3. Epidemiologic risk behaviors, risk exposures, and groups at risk for hepatitis A, hepatitis B, and hepatitis C

Hepatitis A	Hepatitis B	Hepatitis C
• Injection drug use • Non-injection drug use • Incarceration • Experience of homelessness/ unstable housing • Household contact (non-sexual) • Sexual contact with a person with confirmed or suspected hepatitis A • Sexual or other practices that lead to fecal-oral contact • Men who have sex with men* • Exposure to contaminated food or water • Close contacts of adopted children newly arriving from countries with high or intermediate hepatitis A endemicity • International travel to high or intermediate endemic countries	• Injection drug use • Non-injection drug use • Incarceration • Experience of homelessness/unstable housing • Surgery, dialysis, or other medical procedures • IV infusions or injections as part of health care (inpatient or outpatient) • Accidental stick/puncture with a needle or other sharp object contaminated with blood • Receipt of a blood transfusion, tissue product, or organ transplant • Sexual or household contact with a person with confirmed or suspected hepatitis B • History of sexually transmitted infections • Men who have sex with men* • Birth to an infected gestational parent† • Non-commercial tattoo or body piercing • Dental work or oral surgery • Other exposure to blood or bodily fluids (not including risk behaviors or exposures listed above)	• Injection drug use • Non-injection drug use • Incarceration • Experience of homelessness/unstable housing • Surgery, dialysis, or other medical procedures • IV infusions or injections as part of health care (inpatient or outpatient) • Accidental stick/puncture with a needle or other sharp object contaminated with blood • Receipt of a blood transfusion, tissue product, or organ transplant • HIV infection‡ • Sexual practices that result in exposure to blood • Birth to an infected gestational parent† • Non-commercial tattoo or body piercing • Dental work or oral surgery • Other exposure to blood (not including risk behaviors or exposures listed above)

*Men who have sex with men are recommended by the Advisory Committee on Immunization Practices to receive hepatitis A and hepatitis B vaccination.
†Gestational parent is defined in this context as the parent who gave birth.
‡HIV infection is not a risk factor for hepatitis C. People with hepatitis C and HIV share risk behaviors or exposures; therefore, co-infection is common.

1.7. Data Quality Reviews and Dissemination

Frequent evaluation of surveillance data for quality, including completeness and timeliness, is essential for identifying aspects of surveillance that need improvement. The quality and completeness of surveillance data can be improved by increasing awareness of viral hepatitis case reporting requirements among laboratories, health care facilities, and health care providers through outreach and collaboration and providing feedback on missing or invalid data fields. Timeliness of surveillance data can be measured by monitoring the average length of time in days required for each step in the surveillance process (e.g., date of specimen collection, date results were received by the HD, follow-up investigation date, and when the local HD transfers the information to the state/territorial HD).

Jurisdiction Data Quality Reviews and Dissemination

Data Quality Reviews

Jurisdictions conducting viral hepatitis surveillance are encouraged to develop protocols to ensure data quality. The protocol might entail:

- determining if all major clinical and public health laboratories are consistently reporting viral hepatitis laboratory tests,

- performing regular assessments of viral hepatitis surveillance data to assess data quality (e.g., assessment of invalid values and case and condition classification audits), and
- assessing data completeness and supplementing surveillance data with data from other sources to improve data completeness, when available.

Weekly Data Quality Reviews

Weekly data quality procedures might include:

- conducting a quality assurance review of 5% of paper laboratory reports entered by each data entry team member or 5% of electronic laboratory reports received (or fewer, depending on the total volume of laboratory reports) and providing feedback on incomplete or invalid data fields and
- developing a centralized case notification process in which all reports of viral hepatitis conditions that are submitted by field or community-based staff are manually reviewed and approved by viral hepatitis surveillance leads, which can help to improve workflows and data quality prior to transmission to NNDSS.

Quarterly and Annual Data Quality Reviews

Quarterly and annual data quality procedures depend on a jurisdiction's surveillance system and ability to routinely investigate cases. For example, in states and territories using the National Electronic Disease Surveillance System (NEDSS) Base System (NBS), the following procedures can be conducted on viral hepatitis investigations for the prior and current calendar year:

- resolving investigations that have no notification or a pending notification >30 days from the investigation start date;
- updating the case status from probable to confirmed when additional confirmatory information is received after the investigation start date;
- resolving investigations with a case status of "suspected," along with those classified as having an "other non-notifiable case status," that have been open for >30 days from the investigation start date;
- de-duplicating* investigations for the same condition that are not evident of a hepatitis C reinfection;
- conducting a query on viral hepatitis investigations when quarterly and end-of-year CDC DVH quality assurance surveillance reports are received to determine if numbers match; or
- performing end-of-year CDC data validation and completing activities 30 days prior to CDC/CSELS closeout date.

*When de-duplicating, keep the earliest investigation, change the remaining investigations to 'not a case' or append as a single event to the initial report, and associate all laboratory reports with the earliest investigation, if applicable. For cases of hepatitis C reinfection, some jurisdictions are creating a local condition specific for reinfection as opposed to creating a new acute condition to maintain deduplication.

Full data completeness might not be possible for some variables that are often missing on case and laboratory reports (e.g., race, ethnicity, pregnancy status, country of birth, and patient address). Inclusion of demographic information on case and laboratory reports is determined by state/territorial regulations.

Following up on all cases may not be possible, for example on high-volume conditions like chronic hepatitis B and hepatitis C in jurisdictions with large populations. HDs will need to balance the benefits of data completeness with the public health resources needed to obtain this information. Where data collection is resource-intensive, a statistical approach that yields a representative sample of cases to be used to infer demographics or other characteristics might be considered to help direct prevention and resource efforts.

Data Dissemination

Jurisdictions have various mechanisms for sharing viral hepatitis surveillance data internally and externally.

Internal reports might include:

- a weekly line list of acute cases for the week prior and year-to-date, which allows for the timely detection of unusual trends or cases of potential public health importance requiring prompt attention;
- use of workflows and automated reports that allow close monitoring of newly reported acute cases of viral hepatitis infection; or
- regular summary reports of HIV, sexually transmitted infections (STIs), tuberculosis, and viral hepatitis co-infections, which may be distributed to internal staff via secure dashboard (e.g., Tableau or PowerBI).

External reports might include:

- annual surveillance reports containing state/territory- and county-level case counts and incidence rates of viral hepatitis cases, as well as overall summaries of condition-specific risk behaviors or exposures and outcomes (e.g., hospitalizations and deaths);
- a comprehensive epidemiologic profile that includes additional data (e.g., HIV, STI, tuberculosis, and opioid overdose surveillance, vital records, hospital discharge, and testing and treatment data) to complement viral hepatitis surveillance data and document disease burden;
- abstracts on important topics to be submitted to applicable conferences throughout the year; and
- regular (e.g., quarterly) project-specific progress reports to be distributed to partners, stakeholders, and the public (statewide and by region).

Jurisdictions should develop standard operating procedures for managing requests for surveillance data. Data requests should be handled through a secure management and tracking system, with established standards for turnaround time. Data privacy and suppression standards should be established and applied to these requests, considering that some local jurisdictions may have very few cases.

National Data Quality Reviews and Dissemination

Data Quality Reviews

CDC conducts weekly internal analyses to assess the quality of data transmitted to NNDSS. CDC then follows up with HD viral hepatitis surveillance staff to discuss any apparent data inconsistencies (including data entry and transmission errors) along with concerns regarding data timeliness and completeness.

Weekly Data Quality Reviews

Weekly reviews of surveillance data provide valuable information on data quality that may be indicative of coding or data entry errors. Additionally, these reviews can reveal early signals of clusters, outbreaks, or cases of public health importance that may occur along jurisdictional borders or multiple states.

CDC's Center for Surveillance, Epidemiology, and Laboratory Services (CSELS) updates publicly available provisional viral hepatitis data in tables from CDC WONDER, CDC.data.gov, and CDC Stacks and disseminates these each week[16].

Quarterly Data Quality Reviews

On a quarterly basis, DVH provides summaries of data to HDs to ensure data received by CDC are consistent with jurisdictional reports. Any inconsistencies are then addressed through discussions between CSELS, DVH program staff, and the jurisdiction, to ensure agreement of case counts and case information.

Annual Data Quality Reviews

Every April, an end-of-year data quality report for the previous *MMWR* year is produced by CSELS and sent to each state and territorial HD for final review. This step is done before the window for data submission officially closes, by which time the state/territorial epidemiologist reviews and approves the final end-of-year data. After data close-out, which typically occurs in May following the evaluation year, the data are considered frozen, and jurisdictions are unable to make further changes or corrections to the closed-out national data.

Jurisdictions transmitting case data via HL7 can still transmit updates to historical CDC data after the close-out date; however, these updates are not reflected in the closed-out data file used by CSELS and DVH for producing annual surveillance summaries. These processes ensure the continued reliability of reported information.

Data Dissemination

CDC generates annual aggregated summaries of finalized data from states and territories, and publishes the findings on CDC WONDER, CDC.data.gov, and CDC Stacks[16]. Annual surveillance summaries of case-level data from states are published on the DVH website[17]. Annual DVH surveillance summaries contain case counts and incidence rates of cases of hepatitis A, hepatitis B, and hepatitis C as well as overall summaries of condition-specific risk behaviors or exposures and outcomes (e.g., hospitalizations and deaths).

The report also includes hepatitis A, hepatitis B, and hepatitis C-related death counts and rates overall, and by sex, age, race/ethnicity, and geography of residence as obtained from US Multiple Cause of Death data.

1.8. Data Transmission Mechanisms for National Notification

Viral hepatitis case reports are transmitted to NNDSS through one of three separate electronic data transmission streams.

The National Electronic Telecommunications System for Surveillance (NETSS) is the oldest of the three data transmission mechanisms. First launched in 1990, NETSS can capture approximately 50 core and extended variables on a 2-page case report form. The NETSS case report form has not been updated since NETSS was first launched; therefore, variables collected do not necessarily fully characterize the current epidemiology of viral hepatitis infections in the United States. NETSS is not person-based.

The National Electronic Disease Surveillance System Base System (NBS) enables HDs to create and send standards-based case notifications to NNDSS. Through NBS, HDs can send and receive extended data elements, including person-level data and additional laboratory and risk information beyond what can be transmitted using NETSS.

The NNDSS Health Level Seven (HL7) is the most recent standard for viral hepatitis data transmission to NNDSS. Transmitting case reports via HL7 utilizes the most recent case report form[10] and ensures the ability to receive all pertinent case information, including person-level data.

The specifications for HL7 implementation can be found on the CDC NNDSS website[11]. Under the NNDSS Modernization Initiative, CDC encourages all HDs to streamline data transmission using NNDSS HL7 case notification messages. To streamline data transmission and ensure that all relevant information on cases can be received in NNDSS, CDC recommends all HDs work with CDC's CSELS and DVH technical partners to transition data transmission to the HL7 format.

1.9. Cases and Clusters of Potential Public Health Importance

Weekly reviews of acute case surveillance data not only provide valuable information on data quality, but also provide early signals of clusters or outbreaks or cases of significance that require further follow-up. Decisions about follow-up should be prioritized depending on the strength of the signal, whether other indicators of risk are present (e.g., overdose and active HIV or STI transmission), and the available resources to address the problem. To detect cases and clusters of public health interest, jurisdictions should conduct routine data review.

Although not a comprehensive list, the following scenarios provide examples that may signal the need for further public health investigation:

- cases of hepatitis A or acute hepatitis B among people who were previously vaccinated (to characterize possible vaccine failures);
- cases of hepatitis A among people born after 2005 or reported cases of hepatitis B among people born after 1990 (to distinguish between failure of vaccine and failure to vaccinate);
- cases of hepatitis B or hepatitis C among people of childbearing age who are or have the potential to become pregnant (to detect possible perinatal transmission);
- cases of perinatal hepatitis B and hepatitis C (to identify perinatal transmission);
- cases of acute hepatitis B or hepatitis C in unusual or vulnerable demographic groups (e.g., older people [e.g., >70 years of age], and those in a residential facility or other congregate setting [including long-term care or corrections]); and
- cases of seroconversion or acute hepatitis B or hepatitis C in patients receiving hemodialysis.

Possible Outbreaks

An outbreak is defined as the occurrence of more cases of disease than expected in a given area or among a specific group of people over a particular time period.

Prompt detection of outbreaks can significantly reduce further transmission. For example, early detection of hepatitis A transmission among PWUD or people experiencing homelessness can prompt local public health officials to administer hepatitis A vaccine to people at high-risk in the outbreak-affected area quickly.

Similarly, early detection of an outbreak of acute hepatitis B or hepatitis C among PWID may facilitate targeted interventions (e.g., access to SSPs, medication for opioid use disorder [MOUD], viral hepatitis treatment, and contact investigation). Detailed guidance on viral hepatitis outbreaks can be found on the CDC DVH Viral Hepatitis Outbreaks website.

1.10. Case Investigation

Reports from laboratories, health care facilities, health care providers, and other data sources indicative of viral hepatitis should prompt a case investigation. Comprehensive surveillance requires a full investigation of all positive laboratory reports and suspected cases. However, not all HDs have the ability to conduct comprehensive viral hepatitis surveillance due to the high volume of positive laboratory reports and inadequate resources.

Jurisdictions are encouraged to develop a list of cases to prioritize for investigations. Jurisdictions might also consider leveraging intersecting surveillance, prevention, and care systems to obtain case information. Some jurisdictions conduct investigations by interviewing a representative sample of patients and their providers, including cases and clusters of potential public health importance.

This section provides general guidance for viral hepatitis case investigation. More detailed guidance for each viral hepatitis condition can be found in Sections 2.8 (hepatitis A), 3.6.5 (acute and chronic hepatitis B), 3.7.5 (hepatitis B during pregnancy and perinatal hepatitis B), 4.6.5 (acute and chronic hepatitis C), and 4.7.5 (hepatitis C during pregnancy and perinatal hepatitis C).

Cases of viral hepatitis require investigation to

- obtain clinical, laboratory, epidemiologic linkage information to assist in case classification;
- obtain demographic and risk information to more accurately characterize the epidemiology of the infection and inform prevention and control activities;
- assess whether the patient requires education, harm-reduction services, provider referral, or other medical follow-up services, as appropriate; and
- identify contacts requiring post-exposure prophylaxis, testing, or harm reduction services.

Investigation should be conducted to determine whether a case meets the criteria of the CDC/CSTE surveillance case definition. Cases of public health importance will require a more in-depth, timely investigation to collect patient and case-contact information and coordinate referral for counseling, vaccination, and treatment, if appropriate. Case investigation may involve acquiring any of the following types of information:

Information from the Laboratory

Reporting of laboratory test results is mandated by state/territory rules, regulations, or laws. Viral hepatitis surveillance activities generally begin when a HD receives laboratory results of viral hepatitis testing on serum from blood samples submitted by health care providers. The reports generally include demographic information about the patient (e.g., name, date of birth, sex, and identification numbers). The report also includes the name and address of the reporting laboratory, specimen collection date, date the tests were conducted, and name and address of the provider or authority who ordered the tests. Pregnancy status should also be included on the laboratory report if testing was done as part of a prenatal test panel.

Information from the Health Care Provider or Medical Records

The following types of information might be obtainable from medical records:

Demographic Information. Includes name, date of birth, sex at birth, current gender, race, ethnicity, and residential address (including zip code).

Clinical features. Includes reason for testing, illness onset date, clinical signs and symptoms, co-infections, outcomes (e.g., hospitalization status, date of death), and whether an alternate diagnosis is suspected.

Diagnostic test results. Laboratory confirmation of viral hepatitis requires one or more positive test result(s) for the viral hepatitis condition. Laboratory

data also contribute to the determination of acuity of infection and the presence of alternative diagnoses.

Risk behaviors or exposures. If the ordering provider assessed the patient's risk history, this information might be obtainable from the medical records.

Vaccination information. Obtaining hepatitis A and hepatitis B vaccination history might be done via the patient's provider or immunization registry.

Information from the Patient

Unless the source of infection is known, patients should be contacted for an interview using the jurisdiction-specific case investigation form. Decisions to contact the patient are often jurisdiction-specific and depend on available resources. In many situations, patient contact is reserved for those cases deemed highest priority for preventing further transmission or referral to care. The patient interview should ideally include the following components:

Epidemiologic link. Ascertain whether there was an epidemiologic link to a laboratory-confirmed viral hepatitis case consistent with the criteria in the CDC/CSTE case definitions.

Risk behaviors or exposures. Determine the most likely mode of transmission by asking about potential behaviors or exposures relevant to the specific viral hepatitis condition and incubation period.

Education and referral for follow-up services. Assess whether the patient requires education or other follow-up services, including harm reduction and hepatitis A and hepatitis B vaccination, as appropriate. Patients should be counseled on how to prevent transmission to others and referred for further counseling and treatment.

Identification of contacts requiring postexposure prophylaxis. If resources allow, assess whether the window to provide postexposure prophylaxis is still open and coordinate referral for postexposure prophylaxis, testing, and treatment as appropriate.

Risk behaviors or exposures can be obtained from the provider and/or patient. Under the HIPAA Privacy Rule (45 C.F.R. 164.512(b))[18], a public health authority is authorized to collect and receive patient health information for the purpose of preventing and/or controlling disease, injury or disability, including public health surveillance, public health investigations, and public health interventions. Therefore, acquiring these records and/or speaking with the provider should be considered routine for authorized public health professionals.

Considerations for Investigating Populations or Settings at Risk for Rapid Disease Transmission

People experiencing homelessness. The circumstances surrounding homelessness vary widely, not just geographically, but also from person to person. These factors will likely present challenges for viral hepatitis investigations and should be considered when attempting to contact, investigate, and navigate people experiencing homelessness through the investigation and needed services. People experiencing homelessness often do not have a reliable phone number, necessitating implementation of other strategies (e.g., working with community partners or messaging apps).

It might also be difficult to ascertain risk behaviors or exposures among people experiencing homelessness during their incubation period and to determine potential exposure to others in congregate settings (e.g., homeless shelters and soup kitchens [for hepatitis A]). People experiencing homelessness often have infrequent access to health care; further, they may mistrust government organizations because of past stigma and trauma.

Partnering with those who serve populations experiencing homelessness, including local government, nonprofit, and religious organizations, can facilitate access to this population. These organizations might be able to assist with locating patients and gathering information about exposures and contacts. People experiencing homelessness are effective gatekeepers to their own communities and might be willing to help facilitate outreach efforts. People experiencing homelessness often do not have transportation, health insurance, or resources required for testing and/or treatment. Community resources (e.g., homeless shelters; health care services for the homeless; free testing events; food, housing, and

patient assistance programs; and free clinics) can provide important treatment and prevention services and culturally competent outreach based on trust built over time.

People who use drugs. People who use either injection or non-injection drugs might be difficult to reach and distrustful of government agencies offering help due to past histories of stigma and discrimination as well as fear of arrest for illicit drug use. Further, they might be less likely to share complete information, or they may have incomplete recall. Partnering with organizations that serve this population, (e.g., SSPs, behavioral health providers, and SUD treatment facilities) and identifying and employing a champion within the population might be effective ways to gather information about potential exposures and contacts in need of postexposure prophylaxis and/or treatment.

When reaching PWUD, partnership with SSPs and other harm reduction programs with a proven track record of demonstrated trust with PWUD/PWID is helpful while maintaining information security and confidentiality. People should be educated about viral hepatitis transmission, prevention, treatment options, and harm reduction services (e.g., syringe access, MOUD, and naloxone distribution for overdose prevention). Information should be gathered on contacts in need of postexposure prophylaxis.

When a case is reported by a SUD treatment facility, it is best to work with the facility to discuss options that will allow for timely and accurate reporting while ensuring patient confidentiality and compliance with 42 Code of Federal Regulations (CFR) Part 2[7]. People in SUD treatment facilities should be educated on harm reduction, testing and other prevention interventions (e.g., vaccination and HIV pre-exposure prophylaxis [PrEP]), treatment initiation, and linkage to ongoing medical care. Current guidelines and strategies for the investigation and prevention of viral hepatitis among PWUD can be found on the CDC website[19]. Guidance on how to prepare for, detect, investigate, and respond to a hepatitis C outbreak among PWID can be found on the CDC website[20].

People engaging in sexual practices resulting in fecal-oral contact or exposure to blood. Anyone who engages in sexual activity that involves fecal-oral contact are at increased risk for contracting hepatitis A. For hepatitis B and hepatitis C, engaging in anal intercourse with the possibility of mucosal trauma and having multiple sexual partners increase the risk of transmission. HIV-infected men who have sex with men (MSM) are also reported to have higher rates of HCV infection and reinfection[21,22]. This population might be hesitant to share information about partners or contacts they might have exposed or who might have exposed them. Patients might not have sufficient information about partner contacts to share with public health. Partnering with health care providers and advanced practice providers, including those who serve the lesbian, gay, bisexual, transgender, and queer plus (LGBTQ+) populations, might improve access to this population to enable prevention interventions. Information shared by partners can promote measures to help prevent spread in this community.

People in correctional facilities. Cases of viral hepatitis among people who live or work in correctional facilities require intensive investigations, as these settings are frequently associated with substantial transmission of viral hepatitis infections[23]. The ability to conduct case investigations in correctional facilities can vary by correctional jurisdiction, and many barriers exist for case and case-contact investigation (e.g., limited access, high turnover in correctional facilities and inability to find cases or contacts). When possible, jurisdictions should attempt to develop partnerships with correctional facility health care providers/infection preventionists and management staff to establish partnership and allow for the collection of necessary information. Depending on the correctional facility, health staff might be willing to conduct interviews on behalf of the HD. However, investigations must be conducted in a way that shares minimal information with custodial staff to protect patient confidentiality. Knowing the viral hepatitis testing and vaccination policies of the jurisdictional correctional facilities, including the movement of people through the corrections system, is important.

Vaccination and education are important, particularly in congregate settings such as correctional facilities. People who are incarcerated should be made aware of the risks of sharing personal items (e.g., razors, nail

clippers, and toothbrushes). Education should also be provided on behavioral risks while incarcerated, including IDU, high-risk sexual contact, tattoos, and piercings. It is also important that correctional facilities make supplies available to prevent transmission in these settings.

People exposed in health care settings. There are many challenges to identifying and investigating possible health care-associated transmission of viral hepatitis, including (but not limited to) ensuring that the exposure was truly health care-related, gaining access to medical records for follow-up, potential for patient notification, and identifying potential breach(es) in infection control. If the case involves a person with a complex medical history, it might be challenging to identify which health care facility and procedures were involved in disease transmission. Molecular testing, while not available in all jurisdictions, has proven to be a useful tool in these investigations where available. CDC has developed guidelines and tools to assist in the investigation of health care-associated transmissions[24].

Establish relationships early with state health care-associated infections (HAI) coordinator[25] and the state agencies that oversee licensing and survey of health care facilities within the health jurisdiction, if possible. These colleagues can provide useful support and guidance in health care-associated investigations and might have established relationships with staff who work at these facilities. It is also important to work with infection control practitioners at health care facilities to discuss early reporting and vigilance regarding test conversion. Find ways to provide training on case investigation to providers outside the hospital setting, such as in dialysis or long-term care facilities, to promote awareness of the process.

Drug diversion. Health care professionals who illegally divert drugs can expose large numbers of patients to viral hepatitis and other consequences. CSTE has developed the toolkit entitled, "Healthcare-Associated Infections Drug Diversion Planning and Response Toolkit for State and Local Health Departments," which provides guidance, best practices, and customizable tools to guide investigation and reporting[26].

Considerations for Documenting and Investigating Cases of Suspected Vaccine Failure

Suspected vaccine failure can occur due to factors associated with the vaccine recipient (e.g., reduced response, non-response, or loss of long-term immunity) and those associated with the vaccine and vaccine administration (e.g., issues related to manufacturing, shipping and cold chain, vaccine storage, administration route, and dose). Because most people will develop protective antibody within 30 days of vaccine series completion[27,28], a hepatitis A and hepatitis B vaccine failure can be suspected when a person who completed the vaccine series according to the appropriate immunization schedule becomes infected >30 days after completion of the vaccine series. HD surveillance staff should consult with their immunization registry and check medical records to determine the vaccination status of people reported to have hepatitis A and/or hepatitis B.

Any case among a person for whom vaccine failure is suspected should be referred to the vaccine coordinator, who should follow the jurisdiction's guidelines for investigating vaccine failures. Knowing whether the patient has documentation of being a vaccine responder (e.g., anti-HBs ≥10 mIU/mL following a completed series) and patient immune status is important, as the vaccine should induce long-term immunity in vaccine responders who are immune-competent. Consideration of the testing date is also important because recent vaccination can result in transient IgM anti-HAV positivity for hepatitis A and transient HBsAg positivity for hepatitis B.

The patient's provider should be notified, and vaccine manufacturer and lot number should be obtained, if possible. Though these cases are not common in the United States, systematically tracking and analyzing cases of suspected vaccine failures can identify multiple or clusters of vaccine failure cases, allowing public health staff to explore the cause of the failures and determine the appropriate course of action. HDs should notify CDC of cases of vaccine failure through NNDSS by completing the appropriate vaccine information on the case report form. DVH staff are available to provide consultation.

1.11. Security and Confidentiality Guidelines for Surveillance Data

Ensuring secure and confidential data should be a top priority across all levels of public health. CDC's National Center for HIV/AIDS, Viral Hepatitis, Sexually Transmitted Disease, and Tuberculosis Prevention (NCHHSTP) recommends standards that can be used by HDs for the secure collection, storage, and use of data while maintaining confidentiality[29]. These standards are based on 10 guiding principles that address five major areas: program policies and responsibilities, data collection and use, data sharing and release, physical security, and electronic data security[30]. The full Data Security and Confidentiality Guidelines for HIV, Viral Hepatitis, Sexually Transmitted Disease, and Tuberculosis Programs can be found on the CDC National Center for HIV, Viral Hepatitis, Sexually Transmitted Disease, and Tuberculosis Prevention website[29].

1.12. Limitations of Viral Hepatitis Surveillance

Although many jurisdictions have developed strategies to strengthen viral hepatitis surveillance and data collection systems, several limitations remain. Some examples include

- reporting requirements vary by jurisdiction, resulting in varying levels of quality and completeness of surveillance reports;
- absence of negative laboratory result reporting can hinder case classification, identification of false-positive test results, and development of laboratory-based hepatitis B and hepatitis C care continua;
- asymptomatic people are less likely to be diagnosed and identified (particularly relevant for chronic hepatitis C reporting);
- surveillance data cannot account for undiagnosed infections thus resulting in underreporting and underestimation;
- illegal and stigmatized behaviors are likely to be underreported in medical records and surveillance investigations, and stigma might deter people from seeking testing or medical care; and
- investigation of chronic hepatitis B and hepatitis C cases is challenging in jurisdictions.

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2.1. Background

Hepatitis A is typically a self-limited disease caused by hepatitis A virus (HAV), primarily transmitted fecal-orally after close contact with an infected person or consumption of contaminated food or water[31]. Clinical symptoms are indistinguishable from acute hepatitis B and hepatitis C. Hepatitis A is an acute illness and does not result in chronic disease. The United States is considered a country of low endemicity with most infections occurring among adults reporting risk behaviors or exposures such as SUD, homelessness, sexual practices resulting in fecal-oral contact, and international travel to hepatitis A-endemic countries[3,32].

A safe and effective hepatitis A vaccine was licensed in 1995[33]. Prior to vaccine licensure and use, the number of reported hepatitis A cases was around 21,000 annually, and infections were common among children[34,35]. With the widespread adoption of the universal childhood vaccination recommendations in 2006, the overall incidence rate of hepatitis A decreased by 95% across all age groups from 1995 through 2014[3,33]. However, the incidence rate of hepatitis A has increased since 2016 due to widespread person-to-person outbreaks, primarily among PWUD and people experiencing homelessness[36]. Increases in hepatitis A have also been reported among MSM[36]. A study published in 2020 showed that approximately three-fourths of US-born adults ≥20 years of age were susceptible to hepatitis A during 2007–2016[37]. During 2016–2018, approximately 15,000 hepatitis A cases were reported to CDC, representing a 294% increase compared with 2013–2015[38]. In 2018, a total of 12,474 hepatitis A cases were reported to CDC, with 24,900 estimated infections (95% bootstrap confidence interval [CI]: 17,500–27,400) after adjusting for case under-ascertainment and underreporting[3]. The incidence rate of hepatitis A was 3.8 cases per 100,000 population in 2018, a nearly ten-fold increase from the reported incidence rate of 0.4 cases per 100,000 population in 2014[3].

The purpose of this section is to provide jurisdictional guidance to implement and improve hepatitis A surveillance. Information about reporting requirements, collection of relevant laboratory data, and case investigation is provided. Given that current systems for surveillance differ by jurisdiction, the standards outlined in this document are designed to provide models for best practices based on jurisdictional resources, recognizing that not every jurisdiction is able to meet those standards with available resources.

2.2. Uses of Surveillance Data

Hepatitis A surveillance data can be used to inform and improve public health interventions in the following ways:

Monitoring trends in disease incidence and determining risk behaviors or exposures. Hepatitis A surveillance data should be analyzed at a minimum of weekly by person, place, and time to monitor disease incidence. The proportion of cases reporting specific risk behaviors or exposures should be determined to monitor disease transmission patterns.

Identifying outbreaks. The identification of a hepatitis A geotemporal cluster or increase in incidence can be an early signal of an outbreak and should prompt further investigation. This investigation should include collection of additional information, including risk behaviors or exposures for person-to-person transmission (e.g., non-injection and injection drug use, homelessness, and sexual and other practices leading to fecal-oral contact) or potential exposures to a common-source (e.g., suspected foods and infected food handler). Surveillance data should be analyzed to determine affected areas (e.g., rates by local jurisdiction or zip code) and groups (e.g., age-specific incidence rates and frequencies of reported risk behaviors or exposures). Prospective surveillance should be conducted to identify additional outbreak cases, identify candidates for post-exposure prophylaxis (if indicated), enhance vaccination efforts for populations at risk, and inform communication and infection control measures. If an outbreak is identified, DVH staff are available to provide consultation.

Identifying cases among people who might expose others. The identification of a hepatitis A case in someone in a certain occupation (e.g., food handler) or congregate living situations is important because of the potential to expose additional people. This information can facilitate prompt contact tracing and coordination of postexposure prophylaxis.

Molecular sequencing of viral isolates might help guide response measures. When investigating a possible outbreak, in some instances, collecting sera from patients for diagnosis and molecular characterization (genome sequencing and genotype identification) might provide additional information to guide control efforts and identify outbreaks within outbreaks (e.g., foodborne-related cases during person-to-person outbreak). Public health professionals who need guidance regarding use of nucleic acid testing (NAT) for the investigation of hepatitis A outbreaks should contact CDC's DVH at hepaoutbreaklab@cdc.gov.

Assessing missed opportunities for prevention. Patients whose infection source was reported as a household or sexual contact with suspected or confirmed hepatitis A should be investigated to determine if the patient received post-exposure prophylaxis when the source case was identified. In addition, surveillance data can be used to provide information about people at high risk for infection to provide education and awareness about the importance of vaccinating populations as recommended by the Advisory Committee on Immunization Practices (ACIP).

Assessing the impact of vaccination programs. Age-specific incidence rates for the priority groups and the community as a whole can be compared to historical rates for the same age groups to assess the impact of routine vaccination programs.

2.3. Cases and Clusters of Potential Public Health Importance

Jurisdictions should review and analyze hepatitis A data regularly to identify cases and clusters of hepatitis A that merit further investigation. Ideally, all cases of reported hepatitis A should be investigated. In jurisdictions with limited resources, cases and clusters should be prioritized for investigation in accordance with the degree of public health importance. The following are examples of cases that are high priority for further follow-up:

- **Cases in people who are in higher risk groups (e.g., PWUD, people experiencing homelessness) or who live in congregate settings (e.g., shelters, correctional facilities)** to assure that interventions to prevent further spread are implemented in a timely fashion

- **Cases that were previously vaccinated** to characterize possible vaccine failures (see Section 1.10)
- **Cases of hepatitis A in people born after 2005** to distinguish between failure of vaccine and failure to vaccinate
- **Cases without common risk behaviors or exposures**
- **Two or more cases among patrons at the same store or food service establishment**

2.4. Interpretation of Laboratory Test Results

Immunoglobulin M antibody to hepatitis A virus (anti-HAV IgM) and viremia identified by HAV NAT using polymerase chain reaction (PCR) can detect recent or current acute infection with HAV. A description of hepatitis A laboratory markers can be found in Appendix B. Figure 2-1 illustrates the typical serologic course of HAV infection and recovery.

Caution should be exercised when interpreting a positive anti-HAV IgM laboratory result, as positive tests can occur in people >1 year after infection and false-positive tests can also occur in those without clinical or epidemiologic evidence of recent infection[39]. A person with a positive anti-HAV IgM result may also be positive for anti-HAV IgG and total anti-HAV. Because of the risk of misinterpreting positive results, anti-HAV IgM testing should be limited to people with clinical presentation of hepatitis who are suspected of having hepatitis A. Anti-HAV IgM testing should not be used as a screening tool or as part of testing panels in the workup of abnormal liver function tests. Some conditions might cause cross-reactivity with anti-HAV IgM tests, including infection with the Epstein-Barr virus[40] and hepatitis C virus[41]. Furthermore, some infected people might initially test negative for anti-HAV IgM during the first few days of symptoms[42]. If there is high clinical suspicion of hepatitis A in a person who has a negative test for anti-HAV IgM early in their clinical course, repeat testing may be indicated[42]. One study found that the optimal time for repeat testing is at least 2 days after ALT levels have peaked[42].

Figure 2-1. Typical serologic course of hepatitis A virus infection and recovery

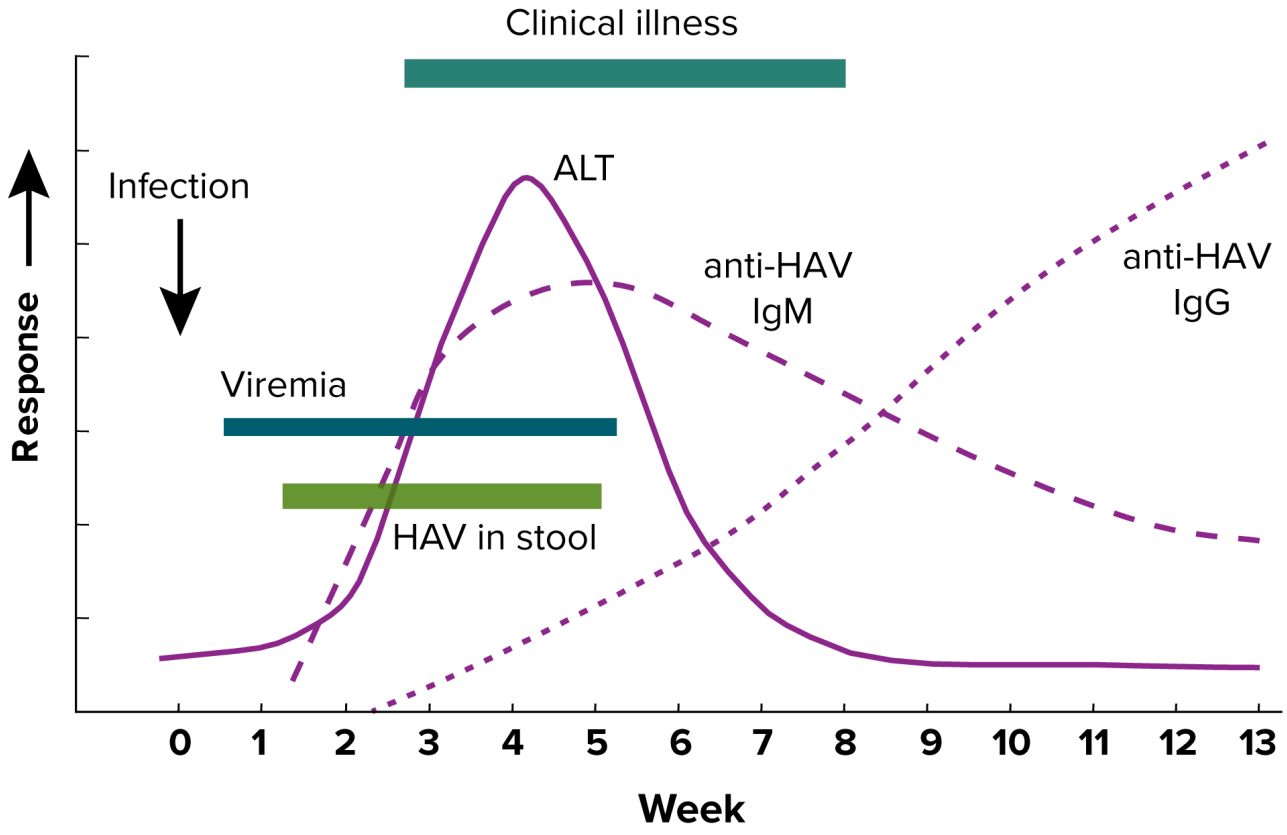


Figure obtained from https://www.cdc.gov/mmwr/pdf/rr/rr5304.pdf.

Table 2-1 interprets the combinations of total anti-HAV and anti-HAV IgM laboratory results frequently available in viral hepatitis test panels, following the biomarker changes over the course of infection as shown in Figure 2-1. If HAV RNA testing is performed, a detectable HAV RNA level indicates the presence of infection.

Table 2-1. Interpretation of hepatitis A laboratory results

Total anti-HAV	Anti-HAV IgM	Interpretation*
Positive	Positive	Current infection, recent infection, or recent vaccination
Positive	Not done	Previous infection or current infection; cannot differentiate recent from remote infection or prior vaccination
Positive	Negative	Previous infection or vaccination
Negative	Negative	Not infected (i.e., susceptible)
Not done or negative	Positive	Current infection or false-positivity/ cross-reactivity

*Ingestion of high levels of biotin can significantly interfere with certain commonly used biotinylated immunoassays, such as those used to detect anti-HAV, and cause false-positive or false-negative laboratory test results. Currently, the US Food and Drug Administration (FDA) is investigating thresholds associated with false-positive and false-negative tests. This section will be updated as more information becomes available. Source: https://www.fda.gov/medical-devices/safety-communications/update-fda-warns-biotin-may-interfere-lab-tests-fda-safety-communication.

2.5. Recommended Reportable Laboratory Markers

To aid in hepatitis A surveillance, the following laboratory markers should be reported to public health agencies:

- Positive anti-HAV IgM;
- Positive/detectable HAV RNA (including qualitative, quantitative, or genotype testing); and
- All concurrent ALT and total bilirubin results reported with positive hepatitis A laboratory results, which can also be helpful in classifying hepatitis A cases that do not have an HAV RNA laboratory result.

2.6. Surveillance Case Definition

Table 2-2 specifies the surveillance case definition for hepatitis A, adopted by CSTE and CDC in 2019. This definition should be used for hepatitis A case classification and national notification[12,43]. See Appendix C for classification scenarios of cases of hepatitis A.

Table 2-2. US Centers for Disease Control and Prevention (CDC) and Council of State and Territorial Epidemiologists (CSTE) case definition for hepatitis A, 2019

Criteria Type	Criteria
Clinical	• An acute illness with a discrete onset of any sign or symptom consistent with acute viral hepatitis (e.g., fever, headache, malaise, anorexia, nausea, vomiting, diarrhea, abdominal pain, or dark urine) **AND** • Jaundice OR peak elevated total bilirubin levels ≥3.0 mg/dL OR peak elevated serum alanine aminotransferase (ALT) >200 IU/L, **AND** • The absence of a more likely diagnosis
Laboratory*	• Positive IgM hepatitis A virus antibody (anti-HAV IgM) **OR** • Positive nucleic acid amplification test (NAAT), such as polymerase chain reaction (PCR) or genotyping for HAV
Epidemiologic Linkage	• Contact (e.g., household or sexual) with a laboratory-confirmed case of hepatitis A 15–50 days prior to the onset of symptoms
Case Status	**Classification**
Confirmed*	• Meets the clinical criteria and is positive for anti-HAV IgM† **OR** • Is positive for HAV RNA **OR** • Meets the clinical criteria and had contact (e.g., household or sexual) with a laboratory-confirmed case of hepatitis A 15–50 days prior to onset of symptoms

*Surveillance programs should provide prevention programs with information on people who have positive test outcomes for post-test counseling, as appropriate.

†And not otherwise ruled out by anti-HAV IgM or NAAT for HAV RNA testing performed in a public health laboratory.

Up to 10% of people with hepatitis A might experience a relapse of symptoms during the 6 months after acute illness. Cases of relapsing hepatitis A should not be enumerated as new cases. In addition, a case should not be counted as a hepatitis A case if there is an alternate, more likely diagnosis.

2.7. Case Ascertainment

The primary method of ascertaining cases is by reviewing reports from clinical laboratories, health care facilities, and health care providers. All states should have rules or regulations requiring that these facilities report evidence of hepatitis A to public health agencies. See Section 1.6 and Section 2.5 for information on the recommended reporting requirements for hepatitis A.

Laboratory Reporting

All states require clinical laboratories to report hepatitis A laboratory markers, such as positive anti-HAV IgM and positive HAV RNA results.

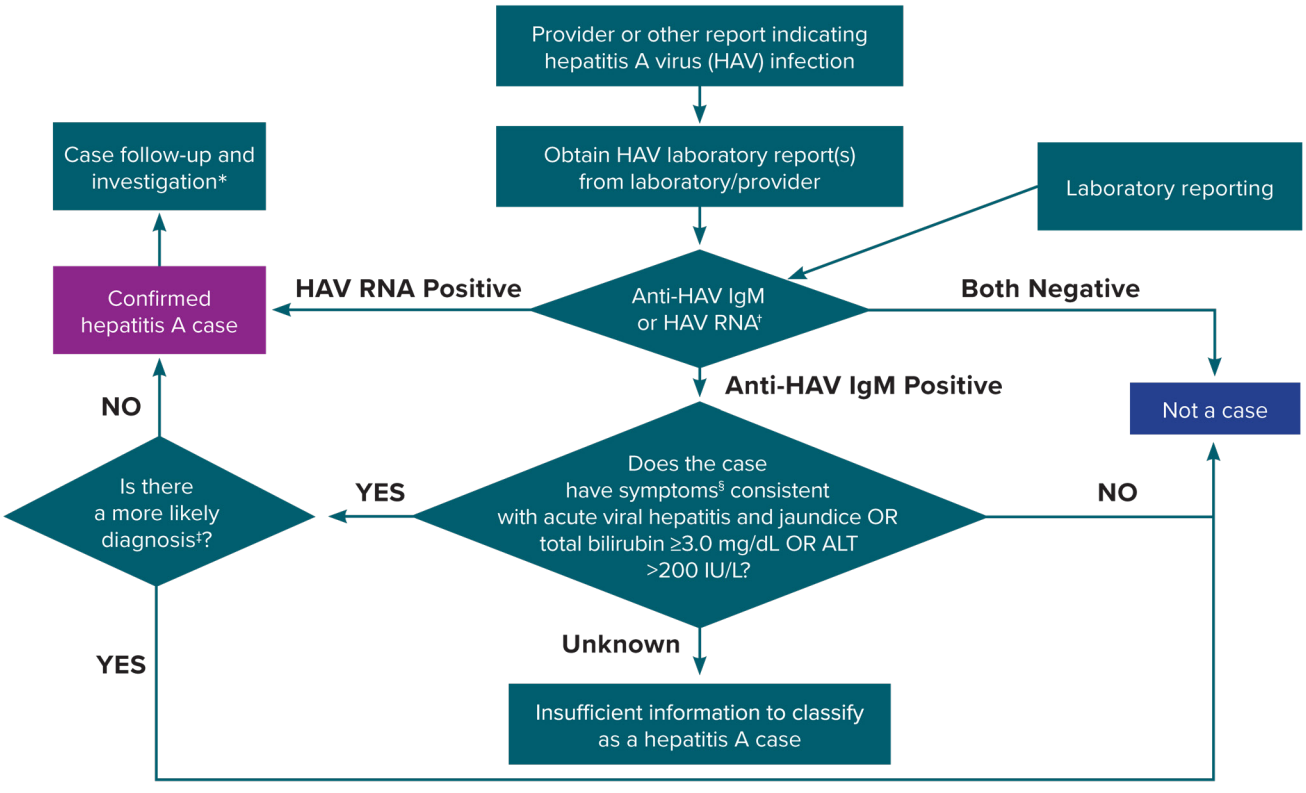
Health Care Facility and Provider Reporting

All states require health care facilities and providers to report hepatitis A diagnoses.

Additional sources that will facilitate case ascertainment and case characterization include medical records, hospital discharge databases, and death certificates. Section 5.4 describes the usefulness of select data sources in supplementing case ascertainment.

Figure 2-2 illustrates one approach for hepatitis A case ascertainment and classification. Specific procedures might vary by jurisdiction, but should generally follow the scheme outlined in Figure 2-2, in accordance with the CDC/CSTE Position Statement for the 2019 hepatitis A case definition[12,43]. See Appendix C for case classification scenarios for hepatitis A.

Figure 2-2. Process for hepatitis A case ascertainment and classification



*A person who had contact with a laboratory-confirmed hepatitis A case 15–50 days prior to onset of symptoms AND meets the clinical criteria should be classified as a confirmed hepatitis A case.

†Surveillance programs should provide prevention programs with information on people who have positive test outcomes for post-test counseling, as appropriate.

‡May include evidence of acute liver injury from infectious, autoimmune, metabolic, drug or toxin exposure, neoplastic, circulatory or thromboembolic, or idiopathic causes.

§Clinical symptoms include fever, headache, malaise, anorexia, nausea, vomiting, diarrhea, abdominal pain, or dark urine.

2.8. Case Investigation

Reports from laboratories, health care providers, and other data sources indicative of hepatitis A should be submitted to HDs (as specified by local regulations) and investigated as soon as possible to ensure adequate time to implement preventive measures (e.g., vaccination of contacts). Suspected cases of hepatitis A should be reported with appropriate laboratory results and clinical information (Table 2-2). For general information on conducting viral hepatitis case investigations, see Section 1.10. The following is a description of the follow-up activities that should be conducted for reported hepatitis A cases:

Information from the Laboratory

Positive anti-HAV IgM and positive/detectable HAV RNA laboratory results should be reported to the HD and investigated immediately. Other laboratory information that can assist with case classification includes ALT and total bilirubin levels.

Information from the Provider or Medical Records

The following information might be available from medical records to confirm the diagnosis, inform case classification, and determine public health priority:

Diagnostic test results. Hepatitis A laboratory markers (e.g., positive anti-HAV IgM and positive/detectable HAV RNA) should be reportable to the HD. If additional laboratory testing (e.g., for ALT and total bilirubin levels) is needed to classify the case, HD staff will work with the provider to obtain these test results.

Clinical features. Includes reason for testing, illness onset date, clinical signs and symptoms (including the presence of jaundice), coinfections, hospitalization status and date of death, and whether hepatitis A or an alternate diagnosis is suspected.

Demographic information. Includes name, date of birth, sex at birth, current gender, race, ethnicity, and residential address (including zip code).

Risk behaviors or exposures. Includes non-injection and injection drug use, experience of unstable housing/homelessness, high-risk sexual practices, occupation, international travel history, international adoption history, and household or sexual contact with someone with a confirmed or suspected case of hepatitis A.

- Patients who deny known risk behaviors or exposures for infection can be interviewed with a supplemental food history questionnaire.
- At the earliest possible point, information regarding whether the patient is in a sensitive occupation (e.g., food handler) or an attendee or resident of a congregate setting should be obtained.

Occupation. While no documented evidence indicates that food handlers or health care workers are at higher risk for infection than people in other occupations, jurisdictions routinely obtain this information to inform contact tracing. Special attention should be given to the job duties of people in sensitive occupations, including whether the patient was symptomatic while at work, which symptoms (if any) were experienced while at work, and the patient's work schedule during their infectious period. Food handlers should be restricted from working in a food handling capacity while infectious, and patrons from food service establishments or health care providers should be notified as appropriate[44].

Vaccination information. Hepatitis A vaccination has been recommended for infants since 2006 in all US states. Depending on age of the HAV-infected person, some cases of hepatitis A should have been vaccinated in childhood, whereas others should have been vaccinated as adults because they met specific risk criteria. Though rare, recent vaccination might result in transient anti-HAV IgM positivity. Obtaining vaccination history can be done via the patient's provider or state immunization registries and is useful in identifying vaccine failure or transient anti-HAV IgM positivity.

Information from the Patient

Resources permitting, all patients with hepatitis A should be contacted for an interview using the jurisdiction-specific case investigation form. At a minimum, all patients who are classified as "confirmed" per the CDC/CSTE case definition should be interviewed. The patient interview should ideally include the following components:

Epidemiologic link. For all laboratory-confirmed cases of hepatitis A, obtain information on contacts where exposure occurred 15–50 days prior to the onset of symptoms and investigate whether contacts met the clinical criteria.

Risk behaviors or exposures. To determine the most likely mode of transmission, ask patients about behaviors and exposures during the 15–50 days prior to illness onset. Patients who deny other risks for infection should be interviewed with a supplemental food history questionnaire.

Education and referral for follow-up. Assess whether the patient requires education or other medical follow-up services, including hepatitis B vaccination, as appropriate. People with hepatitis A should be counseled on how to prevent transmission to others.

Identification of contacts requiring post-exposure prophylaxis. If resources allow, identify contacts and coordinate referral for post-exposure prophylaxis if contact occurred within 14 days. Information regarding hepatitis A vaccination and post-exposure prophylaxis can be found on the Hepatitis A ACIP Vaccine Recommendations website.

Special Considerations when Investigating Certain Populations or Settings at Risk for Rapid Disease Transmission

Certain populations and settings are associated with increased risk for rapid transmission of hepatitis A. Considerations when investigating hepatitis A cases among people experiencing homelessness, PWUD, people engaging in high-risk sexual practices, and people in correctional facilities are provided in Section 1.10.

Outbreak Reporting and Notification

All hepatitis A outbreaks should be reported to the appropriate local authorities for further investigation within the timeframe each jurisdiction has specified. The reporting timeframe to local authorities varies by jurisdiction. Notification to CDC is done through NNDSS and by contacting viralhepatitisoutbreak@cdc.gov, as indicated in CDC-RFA-PS21-2103. See Section 5.3 for guidance on reporting outbreak source to NNDSS.

2.9. Case Reporting and National Notification

Cases of hepatitis A should be reported to HDs as specified by state, territorial, and local regulations. Hepatitis A is a nationally notifiable condition[9]. Hepatitis A cases are identified using an event code (Table 1-2). Data are sent weekly or more frequently, depending on the infrastructure of the jurisdiction sending the data. Cases might be re-classified or removed as needed after the initial transmission to CDC, if the changes occur before surveillance data are finalized each year.

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3.1. Background

Hepatitis B is a disease caused by the hepatitis B virus (HBV) that can be self-limited for some and lifelong for others. HBV is transmitted through the blood or bodily fluids of an infected person. In the United States, injection drug use (IDU) and having multiple sexual partners are the first and second most common risk behaviors or exposures reported for acute hepatitis B, respectively[3]. Approximately 50–70% of people with acute hepatitis B are not symptomatic[45], resulting in many undiagnosed and unreported infections. HBV is highly transmissible and infectious on environmental surfaces for at least 7 days[46].

The epidemiology of hepatitis B in the United States has evolved since the hepatitis B vaccine first became available in 1982[47]. Declines in acute hepatitis B incidence following the expansion of vaccination recommendations ceased beginning in 2010. Furthermore, increases have been detected in people ≥40 years of age and in jurisdictions reporting clusters associated with IDU[3]. The incidence of acute hepatitis B is highest among non-Hispanic White people and non-Hispanic Black people[3]. National chronic hepatitis B prevalence and death rates have remained relatively stable[1,48].

During 2011–2016, approximately 0.28% of the non-institutionalized US population, representing approximately 862,000 people, were estimated to be living with chronic hepatitis B[1]. The prevalence of chronic hepatitis B was highest among non-US-born people and those of Asian/Pacific Islander descent[1]. Approximately two-thirds of people living with chronic hepatitis B during 2013–2016 were unaware of their infection status[49]. Such people could unknowingly transmit their infection to others and are at risk for developing chronic liver disease.

There are clinical guidelines by the American Association for the Study of Liver Diseases (AASLD) for the prevention, diagnosis, and treatment of chronic hepatitis B[50]. Several antiviral medications are available to effectively lower HBV DNA levels and slow the progression of liver disease; however, hepatitis B is not yet curable.

All pregnant people are recommended for universal hepatitis B screening because of the risk for perinatal transmission. Infants who are perinatally exposed to HBV should receive the first dose of hepatitis B vaccine and hepatitis B immune globulin (HBIG) within 12 hours of birth, complete the vaccine series, and receive post-vaccination serologic testing (PVST) for HBsAg and anti-HBs during 9–12 months of age and 1–2 months after the final dose of the vaccine.

Other susceptible people for whom HBV exposure is suspected should receive timely post-exposure prophylaxis and immediate testing, which can prevent HBV infection and interrupt transmission. Without preventive interventions, chronic infection develops in approximately 90% of infected infants compared with 25%–30% of children who acquire HBV infection during 1–5 years of age and about 10% of people infected at >5 years of age[51,52]. Hepatitis B vaccination is recommended for all infants, people at-risk for contracting the virus, and those at increased risk of severe outcomes if infected[53,54].

The purpose of this section is to provide guidance to jurisdictions as they implement and improve hepatitis B surveillance. It contains information regarding reporting requirements, collection of relevant laboratory data, and case investigation. Given that current systems for the surveillance and follow-up of hepatitis B cases differ by jurisdiction, the standards outlined in this document are designed to provide models for best practices, recognizing that not every jurisdiction can meet those standards with available resources.

3.2. Cases and Clusters of Potential Public Health Importance

Jurisdictions should review and analyze hepatitis B data regularly to identify cases and clusters of hepatitis B that merit further investigation. When resources are limited, these should be prioritized for investigation based on the degree of public health importance. The following are examples of high priority cases and clusters:

- **People of childbearing age who are or have the potential to become pregnant,** indicating the potential for perinatal transmission
- **Children ≤24 months of age** to detect perinatal transmission
- **People in age and demographic groups for whom infection may be acute due to recent transmission, including those** ≥70 years of age (indicating possible health care-associated transmission)
- **People who were previously vaccinated** to characterize possible vaccine failures (see Section 1.10)
- **People born after 1990** to distinguish between failure of vaccine and failure to vaccinate
- **People receiving hemodialysis with evidence of acute hepatitis B (including those with test conversions**
- **People lacking typical behavioral risk behaviors or exposures for hepatitis B (e.g., IDU) who have evidence of acute infection (including test conversions)** to identify other potential causes of HBV transmission (e.g., health care-associated exposures) (information on investigation of health care-associated outbreaks can be found on the CDC DVH Viral Hepatitis Outbreaks website)
- **People with other indicator(s) of possible acute or recent infection, including those**
  - » with elevated ALT or jaundice;
  - » with positive immunoglobulin class M antibody to hepatitis B core antigen (anti-HBc IgM);
  - » with recent or current IDU history;
  - » who were tested at locations frequented by people at high-risk for acute infection (e.g., STI and HIV clinics, SSPs, correctional facilities, and medication-assisted treatment for opioid use disorder [MAT] centers); or
  - » who were in a residential facility or custodial care, including long-term care or correctional facilities, for ≥6 months prior to the onset of symptoms.

3.3. Interpretation of Laboratory Test Results

A description of hepatitis B laboratory markers can be found in Appendix B.

Understanding Changes in Biomarkers During Disease Progression

Understanding the changes in HBV biomarkers over the course of a person's infection and recovery is key to interpreting the test results. Figure 3-1 and Figure 3-2 depict the typical biomarker changes over the course of hepatitis B disease.

Figure 3-1. Typical serologic course of acute hepatitis B to recovery

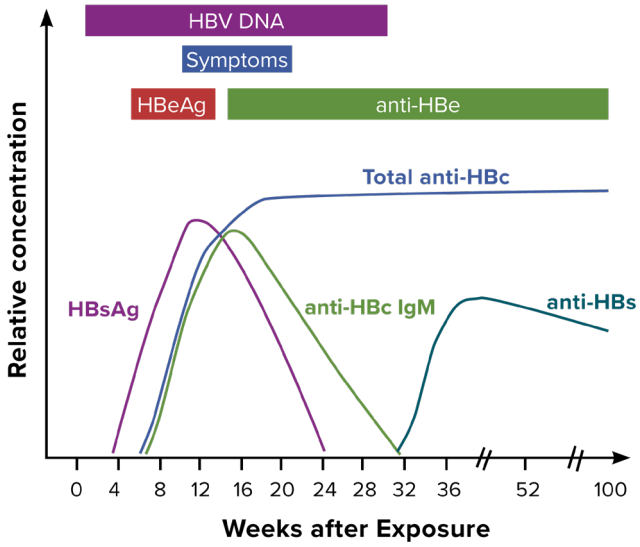


Figure obtained from https://www.cdc.gov/mmwr/preview/mmwrhtml/rr5708a1.htm.

Figure 3-2. Typical serologic course of the progression to chronic hepatitis B

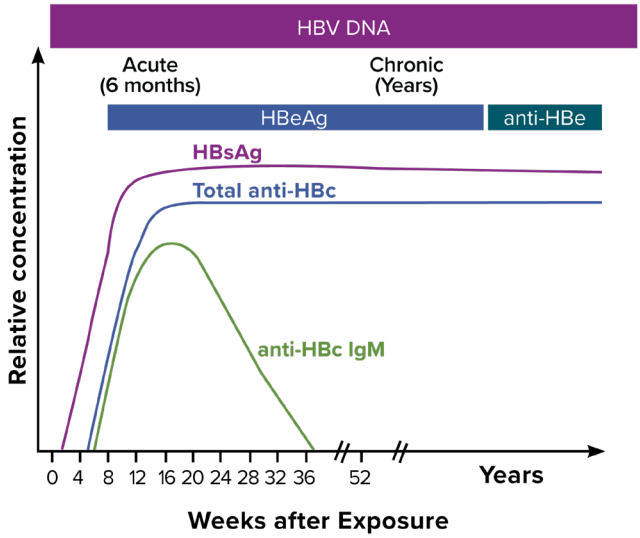


Figure obtained from https://www.cdc.gov/mmwr/preview/mmwrhtml/rr5708a1.htm.

Acute, resolved, and chronic hepatitis B

Approximately 90% of people >5 years of age with acute hepatitis B will spontaneously clear their infection[51,52]. People with resolved hepatitis B will remain positive for total anti-HBc and develop anti-HBs that protect against future HBV infection (Figure 3-1). Chronic hepatitis B is defined as an HBV infection lasting ≥6 months. During the typical course of chronic infection, the total anti-HBc and HBsAg markers will always be present, whereas anti-HBc IgM will disappear (Figure 3-2). Hepatitis B envelope antigen (HBeAg) and hepatitis B envelope antibody (anti-HBe) are variably present. HBV DNA levels vary during the course of chronic infection. Any detectable HBV DNA level is considered positive for surveillance purposes.

Isolated total anti-HBc positive

A person with a positive total anti-HBc with corresponding negative HBsAg and anti-HBs results is considered to be isolated total anti-HBc positive. A small fraction of these people could have low level chronic viremia, also known as occult hepatitis B, in which HBsAg is absent in the serum but HBV DNA is detectable[55] (Table 3-1). Cases of occult hepatitis B may be missed through surveillance in the absence of a provider report indicating occult infection or in the absence of total anti-HBc and HBV DNA results. To determine if occult hepatitis B is present, those who are isolated total anti-HBc positive should be tested for the presence of HBV DNA.

HBV-infected people with mutations in HBsAg that cannot be detected by current serologic assays may present with a negative HBsAg result despite high blood levels of HBV DNA. Some laboratories have the capacity to detect HBsAg mutants. Any HD interested in determining which laboratories can detect HBsAg mutants should follow-up with the major laboratories that perform HBsAg testing in their jurisdiction.

Hepatitis B reactivation

People with inactive chronic hepatitis B or resolved hepatitis B can experience hepatitis B reactivation, characterized by ALT elevation with or without symptoms; in some cases, illness can be severe and result in death[50]. In general, people with inactive chronic hepatitis B (i.e., those positive for HBsAg) are at greater risk for reactivation than are those with resolved hepatitis B (i.e., those negative for HBsAg and positive for total anti-HBc and anti-HBs). People at greatest risk of hepatitis B reactivation include those

- undergoing cancer chemotherapy,
- receiving immunosuppressive therapy (particularly anti-B cell therapy),
- with HIV infection who have discontinued antiretroviral drugs with activity against HBV (e.g., tenofovir),

- undergoing solid organ or bone marrow transplantation, and
- co-infected with hepatitis C virus (HCV) who are undergoing treatment with direct-acting antivirals (DAAs).

Among people with previously **inactive** hepatitis B (i.e., those positive for HBsAg and total anti-HBc), laboratory evidence of reactivation includes meeting any one of the following criteria:

- a ≥100-fold increase in HBV DNA compared to the baseline level,
- HBV DNA ≥1,000 IU/mL in a patient with previously undetectable level, or
- HBV DNA ≥10,000 IU/mL if the baseline level is not available[50].

Among people with **resolved** hepatitis B (i.e., negative for HBsAg and positive for total anti-HBc and anti-HBs), laboratory evidence of reactivation includes meeting either of the following criteria:

- HBV DNA is now detectable or
- HBsAg test conversion occurs (negative HBsAg to positive HBsAg)[50].

A suspected hepatitis B reactivation case might meet either the acute or chronic case classification criteria, depending on laboratory results and symptoms. People with hepatitis B reactivation are frequently positive for anti-HBc IgM. People with previously resolved infection who reactivate can have clinical signs and symptoms while also being transiently positive for anti-HBc IgM, therefore, mimicking acute infection.

Obtaining a clinical history from the patient's provider and/or checking the surveillance system or registry might provide clarification. A history of acute or chronic hepatitis B can help distinguish between a hepatitis B reactivation case (history of hepatitis B) and a newly diagnosed acute or chronic hepatitis B case (no history of hepatitis B). Hepatitis B reactivation cases should not be reported to NNDSS.

Interpreting Hepatitis B Laboratory Results

Many jurisdictions have regulations requiring laboratories to report all positive HBsAg, HBV DNA, and anti-HBc IgM laboratory results to the HD while a subset might also routinely receive positive total anti-HBc and anti-HBs results.

Additionally, some HDs might receive negative hepatitis B laboratory results, which are useful for determining false-positive results and monitoring patients through their infection and recovery. Table 3-1 shows how to interpret the combinations of laboratory results frequently available in hepatitis B test panels, following the biomarker changes over the course of disease as shown in Figure 3-1.

Table 3-1. Interpretation of hepatitis B laboratory results

HBsAg	Total anti-HBc	Anti-HBc IgM	Anti-HBs	HBV DNA	Possible Interpretation*
–	–	–	–	–	Never infected; susceptible if never vaccinated or vaccine failure
+	–	–	–	+ or –	Early acute infection (if HBV DNA is positive); transiently positive for HBsAg after vaccination (if HBV DNA is negative)†
+	+	+	–	+	Acute infection
–	+	+	+ or –	+ or –	Acute resolving infection; "window period" if anti-HBs is negative
–	+	–	+	–	Recovered from past infection and immune
+	+	–	–	+	Chronic HBV infection
–	–	–	+	–	Immune from vaccination; passive anti-HBs transfer after hepatitis B immune globulin administration
–	+	–	–	+ or –	Isolated total anti-HBc positive‡
–	+ or –	–	+ or –	+	Occult HBV infection§
+ or –§	+	+ or –	+ or –	+	Possible HBsAg mutant infection

Table modified from https://www.cdc.gov/mmwr/volumes/67/rr/pdfs/rr6701-H.PDF.

Abbreviations: – = negative; + = positive; anti-HBc = antibody to hepatitis B core antigen; anti-HBs = antibody to hepatitis B surface antigen; HBsAg = hepatitis B surface antigen; HBV DNA = hepatitis B virus deoxyribonucleic acid; IgM = immunoglobulin class M.

*Ingestion of high levels of biotin can significantly interfere with certain commonly used biotinylated immunoassays and cause false-positive or false-negative laboratory test results. The US Food and Drug Administration (FDA) is investigating thresholds associated with false-positive and false-negative tests. This section will be updated as more information becomes available. Reference: https://www.fda.gov/medical-devices/safety-communications/update-fda-warns-biotin-may-interfere-lab-tests-fda-safety-communication.

†People who receive hepatitis B vaccine might be transiently positive for HBsAg, with reports of transient positivity 18 days post-vaccination[56]. Retesting of patients who are positive for HBsAg shortly after hepatitis B vaccination at a later time is needed to determine the true HBV infection status.

‡Could result from:

- Loss of anti-HBs after past resolved infection. HBV DNA is negative.
- False-positive total anti-HBc, i.e., susceptible. HBV DNA is negative. To resolve the ambiguity of a false-positive total anti-HBc result, test a follow-up sample 4–8 weeks later. If found positive, interpret as a resolved infection. If negative, interpret as false-positive.
- Passive maternal transfer of total anti-HBc to infant born to a HBsAg-positive gestational parent for up to 24 months. HBV DNA is negative.
- Occult HBV infection. HBV DNA is positive, typically at low levels. Anti-HBs might or might not be positive.
- HBsAg mutant infection. HBV DNA is positive, typically at high levels. Anti-HBs might or might not be positive.

§HBsAg mutants will not be detectable if testing was performed using an older assay that cannot detect HBsAg mutants. HBsAg mutant strains can be detected by some HBsAg assays that first became available in the United States in 2015, including Abbot ARCHITECT instrument, ETI-MAK-2 PLUS, and Siemens Advia Centaur XP or XPT instrument. Though specimens should be tested using an assay that can detect HBsAg mutants, older HBsAg assays that cannot detect HBsAg mutants remain available. Reference: Apata I W, Nguyen D B, Khudyakov Y, et al. Hepatitis B virus mutant infections in hemodialysis patients: A case series. Kidney Medicine 2019; 1(6): 347-353. DOI: https://doi.org/10.1016/j.xkme.2019.07.011.

3.4. Recommended Reportable Laboratory Markers

The following laboratory markers are recommended for reporting to public health, as they can aid in case ascertainment, case classification, and monitoring care continua for hepatitis B:

- Positive HBsAg,
- Positive/detectable HBV DNA (including quantitative, qualitative, and genotype testing),
- Positive anti-HBc IgM,
- Positive HBeAg, and
- If any of the above positive results are reported, also report the following:
  - » Pregnancy status
  - » Concurrent ALT and total bilirubin result
  - » Other hepatitis serological results (e.g., hepatitis A, hepatitis C, hepatitis D, and/or hepatitis E)
  - » Negative HBsAg and/or negative/undetectable HBV DNA results

Total anti-HBc is detectable, on average, approximately 5 weeks post-HBV exposure, remains detectable indefinitely following exposure, and indicates past or current infection. In the presence of total anti-HBc, a positive HBsAg, HBeAg, or anti-HBc IgM result is a more reliable indication of recent or current infection. Jurisdictions that receive total anti-HBc laboratory results can use these results to clarify a person's HBV infection status.

3.5. Case Reporting and National Notification

Cases of acute, chronic, and perinatal hepatitis B, and hepatitis B during pregnancy should be reported to HDs as specified by state, territorial, or local regulations. Acute, chronic, and perinatal hepatitis B are nationally notifiable conditions[5]. Hepatitis B cases are identified using an event code corresponding to the hepatitis B condition (Table 1-2). Data are sent weekly or more frequently, depending on the infrastructure of the jurisdiction sending the data. Cases might be re-classified or removed as needed after the initial transmission to CDC, as long as the changes occur before surveillance data are finalized each year.

3.6. Surveillance of Acute and Chronic Hepatitis B

3.6.1. Background

The national incidence of acute hepatitis B dramatically declined after incremental recommendations for vaccinating people at-risk for infection and severe outcomes were released beginning in 1982[47] and for infants and children in 1991[53]. Since 2010, the national incidence rate of acute hepatitis B has remained relatively stable, with increases in people aged ≥40 years and in some jurisdictions affected by the opioid crisis. IDU and having multiple sexual partners are major risk behaviors associated with acute hepatitis B in the United States, and incidence is highest among non-Hispanic White people, non-Hispanic Black people, and those 30–59 years of age[3].

In the United States, chronic hepatitis B occurs primarily among people born in countries with intermediate or high hepatitis B prevalence, where the primary mode of transmission is perinatal transmission. Chronic hepatitis B occurs in about 1.3% of non-US-born adults and about 0.16% of US-born adults[1]. During 2011–2016, approximately 862,000 people were estimated to have chronic hepatitis B in the United States[1].

CDC has provided guidelines for hepatitis B testing during pregnancy and among people with risk behaviors or exposures[57,58]. Undiagnosed hepatitis B cannot be detected using traditional surveillance methods. Improving hepatitis B surveillance by improving screening of those at risk is an important component of national and jurisdictional strategies for the prevention and control of hepatitis B.

3.6.2. Uses of Surveillance Data

Acute and chronic hepatitis B surveillance data can be used to inform and improve public health interventions in the following ways:

Monitoring trends in disease incidence and determining risk behaviors or exposures. Acute hepatitis B surveillance data should be analyzed at regular intervals by person, place, and time to monitor disease incidence. Risk factor information should be analyzed to monitor disease transmission patterns and identify groups at higher risk for infection.

Identifying outbreaks. An outbreak is defined as the occurrence of more cases of disease than expected in a given area or among a specific group of people over a particular time period. Detailed guidance on viral hepatitis outbreaks, including examples of hepatitis B outbreaks, can be found on the CDC DVH Viral Hepatitis Outbreaks website.

Assessing missed opportunities for prevention. Patients whose infection source was reported as being a household or sexual contact should be investigated to determine whether they should have been vaccinated when the source case was identified. Potential barriers to administering post-exposure prophylaxis should be explored to mitigate future missed opportunities for prevention.

Surveillance data can be used to provide information on cases occurring among adults at high risk for infection, creating opportunities to provide education and awareness to the health care community and the public about the importance of vaccinating high-risk populations as recommended by ACIP.

Missed opportunities for vaccination should also be assessed for cases occurring among people born after 1990. Understanding the frequency and characteristics of these cases enables monitoring of the effectiveness of routine childhood vaccination programs and identification of barriers to childhood vaccination.

Assessing the frequency and causes of vaccine failure. When available, vaccination history should be obtained. Though vaccine failure is rare, any case in a person who was previously vaccinated requires additional investigation to identify potential instances of vaccine failure. Where available, jurisdiction immunization registries can provide valuable information for such investigations Section 1.10. Health care professionals or public health authorities who have questions on these cases should contact CDC's DVH at viralhepatitis@cdc.gov. Reporting and investigating these cases through surveillance is important for informing vaccination policies and education.

Tracking cases of chronic hepatitis B. Surveillance systems and databases that track chronic hepatitis B cases can aid in monitoring trends in the prevalence of chronic infection.

Understanding the burden of hepatitis B in the community. Person-based longitudinal databases can provide a better understanding of the burden of hepatitis B in the community. Such databases can help

- determine whether infections have resolved or reactivated;
- identify probable cases that need additional testing for diagnosis;
- identify health-related disparities;
- facilitate identification of HBV-infected pregnant people for enrollment in the Perinatal Hepatitis B Prevention Program (PHBPP);
- facilitate monitoring of perinatal hepatitis B;
- monitor the movement of cases in or out of the jurisdiction; and
- track the occurrence of related adverse health outcomes.

Public health management of chronic HBV-infected people and their contacts. Surveillance data can be used to identify and follow-up on chronic hepatitis B cases (especially among those who were recently diagnosed), link them to appropriate medical care and harm reduction services, and ensure contacts are protected and/or referred to care or testing, as appropriate.

3.6.3. Surveillance Case Definitions

Table 3-2 depicts the surveillance case definition for acute hepatitis B, adopted by CSTE and CDC in 2012[59,60]. See Appendix C for classification scenarios of cases of acute hepatitis B.

Table 3-2. US Centers for Disease Control and Prevention (CDC) and Council of State and Territorial Epidemiologists (CSTE) case definition for acute hepatitis B, 2012

Criteria Type	Criteria
Age	• >24 months of age, **OR** • ≤24 months of age and the mode of exposure was not perinatal
Clinical	• An acute illness with a discrete onset of any sign or symptom consistent with acute viral hepatitis (e.g., fever, headache, malaise, anorexia, nausea, vomiting, diarrhea, and abdominal pain), **AND** • Jaundice **OR** serum alanine aminotransferase (ALT) >100 IU/L
Laboratory*	• Positive hepatitis B surface antigen (HBsAg), **AND** • Positive immunoglobulin M (IgM) antibody to hepatitis B core antigen (anti-HBc IgM) (if done)
HBsAg Test Conversion*	Documented negative HBsAg test within 6 months prior to a positive test of either HBsAg, hepatitis B e antigen, or nucleic acid test (NAT) for HBV DNA (including qualitative, quantitative, or genotype)
Case Status	**Classification**
Confirmed Acute*	• >24 months of age **OR** ≤24 months of age and the mode of exposure was not perinatal, **AND** • Not known to have a history of acute or chronic hepatitis B, **AND** • Meets the clinical and laboratory criteria **OR** meets the HBsAg test conversion criterion

*Surveillance programs should provide prevention programs with information on people who have positive test outcomes for post-test counseling and referral to treatment and care, as appropriate.

Table 3-3 specifies the surveillance case definition for chronic hepatitis B, adopted by CSTE and CDC in 2012[61,62]. See Appendix C for classification scenarios of cases of chronic hepatitis B.

Table 3-3. US Centers for Disease Control and Prevention (CDC) and Council of State and Territorial Epidemiologists (CSTE) case definition for chronic hepatitis B, 2012

Criteria Type	Criteria
Age	• >24 months of age, **OR** • ≤24 months of age and the mode of exposure was not perinatal
Clinical	No symptoms are required. People with chronic hepatitis B might have no evidence of liver disease or might have a spectrum of diseases ranging from chronic hepatitis to cirrhosis or liver cancer.
Diagnostic Laboratory*	• Negative Immunoglobulin M (IgM) antibody to hepatitis B core antigen (anti-HBc IgM) AND a positive result on one of the following tests: HBsAg, nucleic acid test (NAT) for HBV DNA (including qualitative, quantitative, or genotype), or hepatitis B e antigen (HBeAg), **OR** • Positive for any combination of the following tests two times at least 6 months apart: » Hepatitis B surface antigen (HBsAg) » NAT for HBV DNA (including qualitative, quantitative, or genotype testing) » HBeAg
Presumptive Laboratory*	• Does not meet the case definition for acute hepatitis B **AND** • Has one positive HBsAg, NAT for HBV DNA (including qualitative, quantitative, or genotype testing), or HBeAg laboratory result
Case Status	**Classification**
Confirmed Chronic*	• >24 months of age **OR** ≤24 months of age and the mode of exposure was not perinatal, **AND** • Has diagnostic laboratory evidence
Probable Chronic*	• >24 months of age OR ≤24 months of age and the mode of exposure was not perinatal, **AND** • Has presumptive laboratory evidence, **AND** • Does not meet the clinical criteria of the acute hepatitis B case definition
Comments	Multiple laboratory tests indicative of chronic hepatitis B might be performed simultaneously on the same patient specimen as part of a "hepatitis panel." Testing performed in this manner can lead to seemingly discordant results, e.g., HBsAg-negative AND HBV DNA-positive. For the purposes of this case definition, any positive result among the three laboratory tests mentioned above is acceptable, regardless of other testing results. Negative HBeAg results and HBV DNA levels below positive cutoff level do not confirm the absence of HBV infection.

*Surveillance programs should provide prevention programs with information on people who have positive test outcomes for post-test counseling and referral to treatment and care, as appropriate.

3.6.4. Case Ascertainment

The primary method to ascertain suspected cases is through investigation of reports from clinical laboratories, health care facilities, and health care providers suggestive of hepatitis B. Rules or regulations requiring that facilities and providers report hepatitis B to public health agencies vary by jurisdiction. See Section 1.6 and Section 3.4 for information on the recommended reporting requirements for hepatitis B.

Additional sources of information include medical records, hospital discharge databases, death certificates, and birth certificates. Section 5.4 provides more information on these data sources. Figure 3-3 illustrates a potential approach for acute and chronic hepatitis B case ascertainment and classification.

Specific procedures can vary by jurisdiction, but should generally follow the scheme below, in accordance with the CDC/CSTE Position Statement for the 2012 acute and chronic case definitions[60,62]. Cases among infants ≤24 months of age should be classified in accordance with the CDC/CSTE Position Statement for the 2017 perinatal hepatitis B case definition[63,64], unless the exposure mode is not perinatal (e.g., health care-associated). See Section 3.7.4 for case ascertainment guidance of perinatal hepatitis B cases.

Laboratory Reporting

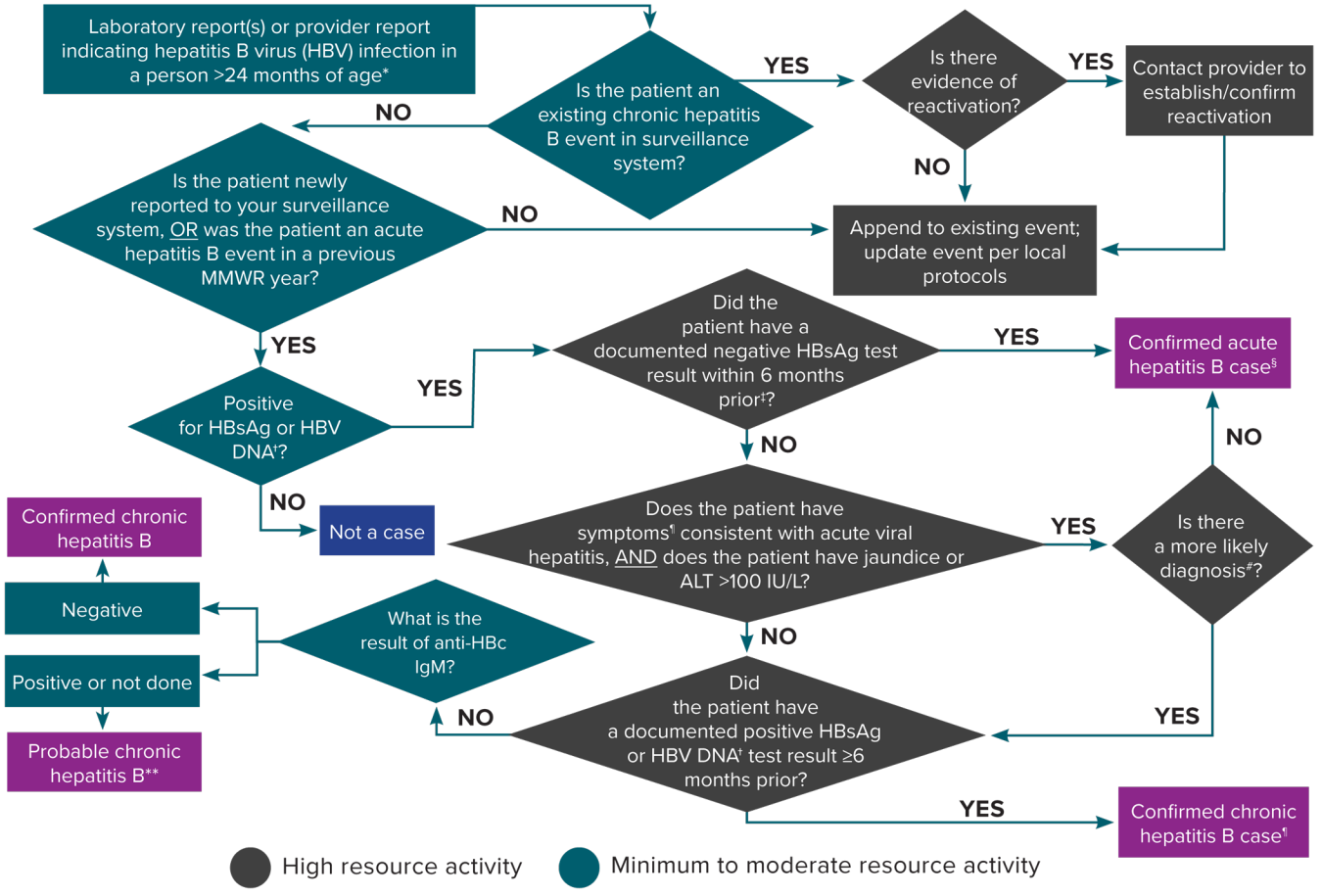
Laboratory reporting of HBV infection is required in all states for which acute and/or chronic hepatitis B are reportable. While case-defining infection markers (e.g., positive HBsAg or anti-HBc IgM) are reportable in most jurisdictions, regulations vary regarding which markers should be reported (e.g., any or all positive indicators within the panel, only positive results of selected biomarkers, or selected combinations of markers).

Some jurisdictions require reporting of negative hepatitis B laboratory results for some or all of the infection markers or when accompanied with positive hepatitis B laboratory results. Receiving negative hepatitis B laboratory results or complete reporting of all tests in the hepatitis panel allows public health officials to more accurately interpret results. However, this also requires more sophistication in information systems to efficiently send, process, and utilize the information received.

Health Care Facility and Provider Reporting

Many states require health care facilities and providers to report hepatitis B diagnoses.

Figure 3-3. Process for acute and chronic hepatitis B case ascertainment and classification



*A person ≤24 months of age whose mode of exposure is not perinatal (e.g., health care-acquired) should be classified under the 2012 acute or chronic hepatitis B case definitions. A person ≤24 months of age whose mode of exposure is perinatal should be classified under the 2017 perinatal hepatitis B case definition. Surveillance programs should provide prevention programs with information on people who have positive test outcomes for post-test counseling and referral to treatment and care, as appropriate.

†Nucleic acid testing for HBV DNA, including qualitative, quantitative, and genotype testing. An isolated positive hepatitis B 'e' antigen (HBeAg) test result should prompt further investigation into the hepatitis B surface antigen (HBsAg) and/or HBV DNA results.

‡A documented negative HBsAg within 6 months prior to a positive test (either HBsAg, HBeAg, or HBV DNA) does not require acute clinical presentation to meet the acute hepatitis B case definition.

§A new acute hepatitis B case is an incident case that has not been previously notified as an acute or chronic hepatitis B case.

¶Acute hepatitis B clinical symptoms include fever, headache, malaise, anorexia, nausea, vomiting, diarrhea, and abdominal pain.

#May include evidence of acute liver injury from infectious, autoimmune, metabolic, drug or toxin exposure, neoplastic, circulatory or thromboembolic, or idiopathic causes.

**May re-classify as confirmed if additional information is later received before the Nationally Notifiable Diseases Surveillance System (NNDSS) close-out date for national notification purposes. Jurisdictions with a longitudinal system can update probable cases to confirmed within their system at any time regardless of the NNDSS close-out date.

3.6.5. Case Investigation

The original report may be sufficient to classify a case as an acute or chronic infection. Resource limitations may not allow all chronic cases to be investigated in the same way as acute cases. Additional investigation may be necessary depending on the priority level of the case. The level of investigation will depend on the situation, the objectives, and the available resources. The following is a description of the type of information that should be collected during case investigations:

Information from the Laboratory

Newly reported positive anti-HBc IgM, HBsAg, or HBV DNA laboratory results should be reported to the HD. Concurrent ALT and total bilirubin results reported with positive hepatitis B laboratory results can be helpful in identifying cases that might be acute. Though not required for case classification, total anti-HBc indicates past or current infection, and in its presence, a positive HBsAg, HBeAg, or anti-HBc IgM result is more likely to be a true positive.

Information from the Provider or Medical Records

Medical records can provide the following types of information:

Demographic information. Includes name, date of birth, sex at birth, current gender, race, ethnicity, country of birth, and residential address (including zip code).

Clinical features. Includes reason for testing, illness onset date, clinical signs and symptoms (including the presence of jaundice), hospitalization status and date of death (if applicable), and whether an alternate diagnosis is suspected. HDs should inquire about the potential of past infection to confirm whether current clinical features are due to a newly acquired infection. Symptoms are not always present at the time of diagnosis for chronic infections. The medical record may also provide evidence of chronic liver disease.

Pregnancy status. Pregnancy status should be checked for all people of childbearing age with childbearing potential. HBV-infected pregnant people should be referred to the PHBPP to ensure their infants receive appropriate post-exposure management according to ACIP recommendations. Children born to an HBV-infected gestational parent should be tested for infection, and if infected, classified according to the CDC/CSTE perinatal hepatitis B case definition.

Diagnostic test results. If additional laboratory testing (e.g., ALT levels, total bilirubin levels, and results from a hepatitis panel) are needed to classify the case, HD staff may work with the provider to order/obtain these test results.

Risk behaviors or exposures. Includes history of IDU, sexual and household exposures, experience of homelessness, recent medical procedures, hemodialysis, incarceration, and residence in a long-term care facility.

Vaccination information. Vaccination history may be obtained from the patient's medical provider or from the jurisdiction's immunization registry. Note that recent hepatitis B vaccination can cause transient HBsAg positivity for up to 18 days post-vaccination[56]. Retesting is needed to determine the true HBV infection status in patients who tested positive for HBsAg shortly after hepatitis B vaccination.

Information from the Patient

All patients with acute hepatitis B should be contacted for an interview using the jurisdiction-specific case investigation form. If resources are limited, at a minimum, all patients who are classified as "confirmed" per the CDC/CSTE case definition and those flagged as having public health importance (Section 3.2) should be interviewed. Decisions to contact the patient are often jurisdiction-specific and depend on available resources. In many situations, patient contact is reserved for those cases deemed highest priority for preventing further transmission or for referral for additional care and treatment, as needed.

The patient interview should ideally include the following components:

Risk behaviors or exposures. This allows identification of a potential source or presence of risk behaviors or exposures for infection during the 60–150 days prior to symptom onset. For chronic cases, if it is determined that the person has current risk behaviors or exposures for ongoing transmission or was identified as part of a cluster of cases, additional information relevant to risk might be prioritized.

Education and referral for follow-up. Newly diagnosed acute and chronic hepatitis B patients should be advised on how to prevent transmission to others. Patients should also be referred for hepatitis B-directed medical care and recommended to receive vaccination against hepatitis A, if indicated.

Identification of contacts requiring post-exposure prophylaxis and testing. If resources allow, contacts should be identified and testing, post-exposure prophylaxis, counseling, and linkage to care coordinated, as appropriate. Information regarding hepatitis B vaccination and prophylaxis can be found on the Hepatitis B ACIP Vaccine Recommendations website.

Special Considerations When Investigating Certain Populations or Settings at Risk for Rapid Disease Transmission

Considerations when investigating hepatitis B cases among certain populations at risk for rapid transmission are provided in Section 1.10.

Case Investigation Prioritization

Providers are required to report acute infections directly to the HD, and laboratories should provide HDs with hepatitis B test results electronically. The automated collection of hepatitis B laboratory results will, in many jurisdictions, lead to a high volume of reporting. Many HDs might lack the resources needed to conduct investigations for all acute cases. If resources allow, automate the collection of ALT and total bilirubin results through electronic laboratory reporting (ELR) or electronic medical record (EMR) reporting, and prioritize data collection to confirm those cases with abnormal results. Jurisdictions can also consider the following when prioritizing case follow-up:

- Semi-automated/preliminary collection of risk data combined with more targeted follow-up on cases **without** identified risk history
- Demographic groups that might be at higher risk for acquiring or transmitting infection
  - » Pregnant people
  - » Elderly patients (e.g., >70 years of age)
  - » Cases that might represent emerging risks
  - » People infected with HIV, hepatitis C virus (HCV), or STIs
- Groups where infection is unexpected
  - » Children and adult cases who were born after 1990
  - » Cases who are documented to have received hepatitis B vaccination
- Target populations based on specific settings within a particular jurisdiction
  - » SSPs or SUD treatment facilities
  - » Correctional facilities
  - » Retirement/nursing facilities
  - » Providers of people experiencing homelessness
  - » Areas where known risk behaviors are occurring, or rates of newly reported infections are increasing
- Ease of data collection
  - » People tested at public health clinics
- Supplement case surveillance data with data sources identifying populations at high risk and the evolving epidemiology of acute infections
  - » SAMHSA/state drug use, overdose, and EMS data
  - » HIV, HCV, and STI incidence data to identify coinfections
  - » Ongoing outbreak and cluster investigations, if applicable
  - » Hospital discharge data
  - » Syndromic surveillance data on IDU-related emergency department care

Considerations for Conducting a Chronic Hepatitis B Case Investigation

Conducting an investigation on a chronic hepatitis B case can involve the following considerations:

1. Check the jurisdiction's hepatitis B registry/surveillance system to ensure the case is newly reported and not previously documented.
2. Review the information in the initial report to determine if the case potentially falls within a group prioritized for investigation, such as those outlined in Section 3.2. At a minimum, pregnancy status should be checked for all people with chronic hepatitis B who are of childbearing age with childbearing potential; reports of HBV-infected pregnant people should be shared with the PHBPP.

3. When possible, contact the health care provider and/or review medical records to obtain additional information to help prioritize which cases should receive a patient interview.
4. If the case has one of the risks for hepatitis B reactivation outlined in Section 3.3 under the subsection "Understanding Changes in Biomarkers during Disease Progression" (e.g., the patient is hepatitis C co-infected and is receiving DAA treatment), consider follow-up with the health care provider to ensure the patient receives medical management according to clinical guidelines[65].
5. For patients who are interviewed, collect relevant demographic and risk history information using the jurisdiction-specific case report form.
6. Investigate likely health care exposures according to the jurisdiction's procedures, ideally in collaboration with the health care-associated infection team.
7. Provide patient education about ways to avoid the spread of infection to others and ways to avoid further harm to the liver.
8. Educate long-term sexual contacts and people who have had direct exposure to the patient's blood about HBV transmission and the need to be tested for hepatitis B if they are not known to be immune or infected. If a contact is susceptible, they should complete the hepatitis B vaccine series; contacts deemed unlikely to return for test results should be vaccinated when testing is initiated.
9. If the patient is a child, screen the parents and household members for evidence of infection.
10. If resources allow, contact the provider and/or refer the patient to a patient navigator to ensure the patient is receiving care services.

3.6.6. Case Reporting and National Notification

Cases of acute and chronic hepatitis B are nationally notifiable to CDC using a condition-specific event code (Table 1-2). Cases might be re-classified, removed, or changed between acute or chronic after the initial transmission to CDC as long as changes are made before surveillance data are finalized each year.

A case initially transmitted to NNDSS as "probable" might later be reclassified as "confirmed" or "not a case." If additional laboratory results are received on an acute hepatitis B case to indicate progression to chronic infection in the same *MMWR* year, only the acute event is transmitted (e.g., a person meets the confirmed acute hepatitis B case definition, including is positive for anti-HBc IgM, but later becomes negative for anti-HBc IgM in the **same** reporting year).

In addition, an acute case might be classified as a new chronic case in a subsequent reporting year. Events for a person should be linked in NNDSS using the same patient ID if submitting via HL7 messages or NBS. See Section 5.2 for additional guidance on transmitting multiple viral hepatitis events for the same person. See Section 3.5 for more information on hepatitis B case reporting and national notification.

3.6.7. Surveillance Activities for Chronic Hepatitis B

The following section describes best practice models for core and enhanced surveillance activities that jurisdictions should consider. Enhanced surveillance activities should be defined based on local priorities.

Best Practice Models for Core and Enhanced Chronic Hepatitis B Surveillance

Core Surveillance

Ascertainment and Reporting

- Create or maintain an electronic system for systematically collecting and storing hepatitis B laboratory results and other case data (e.g., demographic, risk, and clinical information) longitudinally for unique (deduplicated) persons.
- Establish or maintain a method to receive hepatitis B laboratory data and enter it into the hepatitis B surveillance system or registry, preferably through an automated ELR system. ELR is the most efficient way to receive these data, especially if the ELR system can automatically enter the hepatitis B records into the surveillance system.
  - » If an ELR system for other conditions is used in the jurisdiction, include hepatitis B.
  - » If ELR is not possible, work with high volume testers to receive data in another way (e.g., periodic flat files).
- Implement a process to review and classify cases within the surveillance system or registry.

- Extract data from the hepatitis B surveillance system or registry and transmit cases to CDC according to NNDSS procedures.
  - » Include extended data elements in addition to core data elements, when feasible.

Investigations

- Document local procedures for investigations, including defining priority populations, or identifying priority reports for investigation. See Section 3.2 for types of priority cases.
- Conduct investigations for priority reports or populations. See Section 3.6.5 for chronic hepatitis B case investigation guidance.
- Establish a protocol for identifying and investigating health care-associated infections or coordinate with the department's health care-associated infections program. Use CDC's health care-associated infection toolkit as a resource.
- Establish a protocol for identifying and investigating other unique exposures.

Quality Assurance

- Identify and review potential duplicate reports so that only the initial report of each chronic hepatitis B case is counted, and subsequent reports can be used for confirming cases or longer-term monitoring.
- Establish a process for cleaning, reviewing, and standardizing case data and test results.
- Assess case reports and test results for completeness and accuracy.

Analyses

- Create an annual report, situational analysis, or other data product that can be widely shared with providers, advocates, and other public health professionals.

Policy

- Research existing health code/policy related to hepatitis B reporting and the process for changing such policies (if necessary).
- Identify who should report hepatitis B cases – health care providers, health care facilities, and/or laboratories.
- Determine what should be reportable. At a minimum, positive HBsAg, HBeAg, anti-HBc IgM, and HBV DNA results (including genotype) should be reportable. If possible, pregnancy status and concurrent ALT and total bilirubin results should be reported with positive hepatitis B laboratory results, and negative HBsAg and undetectable HBV DNA results should also be reportable. Surveillance programs should provide prevention programs with information on people who have positive test outcomes for post-test counseling and referral to treatment and care, as appropriate.

Other Data Sources

- Explore how to obtain access to additional sources of data (e.g., vital statistics person-level data).

Enhanced Surveillance (where resources permit)

Ascertainment and Reporting

- Use additional data sources to identify cases not reported to the hepatitis B surveillance system or registry (e.g., vital records and medical records review). See Section 5.4 for a description of optional data sources.
- Use additional data sources to supplement data in the surveillance system or registry. For example:
  - » Conduct vital statistics death registry matches to update vital status and death date
  - » Conduct vital statistics birth registry matches to update pregnancy information, and to link gestational parent-infant pairs within the surveillance system in coordination with perinatal hepatitis B prevention program
  - » Conduct data linkage matches to other disease registries (e.g., HIV, cancer) to find missing information (e.g., race, ethnicity, co-infection, co-morbidities)
  - » Use a medical record extraction system to identify additional cases and pregnancy status that might not otherwise be reported or to improve efficiency of those reports
- Implement a process for updating cases in the surveillance system or registry with potential health care systems data to track patients along the care continuum (e.g., insurance and pharmacy claims data, hospital discharge data).

Investigations

- Conduct chronic hepatitis B case investigations for additional priority populations. See Section 3.6.5 for chronic hepatitis B case investigation guidance.
- Establish a protocol for identifying and investigating other unique exposures, including clusters or outbreaks.
- Establish methods for identifying reactivations (i.e., determine whether the patient has a history of acute or chronic hepatitis B) to distinguish a new case of disease from reports or notifications that should not be enumerated as a new case.
- If personnel and other resources allow, consider in-depth investigation of a random sample of chronic cases to evaluate demographic variables, reason for testing, access and barriers to prevention and treatment services, and other questions of importance for viral hepatitis elimination activities in the jurisdiction. Personnel with expertise in study design, data collection, and analytic skills should develop and oversee these types of in-depth investigations.
- Assure linkage to care, treatment, and harm reduction services for priority populations where resources allow.

Quality Assurance

- Establish additional quality assurance processes for case reports and test results.
- Implement quality assurance improvement measures to ensure completeness and accuracy of case investigations and interpretation of laboratory results.
- Establish systems to identify and address decreases in laboratory reporting by test type volume and laboratory that might represent coding or transmission issues.
- Establish systems to identify and address deficiencies in provider reporting (e.g., incomplete or missing reports).

Analyses

- Use data linkage matches to other disease databases/registries (e.g., HIV, HCV, and cancer) for analysis of co-infections and identification of receipt of care.
- Use vital statistics birth registry matches for analysis of infants born to HBV-infected gestational parents.
- Use death registry matches to describe hepatitis B-associated mortality.
- Create provider-level indicators (such as complete reporting, complete diagnostic testing, linkage to care, and treatment initiation) to work with providers to improve these outcomes.
- Identify methods for establishing surveillance-based chronic hepatitis B prevalence estimates.
- Identify and describe trends and disparities in liver cancer incidence and mortality.
- Create hepatitis B care continua, including determining and validating surveillance-based definitions for hepatitis B treatment and outcome indicators.
- Identify and describe trends and disparities along the care continuum (e.g., disparities in screening, viremia, linkage to care, and treatment initiation).
- Expand the data reports available to external partners.

Policy

- Use surveillance data and best practices from other jurisdictions to recommend health code changes related to reporting (e.g., obtaining non-positive test results), as allowable within the jurisdiction.
- Use surveillance data to support evidence-based for health code changes related to expanding access to syringe services programs and other harm reduction services for populations affected by hepatitis B, as allowable within the jurisdiction.
- Use analysis of surveillance data on trends and disparities to guide resource allocation and inform public health action, prioritizing those communities most disproportionately affected.

Other Data Sources

- Obtain access to supplemental data sources wherever possible and incorporate their usage into routine practices. See Section 5.4 for a description of optional data sources.

3.6.8. Considerations for Hepatitis B Cases who were Transplant Recipients

Organ and tissue donor-derived HBV infection is rare and commonly associated with IDU in a deceased donor[66]. In the 2020 Public Health Service (PHS) guidelines[67], it is recommended that all organ recipients in the United States receive hepatitis B vaccination, pre-transplant testing for total anti-HBc, HBsAg and anti-HBs, and post-transplant testing for HBV DNA at 4–6 weeks.

However, clinical manifestations of post-transplant HBV infection can be delayed by many months after liver transplantation[68,69]. As such, the 2020 PHS guidelines also recommend that health care providers caring for liver recipients consider conducting additional testing by HBV NAT or assessing signs or symptoms of liver injury (e.g., jaundice or elevated liver function tests) at one-year post-transplant. All donors are screened for total anti-HBc, HBsAg, and HBV DNA prior to organ procurement. In situations where the donor is known to be positive for any of these tests, recipient HBV infection is expected and does not require investigation by the HD beyond notifying CDC that the recipient case is donor derived. As these patients are already linked to testing and treatment, these infections are notifiable to CDC as new acute cases, but the jurisdiction need not investigate beyond indicating that the infection was donor-derived.

Organ transplantation from deceased donors dying of overdose and IDU has increased recently[70]. To facilitate identification of suspected donor-derived cases of viral hepatitis, jurisdictional viral hepatitis surveillance programs should consider reaching out to transplant centers proactively. In most jurisdictions, there are a relatively small number of medical centers that perform transplantation[71]. A listing of transplant facilities in the United States, including facility location and phone number, can be found on the Organ Procurement and Transplantation Network (OPTN) website[71].

Knowing whether the transplant center is using organs from deceased donors who injected drugs or who were positive for anti-HCV or HCV RNA is important, as this might increase the very small risk of donor-derived HBV infection[69]. When donor-derived viral hepatitis is suspected, the transplant center is required to report the infection to the Disease Transmission Advisory Committee (DTAC) of OPTN, which often consults with CDC about a possible investigation. If CDC accepts the investigation, it is coordinated by the CDC Office of Blood, Organ, and Other Tissue Safety with consultation from CDC DVH. CDC only investigates selected reports of "unexpected" viral hepatitis transmission, meaning that both the donor and recipient tested negative for hepatitis B (including anti-HBc, HBsAg and HBV DNA, if available) prior to the transplant.

Investigation includes review of all laboratory and clinical data for donor and recipients and testing archived donor samples (e.g., serum, lymphocytes, and liver biopsy), if available, for HBV DNA. When the initial investigation is complete, CDC DVH contacts the public health jurisdiction to complete the rest of the investigation. Typically, there are two outstanding questions that only the public health jurisdiction can answer: 1) Did the recipient have any behavioral or other risks for hepatitis B (e.g., IDU) and 2) Does the jurisdiction have any ongoing investigations of health care-associated hepatitis B that might be related to this investigation?

Case classification in patients with a documented transplant should consider reports of laboratory test results prior to and post-transplant and potential health care exposures, if suspected. Table 3-4 outlines considerations for hepatitis B cases who were transplant recipients of a solid organ.

Table 3-4. Considerations for hepatitis B cases who received a solid organ from a donor*

Organ Recipient Pre-Transplant Laboratory Results†	Organ Recipient Post-Transplant Laboratory Results†	Case Classification
Positive hepatitis B surface antigen (HBsAg) or HBV DNA	Positive HBsAg or HBV DNA	Should not be considered a new case due to organ transplant, but rather an infection documented prior to transplant. To determine whether this case should be considered newly reported, follow Figure 3-3.
Evidence of resolved prior infection: • Positive total hepatitis B core antibody • Negative HBsAg • Hepatitis B surface antibody (could be detectable, undetectable, or not done)	Evidence of reactivation: • Detectable HBV DNA, OR • Positive HBsAg	Should not be considered a new case, but reactivation of prior infection. Reactivation information should be appended to the case record of the existing case in the jurisdiction's surveillance system.
Negative HBsAg Negative total anti-HBc	Positive HBsAg or HBV DNA	Three major potential possibilities should be considered: • Donor-derived infection, • Transmission related to recipient risk behaviors or household exposures, and • Health care-associated infection. Centers for Disease Control and Prevention (CDC)'s Division of Viral Hepatitis (DVH) might already have been notified and is available for consultation and coordination of investigation.
No prior HBV laboratory results‡		

*All donors should be tested for total anti-HBc, HBsAg and HBV DNA prior to organ procurement[67]. This table applies to recipients of organs from donors who tested negative for all these markers.

†Because of the large number of tests performed on transplant recipients, irreproducible positive results are rarely reported. Investigators should evaluate all available results in context. CDC DVH is available for consultation.

‡Pre-transplant hepatitis B screening (total anti-HBc, HBsAg and anti-HBs) is recommended for all transplant recipient candidates in accordance with guidelines published by the US Public Health Service[67]. If a transplant recipient does not have hepatitis B laboratory results prior to transplantation of an organ, consider following-up with the transplant facility to discuss appropriate pre-transplant hepatitis B screening protocols.

Cases of viral hepatitis identified among living organ transplant donors and recipients should be submitted to NNDSS in a standardized way, when possible. The CDC case report forms used for NBS and HL7 transmission both include a reason for testing variable in the core section of the form. For HDs transmitting data via NBS or HL7, under the "reason for testing" field, "blood/organ donor screening" should be selected for organ donor cases; "other" should be selected for organ transplant recipient cases with a specification of "transplant recipient" in the free text for the "other reason for testing" field. For state and territorial HDs transmitting case data via NETSS, there is no field on the case report form to indicate that the case was an organ transplant donor or recipient.

3.6.9. Monitoring Infection Trends and Disease Outcomes Using a Person-Level Database and Supplemental Data Sources

A person-level surveillance database can support hepatitis B elimination efforts by allowing a jurisdiction to document hepatitis B laboratory results and testing history. By doing so, jurisdictions are able to:

- track the number of unique persons living with hepatitis B longitudinally, which can inform more accurate estimates of incidence and prevalence;
- identify pregnant people and infants for the PHBPP;
- identify and link people living with hepatitis B to medical care;

- evaluate the impact of public health and clinical services;
- match with secondary data sources (e.g., Vital Statistics, Medicaid, cancer registry, HIV registries); and
- provide information on the number of people at each phase of the hepatitis B care continuum to identify areas for improvement, for example, by supplementing surveillance data with clinical and pharmacy data.

Some of these monitoring capacities may only be possible in jurisdictions capable of capturing negative hepatitis B laboratory results. Linking a person-level surveillance database to other data sources not only allows for longitudinal monitoring of disease outcomes, but can also improve completeness of information in the surveillance system[72]. Supplemental data sources are helpful for understanding the burden of co-morbidities (e.g., infection with HCV or HIV) by providing cross-sectional data over time and can inform interpretation of prevalence estimates. Section 5.4 describes supplemental data sources for HDs to consider.

3.7. Surveillance of Hepatitis B During Pregnancy and Perinatal Hepatitis B

3.7.1. Background

Knowledge of a pregnant person's HBV infection status is essential for preventing perinatal hepatitis B. The American College of Obstetrics and Gynecologists (ACOG) supports CDC's recommendation that prenatal care providers should screen every pregnant person for HBV infection during an early prenatal visit, even if the person has already been vaccinated or tested for hepatitis B[73]. HBV particles have also been detected in ova[74,75]; though uncommon, the potential to vertically transmit HBV exists when an HBV-infected genetic parent donating ova elects to use a gestational carrier (i.e., surrogate). Transmission of HBV infection at birth leads to chronic infection in approximately 90% of infants who are not given immunoprophylaxis[76].

To improve the prevention and identification of perinatal hepatitis B and to facilitate the clinical care of pregnant and postpartum people, universal HBsAg screening during an early prenatal visit and treatment of infants born to HBsAg-positive gestational parents with hepatitis B immunoglobulin and hepatitis B vaccine at birth were recommended in 1988 by ACIP[73]. To reduce perinatal transmission risks, it is recommended that pregnant people with an HBV DNA level >200,000 IU/mL receive antiviral therapy at 28–32 weeks of gestation and infants born to HBV-infected gestational parents receive HBIG at birth[50,73]. However, it is estimated that approximately 1,000 newborns are infected annually despite these longstanding recommendations[77].

Surveillance should include monitoring HBV-infected pregnant people and monitoring infants born to them for receipt of immunoprophylaxis at birth, completion of the infant hepatitis B vaccination series, and PVST for evidence of infection (HBsAg-positivity or HBV DNA-positivity) and immunity (anti-HBs ≥10 mIU/mL). PVST identifies infants who failed to respond to the hepatitis B vaccine and require re-vaccination.

The overall surveillance goals of hepatitis B during pregnancy include: 1) identifying pregnant people currently infected with HBV (as indicated by the presence of HBsAg or HBV DNA), and 2) among HBV-infected people of childbearing age with childbearing potential, identifying those who are currently pregnant or who have recently delivered a live birth to identify exposed infants for referral to the PHBPP.

Perinatal hepatitis B surveillance relies on screening for HBsAg during each pregnancy and conducting the appropriate follow-up tests on infants born to HBV-infected gestational parents. The overall goals of perinatal hepatitis B surveillance are to identify exposed infants and evaluate the effectiveness of the PHBPP to prevent perinatal transmission, and also the following:

- identify HBV-infected people of childbearing age with childbearing potential to link them to care to prevent infant HBV exposure during future pregnancies;
- provide data to improve assessment of the burden of perinatal hepatitis B;
- evaluate health outcomes of HBV-infected infants;
- educate clinicians and guardians on HBV transmission, clinical progression, and treatment; and

- measure the rate of progression to chronic hepatitis B, as determined by HBsAg-positivity or by the detection of HBV DNA after 24 months of age.

3.7.2. Uses of Surveillance Data

Surveillance data are used in the following ways to accomplish the above goals:

Identifying HBV-infected pregnant people to prevent perinatal HBV transmission.

Monitoring and evaluating the effectiveness of PHBPP*

The following key indicators are used for pregnant people:

- Number of HBV-infected pregnant people identified
- Number of births to HBV-infected pregnant people identified

The following key indicators are used for exposed infants:

- Number and percentage of exposed infants who receive first dose of hepatitis B vaccine and HBIG within 12 hours of birth.
- Number and percentage of exposed infants who receive HBIG and complete the hepatitis B vaccine series by 6 months of age.
- Number and percentage of exposed infants who receive PVST consisting of HBsAg and anti-HBs:
  - » **Infants at 9-24 months of age**
    - › Number who tested positive for HBsAg
    - › Number with anti-HBs titer level of <10 mIU/mL
  - » **Children at >24 months of age**
    - › Number who test positive for HBsAg (reported as chronic hepatitis B)
  - » **Infants at 0-24 months of age**
    - › Number of erroneous tests performed (e.g., testing performed outside of the recommended age windows or wrong test ordered)
- Number of exposed infants who require additional doses of vaccine (non-responders)
- Number of exposed infants lost to follow-up

*Note that the outcome indicators for PHBPP are slightly different from the ACIP recommendations[56].

Assessing the frequency and evaluating the causes of missed opportunities. This includes evaluating missed opportunities for testing during pregnancy and for antiviral therapy, when indicated. For HBV-exposed infants, this includes failure to provide timely immunoprophylaxis and vaccination failure. It is recommended that all exposed infants receive the first dose of the hepatitis B vaccine and HBIG within 12 hours of birth, even those with low birth weight (i.e., birth weight <2,000 g). Investigation of perinatal hepatitis B cases should evaluate causes of possible breakthrough infections and should include obtaining sera from the infant and gestational parent to test for the presence of HBV variants.

Monitoring adherence to screening recommendations among pregnant people. Surveillance programs should ideally collect negative HBV laboratory results. Alternatively, surveillance can help track changes in hepatitis B incidence and be used to implement quality measures to monitor adherence to screening recommendations.

Monitoring trends in disease incidence and prevalence among people of childbearing age with childbearing potential. Knowing the incidence and prevalence of hepatitis B in the population who are or can become pregnant is critical to the prevention and control of hepatitis B, and this population should be assessed independently from surveillance in the general population.

3.7.3. Surveillance Case Definition

No CDC/CSTE surveillance case definition exists for HBV infection during pregnancy. Instead, these cases should be classified in accordance with the CDC/CSTE acute and chronic hepatitis B case definitions (see Section 3.6.3).

Table 3-5 depicts the surveillance case definition for perinatal hepatitis B, adopted by CSTE and CDC in 2017[63,64]. See Appendix C for classification scenarios of cases of perinatal hepatitis B.

Table 3-5. US Centers for Disease Control and Prevention (CDC) and Council of State and Territorial Epidemiologists (CSTE) case definition for perinatal hepatitis B, 2017

Criteria Type	Criteria
Demographic	Diagnosis of hepatitis B in a child 1–24 months of age who was born in the United States
Clinical	Can range from asymptomatic to fulminant hepatitis
Laboratory*	Child ≤24 months of age with evidence of hepatitis B as shown by the following laboratory results: • Positive HBsAg† from 1–24 months of age only if at least 4 weeks after last dose of Hep B vaccine **OR** • Positive HBeAg from 9–24 months of age **OR** • Positive nucleic acid test (NAT) for HBV DNA (including qualitative, quantitative, or genotype testing) from 9–24 months of age
Epidemiologic Linkage	Born to an HBV-infected mother
Case Status	**Classification**
Confirmed Perinatal*	• Child ≤24 months of age **AND** • Born in the United States **AND** • Meets laboratory criteria **AND** • Born to an HBV-infected mother
Probable Perinatal*	• Child ≤24 months of age **AND** • Born in the United States **AND** • Meets laboratory criteria **AND** • HBV infection status of mother is unknown (i.e., no epidemiologic linkage)

*Surveillance programs should provide prevention programs with information on people who have positive test outcomes for post-test counseling and referral to care, as appropriate.

†Positive HBsAg results obtained from infants ≤9 months of age who received hepatitis B vaccine should not be interpreted as positive due to the potential for transient HBsAg positivity.

HBsAg test results obtained from infants ≤1 month of age, and HBeAg and HBV DNA results from those ≤9 months of age should not be used for classification. Cases in the specified age range that are known to have been exposed to HBV through health care and not perinatally should also be classified under the 2012 acute and chronic hepatitis B case definition. The event date of the perinatal hepatitis B case should be based on the earliest relevant laboratory test collection date within the test-specific age window.

3.7.4. Case Ascertainment

To facilitate identification of HBV infection during pregnancy, the following measures are recommended:

- Screen for HBsAg during each pregnancy as part of prenatal care at an early prenatal visit (i.e., during the first trimester)
- For pregnant people who are isolated total anti-HBc positive, check HBV DNA status to determine if occult HBV infection or HBsAg mutant infection is present
- Document maternal HBV infection status on newborn metabolic screening card or birth certificate
- Report laboratory results indicating HBV infection for all pregnant people to the appropriate health jurisdiction
- Ensure delivery facilities have standing orders to check HBV infection status upon admission. The following groups should be tested for HBsAg at the time of admission for delivery[56]:
  - » Those whose HBsAg status is unknown
  - » Those with clinical hepatitis
  - » Those with high-risk behaviors (e.g., history of recent or current IDU, multiple sexual partners within the past 6 months or an HBsAg-positive sexual partner, or evaluation or treatment for a sexually transmitted infection)
- Report admission of HBV-infected pregnant people to delivery facility
- Ensure health care providers have protocols to:
  - » Test HBV infection status during each pregnancy at an early prenatal visit (i.e., during the first trimester)
- Ensure that state, territorial, and local health jurisdictions can:
  - » Receive and integrate electronic laboratory reports, electronic health records, and facsimiles into a disease surveillance system

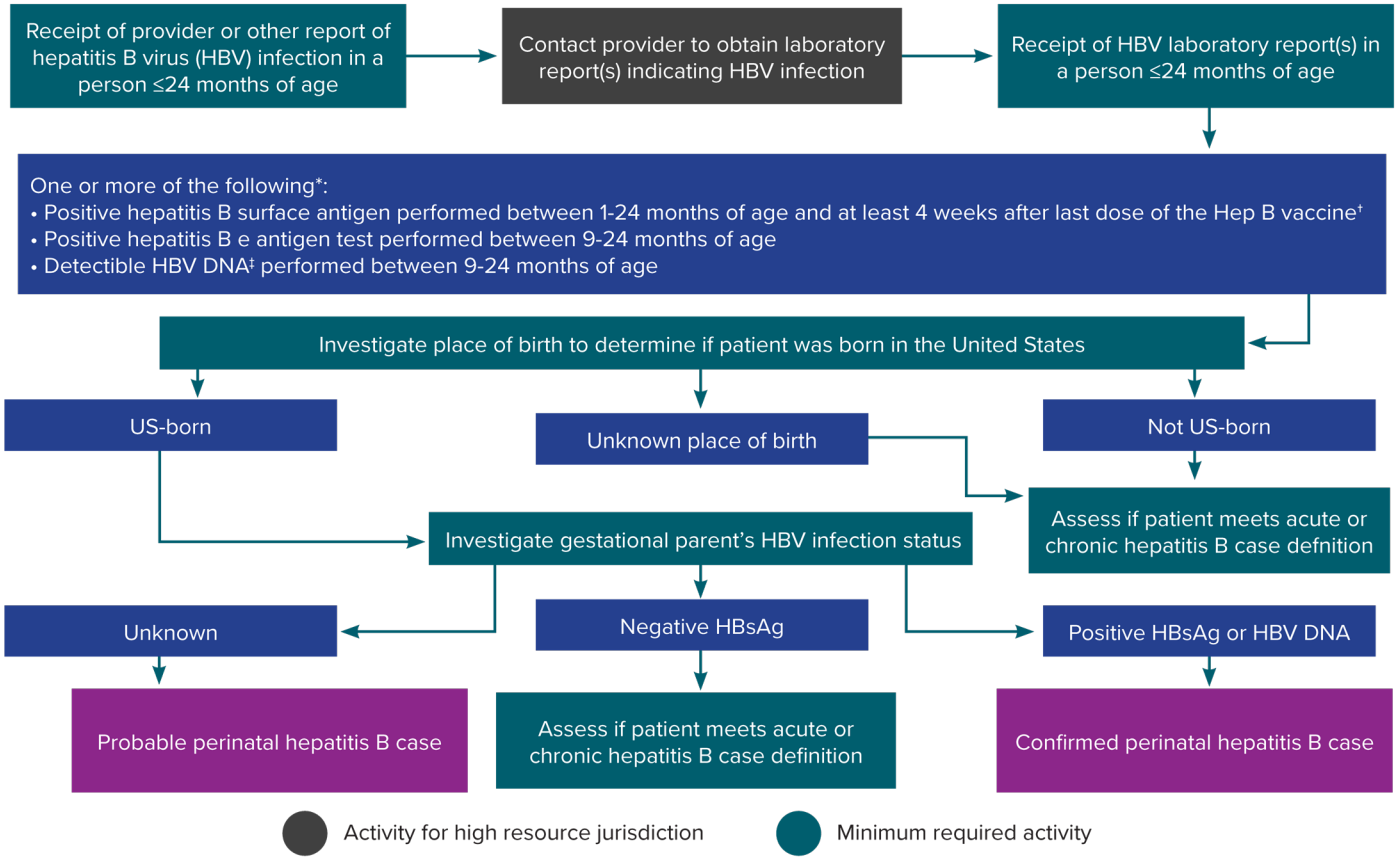
- » Perform enhanced surveillance methods to identify previously unreported HBV-infected people who have recently given birth by comparing birth certificate data to known HBV-infected cases in the disease surveillance system
- » Determine pregnancy status of all HBsAg-positive people of childbearing age with childbearing potential
- » Determine pregnancy status for all existing cases of hepatitis B among people of childbearing age with childbearing potential

The following steps are recommended to facilitate identification of perinatally HBV-exposed infants:

- Ensure delivery facilities have standing orders to report all births to HBsAg-positive or HBV DNA-positive gestational parents to local PHBPP jurisdiction
- Ensure health care providers have protocols to:
  - » Test all exposed infants for HBsAg and anti-HBs (PVST) at 9–12 months of age
  - » Routinely report the hepatitis B PVST results of exposed infants to the local health jurisdiction

Figure 3-4 illustrates a potential approach for perinatal hepatitis B case ascertainment and classification. Specific procedures vary by jurisdiction, but should generally follow the scheme below, in accordance with the CDC/CSTE Position Statement for the 2017 perinatal hepatitis B case definition[63,64].

Figure 3-4. Process for perinatal hepatitis B case ascertainment and classification



*Surveillance programs should provide prevention programs with information on people who have positive test outcomes for post-test counseling and referral to care, as appropriate. HBsAg test results obtained from infants ≤1 month of age and hepatitis B e antigen and HBV DNA results obtained from those ≤9 months of age should not be used for classification. Cases among children ≤24 months of age who are known to have been exposed to HBV through health care (not perinatally) should be reported according to the 2012 acute and chronic hepatitis B case definitions.

†Positive HBsAg results obtained from infants ≤9 months of age who received hepatitis B vaccine should not be interpreted as positive due to the potential for transient HBsAg positivity.

‡Nucleic acid testing for HBV DNA, including qualitative, quantitative, and genotype testing.

3.7.5. Case Investigation

The following elements can inform investigation and management of HBV-infected pregnant people and infants:

Demographic information. For the pregnant person, obtain date of birth, current gender, race, ethnicity, residential address (including zip code), insurance status, country of birth, and primary language spoken. For the infant, obtain the date, time, and place of birth, birth weight, sex, race, ethnicity, and insurance status. The contact information of the legal guardian(s) should also be collected.

Patient and health care provider information. Includes prenatal care provider's name and phone number to coordinate follow-up HBV DNA testing and treatment, if indicated. The contact information of the infant's health care provider (to obtain PVST results) and legal guardian(s) as well as adoption or foster care status should also be collected.

Delivery information. Includes the expected and actual due dates and the expected and actual delivery facilities.

Diagnostic test results. Obtain documentation of positive HBV test results for both gestational parent and infant; obtain anti-HBs test result(s) for the infant.

Clinical features. For the pregnant person, document the presence of symptoms and jaundice. Most infants with hepatitis B are asymptomatic. Obtain documentation of the gestational parent's HBV DNA level and whether antiviral medication was administered during 28–32 weeks of gestation.

Immunization and prophylaxis history. Ascertain the date and time for all administered doses of hepatitis B vaccine and HBIG.

Epidemiologic link. For the infant, confirm birth to an HBV-infected gestational parent.

Reporting information. Date reported to health jurisdiction, date of diagnosis, date investigation initiated, date of first contact with patient and/or health care provider, and date referred for medical evaluation.

Education and referral for follow-up. Provide education to the patient/provider regarding the role of PHBPP, importance of immunoprophylaxis for the infant within 12 hours of birth, and timely completion of the hepatitis B vaccine series and PVST. Determine medical care provider for HBV-infected pregnant cases and educate on the importance of regular care and monitoring of hepatitis B, even after delivery.

Case Investigation Prioritization

The following factors should be considered of high priority for investigation and follow-up:

- Investigation and follow-up should occur during pregnancy or as soon as possible thereafter. Successful follow-up might be more likely if contact information is utilized sooner. Early identification and timely follow-up will facilitate the prevention of perinatal HBV transmission.
- Investigation and follow-up should occur for those who can become pregnant and those whose pregnancy status is unknown who are co-infected with HIV/HCV/STIs or who have high HBV DNA levels (>200,000 IU/mL).

3.7.6. Case Management

HBV-infected gestational parents and their infant(s) should be tracked in a surveillance database/system that can track case management processes and allow for sharing and/or linking parent and child events. The system should allow for each pregnancy to be considered unique and the pregnancy-specific data to be captured and maintained. It should also contain a mechanism to track hepatitis B vaccine doses given to the infant to ensure the proper number and spacing of doses.

HBV-infected pregnant people should be enrolled in the PHBPP. Upon enrollment, the hepatitis B coordinator should undertake the following case-management actions:

- Obtain a copy of the original laboratory results to provide to the anticipated delivery facility and infant's anticipated health care provider. Original laboratory reports are strongly recommended to prevent misinterpretation or transcription errors.
- Follow-up with the infant's anticipated health care provider.
  - » Notify of gestational parent's HBV infection status (i.e., positive HBsAg or HBV DNA) and communicate the need for timely vaccination and PVST.

  - » Provide instructions on how to report each hepatitis B vaccine dose administered and the HBsAg and anti-HBs results at 9–12 months of age.
    - › For low birth weight babies (i.e., those <2,000 g), the initial dose of hepatitis B vaccine should still be administered as early as possible, but should not be counted as part of the vaccine series. The infant should receive 3 additional doses of the vaccine, typically starting at 1 month of age.
  - » Send a reminder (preferably a phone call) regarding the need for PVST after the final dose of hepatitis B vaccine is administered.
    - › PVST should include HBsAg testing to ensure the infant has not become infected and anti-HBs testing to ensure that immunity has been conferred (i.e., anti-HBs ≥10 mIU/mL). Table 3-6 lists the most common laboratory codes for PVST.
  - » Ensure that susceptible children (i.e., anti-HBs <10 mIU/mL performed >4 weeks after the last dose of hepatitis B vaccine) receive a booster dose and are retested to confirm immunity.
    - › If the child's anti-HBs titer is still <10 mIU/mL, complete the second revaccination series and retest for HBsAg and anti-HBs.
    - › If the anti-HBs titer is still <10 mIU/mL after full vaccination series, the child is considered a vaccine non-responder. Provide guidance to the parent(s) or legal guardian(s) of the child that remains susceptible. For more detailed guidance, see the Epidemiology and Prevention of Vaccine-Preventable Diseases from The Pink Book.
- Refer for HBV DNA testing to determine if antiviral treatment is recommended.
  - » It is recommended that pregnant people with an HBV DNA level >200,000 IU/mL start antiviral therapy at 28–32 weeks of gestation to reduce perinatal transmission risks[50].
  - » Document the gestational parent's HBV DNA level at the time of delivery and whether antiviral medication was received during pregnancy.
- Obtain information on anticipated due date, anticipated delivery facility, actual delivery date, and actual delivery facility.
  - » Ensure anticipated birth facility is aware of the pregnant person's HBV infection status and anticipated due date and will report to local jurisdiction's PHBPP upon delivery of infant.
- 2–4 weeks prior to anticipated due date, send communication to:
  - » Parent or provider to confirm anticipated delivery facility, and
  - » Anticipated delivery facility to communicate the need to
    - › provide timely post-exposure prophylaxis for infant,
    - › report birth and prophylaxis information to public health, and
    - › administer the first dose of the hepatitis B vaccine and HBIG in separate anatomical sites.
- Document the first dose of hepatitis B vaccine given within 12 hours of birth.
- Document completion of hepatitis B vaccine series in accordance with ACIP recommendations.
- Refer children with positive HBsAg test results for evaluation (by referral or consultation, if appropriate), ensuring
  - » confirmation of chronic hepatitis B (tests positive for HBsAg after 24 months), as spontaneous clearance is possible;
  - » assessment of evidence of chronic liver disease; and
  - » assessment of severity of disease and possible treatment according to current practice guidelines in consultation with, or by referral to, a specialist knowledgeable in this area.
- All parents should be provided with education regarding HBV vertical transmission and testing recommendations. Providers should also be provided with information on HBV transmission risk to the infant, hepatitis B testing recommendations (PVST), and HBV infection clinical care. Education should be provided according to evidence-based guidelines and include perinatal transmission risk, testing for the infant, and current treatment recommendations.

The following case management actions are recommended for delivery facilities:

- Report gestational parent's HBV infection status (i.e., positive HBsAg or HBV DNA) on infant's birth certificate and metabolic screening card (as applicable).
- Report birth to an HBV-infected gestational parent to appropriate health jurisdiction. This can be achieved by completing the jurisdiction-specific reporting form with all requested information.
- Facilities that need information regarding immunoprophylaxis for infants born to HBV-infected gestational parents can contact the Perinatal Hepatitis B Prevention Program in their state or territory.

Case management is considered completed when the

- child has evidence of immunity,
- child has moved to another jurisdiction and notification to that jurisdiction and PHBPP has been completed, or
- gestational parent-infant pair is lost to follow-up.

Sources of data on immunization and PVST include, but are not limited to

- jurisdiction's immunization registry/information system,
- report from infant's health care provider, and
- electronic health and laboratory records.

Table 3-6. Common laboratory codes for hepatitis B post-vaccination serologic testing

Laboratory	Hepatitis B Surface Antigen	Antibody to Hepatitis B Surface Antigen
Affiliated Medical Services	5196-1	10900-9
LabCorp	006510	006530
Mayo Medical Labs	9013	8254
Quest Diagnostics	498	8475

3.7.7. Case Reporting and National Notification

HBV infection during pregnancy should be a reportable event to the HD. Although no specific NNDSS event exists for hepatitis B during pregnancy, CDC recommends classifying these cases as acute or chronic using the appropriate event code (Table 1-2) in accordance with the CDC/CSTE case definitions, and transmitting the pregnancy status to NNDSS for all cases among people of childbearing age with childbearing potential to allow for national tracking. At the jurisdiction-level, there may be classification category specifically for hepatitis B during pregnancy. Cases of perinatal hepatitis B are nationally notifiable to CDC and are submitted using a condition-specific event code (Table 1-2). As more information is learned about how jurisdictions are counting and submitting perinatal hepatitis B cases that progress to chronic infection, information in this section will be updated.

4. Hepatitis C Surveillance Guidance

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4.1. Background

Hepatitis C is a disease caused by the hepatitis C virus (HCV) that can be a short-term illness, but for more than one-half of people who become infected, it can become a long-term, chronic infection[78]. HCV is one of the most common bloodborne pathogens in the United States[58,79,80]. It is highly infectious and can survive on dry surfaces and equipment for up to 6 weeks, resulting in a longer period for potential transmission than for other bloodborne pathogens (e.g., HBV and HIV)[81]. HCV is most efficiently transmitted through blood-to-blood contact or through percutaneous exposure to blood[79]. IDU is the most common risk behavior reported for HCV infection[3]. Among PWID, sharing of needles and syringes is most strongly associated with hepatitis C[82]. Populations at highest risk for having hepatitis C include PWID, HIV-positive MSM, people with a history of incarceration, and people born during 1945–1965 (baby boomer birth cohort)[83]. Approximately 75%–85% of people with acute hepatitis C are not symptomatic[84-86]; as such, measuring the true burden of disease is difficult.

The epidemiology of hepatitis C in the United States has changed substantially. After decades of decline in acute hepatitis C incidence, rates began increasing in 2010. Increases in both acute and chronic hepatitis C, associated with IDU, shifted from people born during 1945–1965 to a younger population[15] that is typically non-Hispanic White. People of American Indian/Alaska Native and non-Hispanic Black race/ethnicity also experience disproportionately high rates of infection and mortality[3]. Though these groups are disproportionately affected by hepatitis C at the national level, disparities vary among jurisdictions.

During 2013–2016, the US prevalence of chronic hepatitis C, as measured by the presence of HCV RNA in blood, was estimated to be 1.0% (95% CI, 0.8%–1.1%), representing approximately 2.4 million adults[2]. This national estimate was adjusted to include incarcerated, unsheltered people experiencing homelessness, active-duty military, and nursing home populations (those not surveyed in NHANES). Jurisdictional-specific estimates would be more useful for program planning and evaluation at the state, territorial, and local level. Without treatment, 20%–30% of people with chronic hepatitis C progress to cirrhosis over a 25–30-year period[87].

In addition, nearly one-half of people with hepatitis C are unaware of their infection status and can unknowingly transmit the virus to others[49]. Hepatitis

C- and liver cancer-associated death rates were highest among decedents who were born during 1945–1965[88]. Hepatitis C-associated death rates have declined each year since 2013[3]. The decline in the national hepatitis C-associated death rate is likely due to the evolving epidemiology of hepatitis C, as people disproportionately affected by hepatitis C have died in earlier years and more HCV-infected people are being cured with DAA drugs.

Children born to HCV RNA-positive gestational parents are also at risk for hepatitis C. The rate of perinatal HCV transmission is approximately 5.8% in HCV RNA-positive/HIV-negative mothers and 10.8% in HCV RNA-positive women who have HIV coinfection[89]. At the time of this writing, treatment during pregnancy is not recommended due to limited safety and efficacy data.

There is no vaccine to prevent hepatitis C. Therefore, the best way to prevent infection is by avoiding behaviors that can transmit the virus, such as sharing drug injecting equipment (e.g., needles, syringes, works, and cookers). Research has shown that maintenance MOUD can also be effective in reducing HCV transmission among PWIDs. If exposure is suspected to have occurred, getting tested and seeking treatment can prevent complications related to HCV infection and interrupt transmission.

In 2011, DAA therapies were approved for the treatment of chronic hepatitis C[90]. In 2014, therapies became all-oral and highly effective[91]. In 2019, as part of the "test and treat" strategy, the AASLD/Infectious Diseases Society of America (IDSA) updated their hepatitis C treatment guidance to recommend initiating treatment in patients with acute hepatitis C upon first diagnosis without waiting for spontaneous resolution to occur[92]. In addition, some DAAs are now approved by FDA for children ≥3 years of age and are recommended by AASLD/IDSA for treatment[92].

Recommendations for universal hepatitis C screening were released by the CDC in 2020[15]. They recommend that all adults ≥18 years of age be tested at least once and that all pregnant people be tested during each pregnancy, except in settings where the prevalence is known to be less than 0.1%. All people with risk behaviors or exposures should be tested for hepatitis C, with periodic testing while risk behaviors or exposures persist. In addition, any person who requests hepatitis C testing should receive it, regardless of disclosure of risk, because many people might be reluctant to disclose stigmatizing information. If the HCV RNA prevalence is unknown in a setting, health care providers should test all adults and pregnant people for hepatitis C until the HCV RNA prevalence is determined to be less than 0.1%, at which point providers can screen at their discretion[93].

To determine the HCV RNA prevalence, health care providers and program directors are encouraged to consult with their state, territorial, or local HDs or with CDC to determine a method for calculating the HCV RNA baseline prevalence in their setting. Approximately 59% of people positive for anti-HCV are positive for HCV RNA[93]. Therefore, as a general guide, an estimated 507 randomly selected patients in any sized setting would need to be tested for anti-HCV in order to detect an anti-HCV prevalence of ≤0.17%, corresponding to an expected HCV RNA prevalence of 0.1%[93].

The purpose of this document is to provide jurisdictional guidance to implement and improve hepatitis C surveillance, including reporting requirements, collection of relevant laboratory data, and case investigation. Given that current systems for the surveillance and follow-up of hepatitis C cases differ by jurisdiction, the standards outlined in this document are designed to provide models for best practices, recognizing that not every jurisdiction can meet those standards with available resources.

4.2. Cases and Clusters of Potential Public Health Importance

Jurisdictions should review and analyze hepatitis C data regularly to identify cases and clusters of hepatitis C that merit further investigation. When resources are limited, these should be prioritized for investigation according to degree of public health importance. The following are examples of high priority cases and clusters:

- **People of childbearing age who are or have the potential to become pregnant,** indicating the potential risk for perinatal transmission.
- **Children ≤36 months of age,** indicating possible perinatal transmission.

- **People in age and demographic groups among whom infection might be acute due to recent transmission.** This includes people
  - » <40 years of age (population experiencing greater increase in acute hepatitis C incidence) and
  - » ≥70 years of age (possible health care-associated transmission).
- **People receiving hemodialysis with evidence of acute hepatitis C (including test conversions).**
- **People who do not have typical risk behaviors for hepatitis C (e.g., IDU) but who have evidence of acute infection (including test conversions).** These people should be investigated to identify other potential causes of HCV transmission (e.g., exposure through health care). Information on investigation of health care-associated outbreaks is available through CDC's DVH.
- **People with other indicator(s) of possible acute or recent infection, including those**
  - » with elevated ALT or total bilirubin levels;
  - » with current or recent IDU history;
  - » who were tested at locations where people at high risk for acute infection are typically seen (e.g., STI and HIV clinics, SSPs, correctional facilities, and MAT centers); or
  - » who were in a residential facility or custodial care (including long-term care or correctional facilities) for ≥6 months prior to the onset of clinical signs.

4.3. Interpretation of Laboratory Test Results

The two tests used primarily for hepatitis C screening and diagnosis are an antibody test (often an immunoassay) and an RNA test (NAT), respectively[94]. A description of hepatitis C laboratory markers can be found in Appendix B. Figure 4-1 describes the typical serologic course of HCV infection[95].

Figure 4-1. Typical serologic course of hepatitis C virus infection

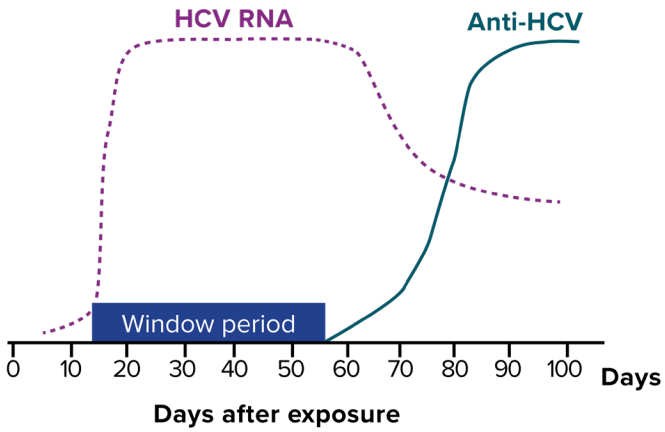


Figure obtained from https://www.aphl.org/aboutAPHL/publications/Documents/ID-2019Jan-HCV-Test-Result-Interpretation-Guide.pdf.

In 2013, CDC provided updated guidance on the recommended testing sequence for identifying current hepatitis C[96]. Hepatitis C testing should be initiated with an anti-HCV screening test, and if positive, an HCV RNA test should be performed. In settings serving high-risk populations (e.g., SSPs), rapid anti-HCV testing (also called point-of-care testing) can be used in lieu of laboratory-based anti-HCV testing to deliver results to the patient at the time of visit. For people who tested anti-HCV positive through rapid screening, an on-the-spot blood draw to be sent for HCV RNA testing should be performed or a referral and/or evaluation for HCV RNA testing should be provided. For blood draws collected for anti-HCV testing, all positive specimens should reflex to HCV RNA testing to reduce the number of patients lost to follow-up.

Many jurisdictions have regulations requiring laboratories to report all positive results of hepatitis C markers to the HD, and some also receive negative laboratory results (anti-HCV and/or HCV RNA). Liver function tests (ALTs and total bilirubin results) can provide information on acute infection status; if testing is conducted as part of a pregnancy panel, pregnancy test results can identify HCV-infected pregnant people. To obtain data that will enable HCV infection status to be determined and follow-up care received, jurisdictions should have all positive laboratory results indicative of HCV infection reportable

(i.e., anti-HCV, HCV RNA, HCV genotype, and any other tests indicating the presence of HCV). Section 4.4 (Recommended Reportable Laboratory Markers) provides information on what might be made reportable in different jurisdictions and the rationale for collecting these results. Table 4-1 describes the interpretations of hepatitis C laboratory results and actions that should be taken by anyone advising confirmed HCV-positive patients about necessary next steps[97]. Anti-HCV indeterminate/borderline results are not interpretable and should be retested according to the Instructions for Use provided with the test assay.

Table 4-1. Interpretation of hepatitis C laboratory results

Test Outcome*	Interpretation†	Further Actions
Nonreactive hepatitis C virus (HCV) antibody	No HCV antibody detected	No further action required in most cases. Though this would not be considered a case, some jurisdictions do require reporting (especially among children ≤36 months of age). There might be some instances where further testing is recommended.‡
Reactive HCV antibody§	Presumptive hepatitis C	A reactive result is consistent with current HCV infection, past HCV infection that has resolved, or biologic false positivity for HCV antibody. Recommend testing for HCV RNA to identify current infection.
Reactive HCV antibody **AND** • Positive nucleic acid test (NAT) for HCV RNA (including qualitative, quantitative, or genotype testing) **OR** • Positive HCV antigen*	Current hepatitis C	Provide patient with appropriate counseling and linkage to care.
Reactive HCV antibody **AND** • Negative NAT for HCV RNA (including qualitative, quantitative, or genotype testing) **OR/AND** • Negative HCV antigen	Cleared hepatitis C	Result might be consistent with natural clearance or successful treatment or with a false-positive HCV antibody result. No further action required in most cases. Further testing may be recommended in some instances.¶

Table modified from https://www.cdc.gov/mmwr/pdf/wk/mm62e0507a2.pdf.

*Surveillance programs should provide prevention programs with information on people who have positive test outcomes for post-test counseling and referral to treatment and care, as appropriate. No HCV antigen tests have been approved by the US Food and Drug Administration (FDA). When an FDA-approved test becomes available, it will be acceptable laboratory criteria, equivalent to HCV RNA testing. For surveillance purposes, the reporting of positive genotype test results should be considered equivalent to HCV RNA detection, as RNA is required for this test. However, a genotype test in which the genotype cannot be determined is not the same as a "not detected" HCV RNA result.

†Ingestion of high levels of biotin can significantly interfere with certain commonly used biotinylated immunoassays and cause false-positive or false-negative laboratory test results. Currently, the FDA is investigating thresholds associated with false-positive and false-negative tests. Reference: https://www.fda.gov/medical-devices/safety-communications/update-fda-warns-biotin-may-interfere-lab-tests-fda-safety-communication.

‡Further testing might be recommended if a recent HCV exposure is suspected in the past 6 months (or longer in people who are immunocompromised) or if there is concern regarding the handling or storage of the specimen. If recent exposure is suspected, test for the presence of virus using either a NAT for HCV RNA or a test for HCV antigen (if available). If HCV RNA testing is not feasible, conduct follow-up testing for HCV antibody to demonstrate test conversion.

§If the HCV RNA result is indeterminate, consider provider follow-up to discuss interpretation of result and re-testing strategy.

¶Further testing might be recommended if a recent HCV exposure is suspected in the past 6 months, or if there is concern regarding the handling or storage of the specimen. If distinction between true positivity and biologic false positivity for HCV antibody is desired and the sample is repeatedly reactive, testing with an alternative HCV antibody assay may be useful. In certain situations (e.g., suspected HCV infection within the past 6 months, clinical evidence of HCV infection, and questionable specimen integrity), follow up with another HCV RNA test and appropriate counseling.

4.4. Recommended Reportable Laboratory Markers

The following laboratory markers are recommended for reporting to public health to aid in case ascertainment, case classification, and monitoring cure continua for hepatitis C:

- Anti-HCV (all positive results, negative results for children ≤36 months of age);
- HCV RNA (positive/detectable and negative/undetectable results), including quantitative, qualitative, and genotype testing;
- HCV antigen (positive, negative, and indeterminate results) when and if a test is approved by FDA; and
- If any of the above positive results are reported, also report the following:
  - » Pregnancy status,
  - » Concurrent ALT and total bilirubin results, and
  - » Other hepatitis serological results (e.g., hepatitis A, hepatitis B, and/or hepatitis E).

Jurisdictions are strongly encouraged to incorporate the reporting of negative/undetectable HCV RNA test results into their surveillance regulations and systems to support improved understanding of their local epidemic. Such reporting may increase awareness regarding

- acute infections (new and re-infections) and cleared (resolved and cured) infections,
- completeness of testing, and
- availability of reflex testing.

Jurisdictions might also wish to receive negative anti-HCV results to assist in identifying cases of test conversion and examine trends in screening; however, they must be mindful of their ability to process and store high volumes of data. Further, caution must be taken in the collection and use of these results, as people with non-reactive anti-HCV tests do not have a reportable condition. Jurisdictions must have legal authorization for receipt of these data.

In 2019, of 43 state, territorial, and major city HDs participating in the National Alliance of State and Territorial AIDS Directors (NASTAD) viral hepatitis surveillance and prevention capacity assessment, 17 (40%) received negative HCV RNA test results, and nine (21%) received negative anti-HCV test results. An additional 12 (28%) jurisdictions indicated that they received negative HCV RNA test results, and 10 (23%) indicated that they received negative anti-HCV test results, but either did not mandate negative hepatitis C laboratory reporting in their jurisdiction or were in the process of changing local laws or regulations to require reporting of negative hepatitis C laboratory results. Some jurisdictions have changed policy to allow reporting of negative HCV test results but have not yet modified their surveillance system to receive and process these negative test results because of limited resources and competing priorities.

4.5. Case Reporting and National Notification

Cases of acute, chronic, and perinatal hepatitis C and hepatitis C during pregnancy should be reported to HDs as specified by state, territorial, or local regulations. Acute, chronic, and perinatal hepatitis C are nationally notifiable conditions[5]. Hepatitis C cases are identified using an event code corresponding to the hepatitis C condition (Table 1-2). Data are sent weekly or more frequently, depending on the infrastructure of the jurisdiction sending the data. Cases might be re-classified or removed as needed after the initial transmission to CDC, as long as the changes occur before surveillance data are finalized each year.

4.6. Surveillance of Acute and Chronic Hepatitis C

4.6.1. Background

New cases of acute hepatitis C have increased rapidly in the United States since 2010, most being associated with IDU. The highest incidence of acute hepatitis C is typically found among people in younger age groups. For hepatitis C surveillance statistics for the United States, visit the CDC Viral Hepatitis Surveillance website[17].

Most people with chronic hepatitis C are asymptomatic[86,98,99]; however, approximately 10%–20% of people living with chronic hepatitis C who have

persistent liver inflammation will develop cirrhosis over the course of 20 years, and people with cirrhosis are at risk for developing liver cancer and other serious consequences[100]. Those with hepatitis C who do not develop liver-related complications can still suffer from extrahepatic manifestations of chronic hepatitis C (e.g., severe fatigue, certain types of renal diseases, and certain autoimmune diseases)[101-104]. Additionally, those living with chronic hepatitis C can continue to transmit the infection to others, and antibodies to HCV are not protective against reinfection[105].

Improving hepatitis C surveillance is an important component of national, state, and local strategies for eliminating hepatitis C as a public health problem. In addition to the general goals of viral hepatitis surveillance (Section 1.2), the overall goals of chronic hepatitis C surveillance are to measure and characterize the burden of infection and disease, and if feasible, create person-level systems/registries. Person-level data enable classification of those infected along the care continuum, from screening and diagnosis to linkage to care, treatment, and cure, helping jurisdictions inform and evaluate the impact of hepatitis C elimination activities. Goals specific to chronic hepatitis C surveillance include:

- monitoring trends in the prevalence of chronic infection;
- identifying cases for further investigation to better describe the epidemiology, including characterizing behaviors or exposures related to infection and identifying health disparities;
- detecting and responding to clusters and/or outbreaks (many acute infections have no clinical signs and will be classified as chronic cases);
- identifying infected people who require linkage to care and harm reduction resources, including through matches with other surveillance registries for HIV, cancer, and hepatitis B; and
- cross-referencing person-level systems/registries with vital statistics data to assess the burden of hepatitis C-associated deaths and perinatally-acquired hepatitis C.

4.6.2. Uses of Surveillance Data

Acute and chronic hepatitis C surveillance data can be used to inform and improve public health interventions in the following ways:

Monitoring trends in disease incidence and determining risk behaviors or exposures. Acute hepatitis C surveillance data should be analyzed at regular intervals by person, place, and time to monitor disease incidence. Keep in mind that place might not simply be the provided address of residence, as location of occurrence of risk behaviors might not correspond to the reported address. Risk behavior or exposure information should be analyzed to monitor disease transmission patterns and to identify groups at higher risk for infection for whom prevention efforts should be targeted. Prevention efforts include vaccination for hepatitis A and hepatitis B, expanded access to PrEP to prevent HIV transmission, increased testing for bloodborne diseases, improved access to harm reduction services, and increased access to hepatitis C treatment and SUD treatment including MOUD.

Identifying outbreaks. An outbreak is defined as the occurrence of more cases of disease than expected in a given area or among a specific group of people over a particular time period. Detailed guidance on viral hepatitis outbreaks, including examples of hepatitis C outbreaks, can be found on the CDC DVH Viral Hepatitis Outbreaks website[106].

Assessing missed opportunities for prevention. Surveillance data can be used to provide information on cases occurring among adults at higher risk for infection to identify opportunities for intervention and prevention. Tools (e.g., a cure continuum) can be developed to identify performance measures for prevention of transmission and for access to care and treatment.

Identifying needs for education. Surveillance data can help identify trends in risk or testing patterns and allow for education efforts (targeted to both health care providers and the general public) about transmission, long term consequences of chronic infection, and availability of treatment.

Tracking cases of chronic hepatitis C. Surveillance systems and databases that track chronic hepatitis C cases can aid in monitoring trends in the prevalence of chronic infection.

Understanding the burden of hepatitis C in the community. Person-based longitudinal databases can help describe the hepatitis C cure continuum in jurisdictions, including

- identifying people with positive anti-HCV results who have no HCV RNA result and need HCV RNA diagnostic testing (probable cases),
- identifying health-related disparities where hepatitis C affects specific sub-populations,
- monitoring for perinatal transmission (being born to an HCV-positive gestational parent) to ensure appropriate testing and identification of confirmed infections,
- monitoring movement of cases in or out of the jurisdiction, and
- tracking the occurrence of related adverse health outcomes.

Identifying chronic HCV-infected people who need linkage to care. Surveillance data can be used to identify and follow-up on chronic hepatitis C cases (especially those who have been recently diagnosed), link them to appropriate medical care and harm reduction services, and ensure contacts are referred to testing and care, as appropriate.

4.6.3. Surveillance Case Definitions

Table 4-2 specifies the surveillance case definitions for acute and chronic hepatitis C, adopted by CSTE and CDC in 2020[14,107,108]. See Appendix C for classification scenarios of cases of acute and chronic hepatitis C.

Table 4-2. US Centers for Disease Control and Prevention (CDC) and Council of State and Territorial Epidemiologists (CSTE) case definitions for acute and chronic hepatitis C, 2020

Criteria Type	Criteria
Age	• >36 months of age, **OR** • ≤36 months of age and the mode of exposure was not perinatal
Clinical	• Jaundice, **OR** • Peak elevated total bilirubin levels ≥3.0 mg/dL, **OR** • Peak elevated serum alanine aminotransferase (ALT) >200 IU/L, **AND** • The absence of a more likely diagnosis (which may include evidence of acute liver disease due to other causes or advanced liver disease due to pre-existing chronic hepatitis C or other causes, such as alcohol exposure, other viral hepatitis, hemochromatosis, etc.)
Confirmatory Laboratory	HCV detection test • Positive nucleic acid test (NAT) for HCV RNA (including qualitative, quantitative, or genotype testing), **OR** • Positive test indicating presence of HCV antigen*
Presumptive Laboratory	Positive HCV antibody (anti-HCV) test†
Anti-HCV Test Conversion	Documented negative anti-HCV test followed within 12 months by a positive anti-HCV test
HCV Detection Test Conversion Criteria‡	• Documented negative anti-HCV test followed within 12 months by a positive HCV detection test **OR** • Documented negative HCV detection test in someone without a prior diagnosis of hepatitis C followed within 12 months by a positive HCV detection test **OR** • At least 2 sequential documented negative HCV detection tests at least 12 weeks apart in someone with a prior diagnosis of hepatitis C followed by a positive HCV detection test§

Case Status	Classification
Confirmed Acute‡	• >36 months of age **OR** ≤36 months of age and the mode of exposure was not perinatal, **AND** • Meets the clinical criteria and has confirmatory laboratory evidence **OR** has documentation of an anti-HCV test conversion **OR** has documentation of an HCV detection test conversion
Probable Acute‡	• >36 months of age **OR** ≤36 months of age and the mode of exposure was not perinatal, **AND** • Meets the clinical criteria, **AND** • Has presumptive laboratory evidence, **AND** • Has no or unknown HCV detection test result, **AND** • Has no documentation of an anti-HCV or HCV detection test conversion, **AND** • Has not been previously reported as a confirmed acute or chronic HCV case
Confirmed Chronic‡	• >36 months of age **OR** ≤36 months of age and the mode of exposure was not perinatal, **AND** • Does not meet or is not known to meet the clinical criteria, **AND** • Has confirmatory laboratory evidence, **AND** • Has no documentation of an anti-HCV or HCV detection test conversion
Probable Chronic‡	• >36 months of age **OR** ≤36 months of age and the mode of exposure was not perinatal, **AND** • Does not meet or is not known to meet the clinical criteria **AND** • Has presumptive laboratory evidence, **AND** • Has no documentation of an anti-HCV or HCV detection test conversion, **AND** • Has no or unknown HCV detection test result, **AND** • Has not been previously reported as a confirmed acute or chronic hepatitis C case

*At present, no HCV antigen tests are approved by the US Food and Drug Administration (FDA). These tests will be acceptable laboratory criteria, equivalent to HCV RNA testing, when an FDA-approved test becomes available.

†The presence of a negative HCV detection test result, in the absence of criteria that would allow for confirmation, indicates that the case should not be classified as probable and should not be reported to CDC.

‡Surveillance programs should provide prevention programs with information on people who have positive test outcomes for post-test counseling and referral to treatment and care, as appropriate.

§Timing of these tests may change as standard of care for HCV treatment evolves. Some jurisdictions are creating a local condition specific for reinfection as opposed to creating a new acute condition to maintain deduplication.

People who test positive for anti-HCV and have a negative HCV detection test (with no known prior positive HCV detection test) received before the data closes for that reporting year should be classified as "not a case" and should not be notified to CDC. People who test positive for anti-HCV and HCV RNA are still considered confirmed cases even if they later clear their infection (i.e., negative for HCV RNA). The critical differentiation for the case definition between acute cases and chronic cases is the presence of clinical criteria (i.e., jaundice or elevated total bilirubin or elevated ALT) in the absence of a more likely diagnosis.

To be classified as a probable acute case, provider reports of jaundice or laboratory reports of elevated total bilirubin or ALT must have been received within the reporting year prior to data close-out. Additionally, if HCV RNA is detectable and anti-HCV is undetectable on the same specimen, this could indicate laboratory evidence of early acute hepatitis C when anti-HCV testing was performed during the window period. See Section 5.1.3 on Laboratory Results Indicating Early Acute Hepatitis C for more information.

Cases are classified using the CDC/CSTE case definition at the time the case is reported. A person's case status might change throughout the year as more test results are reported. In addition, a confirmed or probable acute case might be classified as a new confirmed chronic case in a subsequent reporting year, if a positive HCV detection test is reported ≥12 months after the collection date of the first positive test indicating acute infection[14].

Although jurisdictions have varying capability to track reinfection, evidence of reinfection might include someone who was previously a confirmed hepatitis C case who then had at least two sequential negative HCV detection tests at least 12 weeks apart, followed by a positive HCV detection test. Assessment for SVR ≥12 weeks after the completion of treatment is the same for treatment-naïve patients with and without cirrhosis according to the simplified hepatitis C treatment guidance[109]. Other evidence of reinfection should be considered, including a report of a new genotype from a case who had previously cleared an infection from a different genotype[14].

Jurisdictions are encouraged to take measures to ensure that cases of hepatitis C treatment failure are not classified as new cases of hepatitis C[14]. One option for tracking and investigating reinfections is to create a local condition called "possible hepatitis C virus reinfection or possible hepatitis C virus treatment failure" as opposed to creating a new acute condition to maintain a deduplicated registry. Jurisdictions tracking reinfections should consider requesting medical records and collecting data on prior treatment completion (when relevant and possible to document), treatment failure, and the known time frame for reinfection in order to determine true reinfections from possible treatment failures[14].

4.6.4. Case Ascertainment

The primary method for ascertaining suspected cases is by investigating reports from clinical laboratories, health care facilities, and health care providers suggestive of hepatitis C. Rules or regulations requiring facilities and providers to report hepatitis C to public health agencies vary by jurisdiction. See Section 1.6 and Section 4.4 for information on the recommended reporting requirements for hepatitis C.

Laboratory Reporting

Laboratory reporting of HCV infection is required in all states for which acute and chronic hepatitis C is reportable. While case-defining infection markers (e.g., positive HCV RNA tests) are reportable in most jurisdictions, regulations vary regarding which positive indicators within the panel must be reported. It is recommended that jurisdictions require reporting of all negative/undetectable HCV RNA results (to monitor jurisdictional cascade of care), plus negative anti-HCV results in children ≤36 months of age (for perinatal hepatitis C surveillance). Complete reporting of all tests in a hepatitis panel, to include negative hepatitis C laboratory results, allows public health officials to more accurately interpret results. However, this also requires more sophistication in information systems to efficiently send, process, and utilize the information received.

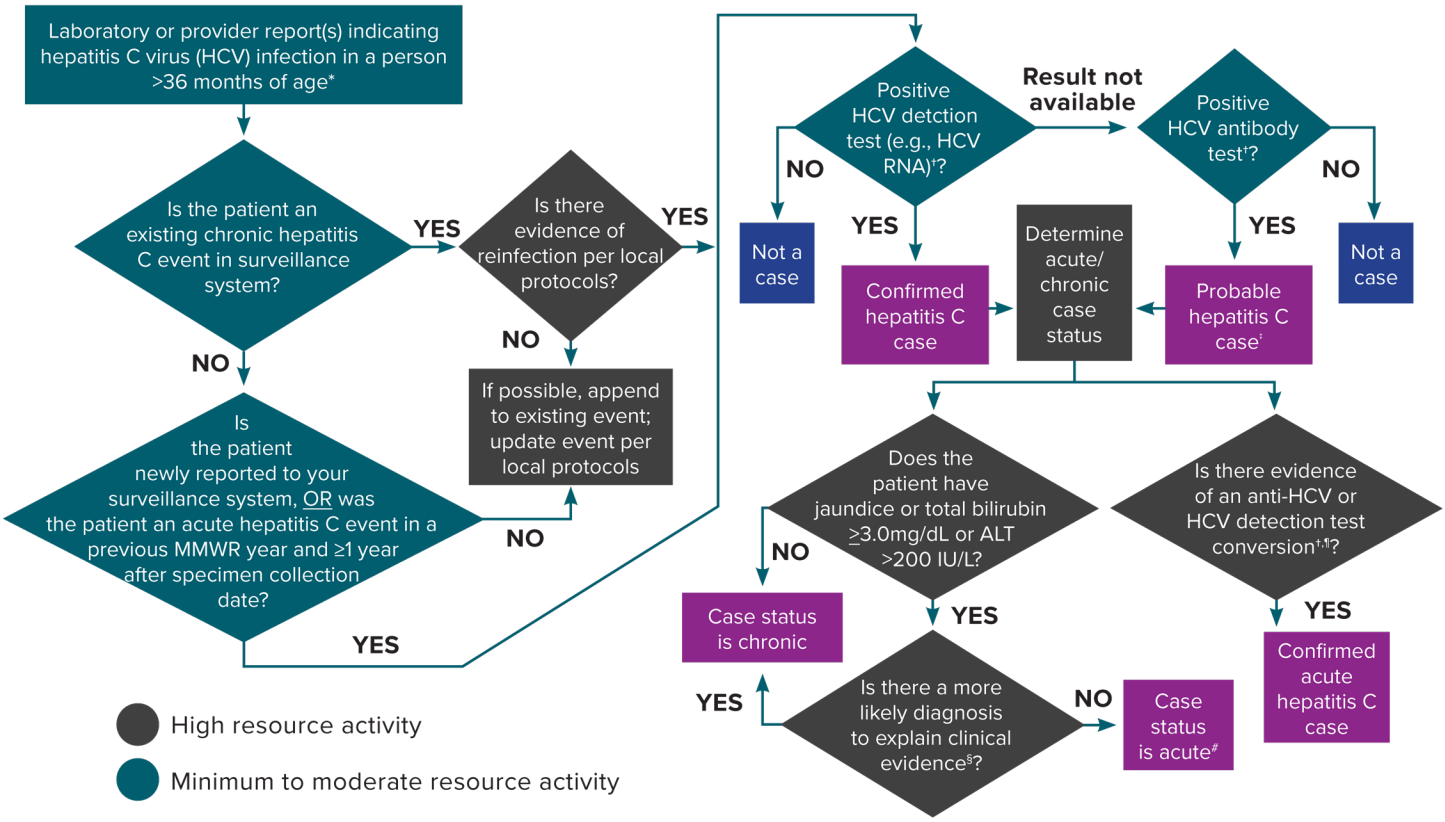
Health Care Facility and Provider Reporting

Many states require health care facilities and providers to report hepatitis C diagnoses.

Additional sources of information include medical records, hospital discharge databases, death certificates, and birth certificates. Section 5.4 provides more information on these data sources. Figure 4-2 illustrates a potential approach for acute and chronic hepatitis C case ascertainment and classification. Specific procedures might vary by jurisdiction, but should generally follow the scheme below, in accordance with the CDC/CSTE Position Statement for the 2020 acute and chronic hepatitis C case definitions[14,107,108].

Cases among children 2–36 months of age should be classified under the Perinatal Hepatitis C Position Statement (17-ID-08) case definition unless the exposure mode is not perinatal (e.g., health care-associated). See Section 4.7.4 for case ascertainment guidance of perinatal hepatitis C cases.

Figure 4-2. Process for acute and chronic hepatitis C case ascertainment and classification



*A child <36 months of age whose mode of exposure is not perinatal (e.g., health care-acquired) should be classified under the 2020 acute or chronic hepatitis C case definition. A child 2–36 months of age whose mode of exposure is perinatal should be classified under the 2018 perinatal hepatitis C case definition.

†Surveillance programs should provide prevention programs with information on people who have positive test outcomes for post-test counseling and referral to treatment and care, as appropriate. HCV detection testing includes nucleic acid testing for HCV RNA (including qualitative, quantitative, or genotype testing) or a test indicating the presence of HCV antigen. At present, no HCV antigen tests are approved by the US Food and Drug Administration (FDA). These tests will be acceptable laboratory criteria, equivalent to HCV RNA testing, when an FDA-approved test becomes available.

‡May re-classify as confirmed if a positive HCV detection test is later received before the National Notifiable Diseases Surveillance System (NNDSS) close-out date for national notification purposes. Jurisdictions with a longitudinal system can update probable cases to confirmed within their system at any time regardless of the NNDSS close-out date.

§May include evidence of acute liver injury from infectious, autoimmune, metabolic, drug or toxin exposure, neoplastic, circulatory or thromboembolic, or idiopathic causes.

¶A documented negative HCV antibody followed within 12 months by a positive HCV antibody test (anti-HCV test conversion) OR a documented negative HCV antibody OR negative HCV detection test (in someone without a prior diagnosis of HCV infection) followed within 12 months by a positive HCV detection test (HCV detection test conversion).

#A new, acute hepatitis C case is either an incident case that has not been previously reported or a case among someone previously reported as having hepatitis C who has laboratory evidence of reinfection[14]. Some jurisdictions are creating a local condition specific for reinfection as opposed to creating a new acute condition to maintain a deduplicated registry.

Reference:

14. Council of State and Territorial Epidemiologists. Position statement 19-ID-06: revision of the case definition for hepatitis C. Available at: https://cdn.ymaws.com/www.cste.org/resource/resmgr/2019ps/final/19-ID-06_HepatitisC_final_7..pdf. Accessed on January 16, 2020.

4.6.5. Case Investigation

The original case report may be sufficient to classify a case of hepatitis C as being acute or chronic. Resource limitations may not allow all chronic cases to be investigated in the same way as acute cases. Additional investigation may be necessary depending on the priority level of the case. The level of investigation will depend on the situation, the objectives, and the available resources. Below is a description of the type of information that should be collected during case investigations.

Information from the Laboratory

Newly reported positive anti-HCV and HCV detection laboratory results should be reported to the HD. Concurrent ALT and total bilirubin results reported with positive hepatitis C laboratory results can be helpful in identifying cases that might be acute.

Information from the Provider or Medical Records

The following types of information might be available from the medical records:

Demographic information. Includes name, date of birth, sex at birth, current gender, race, ethnicity, and residential address (including zip code).

Clinical features. Includes reason for testing, signs (jaundice) and symptoms (if available*), hospitalization status and date of death (if applicable), and whether an alternate diagnosis is suspected. HDs should inquire about the potential of past infection to confirm whether current clinical features are due to a newly acquired infection. The medical record might provide evidence of chronic liver disease.

*Includes fever, headache, malaise, anorexia, nausea, vomiting, diarrhea, and abdominal pain.

Pregnancy status. Pregnancy status should be checked for all people of childbearing age with childbearing potential. Children born to HCV-positive gestational parents should be tested for infection and classified according to the CDC/CSTE perinatal hepatitis C case definition.

Diagnostic test results. If additional laboratory testing (e.g., ALT levels, total bilirubin levels, and results from a hepatitis panel) is needed to classify the case.

Risk behaviors or exposures. Includes history of IDU, sexual contact resulting in exposure to blood (e.g., anal intercourse), experience of homelessness, recent medical procedures, hemodialysis, incarceration, and residence in a long-term care facility.

Information from the Patient

Unless the source of infection is known (e.g., transplantation of an organ from an HCV-positive donor into an HCV-negative recipient), all patients with acute hepatitis C should be contacted for an interview using the jurisdiction-specific acute hepatitis C case investigation form. If resources are limited, at a minimum, all patients who are classified as "confirmed" per the CDC/CSTE case definition and those flagged as having public health importance (Section 4.2) should be interviewed. Decisions to contact the patient are often jurisdiction-specific and depend on the resources available. In many situations, patient contact might be reserved for those cases deemed highest priority for preventing further transmission or for referral for additional care and treatment, as needed. The patient interview should ideally include the following components:

Risk behaviors or exposures. To identify a potential source or risk behavior or exposure(s) for infection during the 2 weeks to 6 months prior to illness onset. For chronic cases, if it is determined that the person has current risk behaviors or exposures for ongoing transmission or was identified as part of a cluster of cases, additional information might be prioritized.

Education and referral for follow-up. People with newly diagnosed acute and chronic hepatitis C should be advised on how to prevent transmission to others. HDs should assess whether the patient requires education, provider referral for treatment, and other medical and public health follow-up services (e.g., hepatitis A and hepatitis B vaccination, PrEP to prevent HIV transmission, MOUD, SSPs, and/or harm reduction services), as appropriate.

Identification of contacts requiring testing and vaccination. If resources allow, identify contacts and coordinate testing, counseling, linkage to care, and hepatitis A and hepatitis B vaccination in accordance with existing recommendations by ACIP. Identification of contacts might require further work-up to identify HCV infection networks that could potentially result in an outbreak.

Special Considerations When Investigating Certain Populations or Settings at Risk for Rapid Disease Transmission

Considerations when investigating hepatitis C cases among certain populations at risk for rapid transmission are provided in Section 1.10.

Case Investigation Prioritization

The automated collection of hepatitis C laboratory results will, in many jurisdictions, lead to a high volume of reporting. Even with automated reporting, many HDs lack the resources needed to conduct investigations for all acute cases. Jurisdictions might consider the following when prioritizing cases for follow-up:

- Require providers to report clinically identified acute infections directly to the HD
- If resources allow, automate the collection of ALT and total bilirubin results through ELR or EMR reporting, and prioritize data collection to confirm those cases with abnormal results
- Conduct semi-automated/preliminary collection of risk data combined with more targeted follow-up on cases WITHOUT anticipated risk history

- Target efforts to demographic groups that might be at higher risk of acquiring or transmitting infection
  - » Pregnant people
  - » New infections reported in elderly patients (e.g., ≥70 years of age)
  - » People <40 years of age that might represent emerging risks
  - » People infected with HIV*
- Target efforts based on specific settings within a jurisdiction
  - » SSPs or substance use disorder treatment facilities
  - » Correctional facilities
  - » Retirement/nursing facilities
  - » Homeless services providers
  - » Areas where known risk behaviors are occurring, or rates of newly reported infections are increasing
- Implement efficient data collection
  - » Test in public health clinics
- Supplement case-surveillance data with data sources to provide information about higher risk populations and the evolving epidemiology of acute infections
  - » SAMHSA/state drug use, overdose, and EMS data
  - » HIV incidence data to identify coinfection*
  - » Ongoing outbreak and cluster investigations, if applicable
  - » Hospital discharge data

*People with hepatitis C and HIV share risk behaviors or exposures; therefore, co-infection is common.

Considerations for Conducting a Chronic Hepatitis C Case Investigation

Conducting an investigation for a chronic hepatitis C case can involve the following considerations:

1. Check the jurisdiction's hepatitis C registry/surveillance system to ensure the case is newly reported and not previously documented.
2. Review the information in the initial report to determine if the case falls within a group prioritized for investigation, such as those outlined in Section 4.2. At a minimum, pregnancy status should be checked for all people with chronic hepatitis C who are of childbearing age with childbearing potential; reports of HCV-infected pregnant people should be shared with the staff member responsible for perinatal hepatitis C case management.
3. When possible, contact the health care provider and/or review medical records to obtain additional information to help prioritize which cases should receive a patient interview.
4. For patients who are interviewed, collect relevant demographic and risk history information using the jurisdiction-specific case report form.
   - » Investigate likely health care exposures according to the jurisdiction's procedures, ideally in collaboration with the health care-associated infection team.
   - » Provide patient education about ways to avoid the spread of infection to others and ways to avoid further harm to the liver.
   - » Educate people who have had direct exposure to the patient's blood about HCV transmission and provide hepatitis C testing if they are not known to be infected.
   - » If the case is in a child, screen the parents and household members for evidence of infection.
5. If resources allow, contact the provider and/or refer the patient to a patient navigator to ensure the patient is in care and receives treatment.

4.6.6. Case Reporting and National Notification

Cases of acute and chronic hepatitis C are nationally notifiable to CDC using a condition-specific event code (Table 1-2). Acute and chronic cases can be re-classified, removed, or changed after the initial transmission to CDC as long as revisions are made before surveillance data are finalized each year. A case initially transmitted to NNDSS as probable might later be reclassified as "confirmed" or "not a case." A confirmed acute case may be classified as a confirmed chronic case if a positive HCV detection test is reported one year or longer after acute case onset.

4.6.7. Surveillance Activities for Chronic Hepatitis C

Due to varying levels of resources, jurisdictions might be at different stages of implementing surveillance activities for chronic hepatitis C. The following section provides best practice models for core and enhanced surveillance activities for consideration by jurisdictions. Enhanced surveillance activities should be identified based on local priorities.

Best Practice Models for Core and Enhanced Chronic Hepatitis C Surveillance

Core Surveillance

Case Ascertainment and Reporting

- Create an electronic system for systematically collecting and storing hepatitis C test results and other case data (e.g., demographic, risk, and clinical information) longitudinally for unique (de-duplicated) persons.
- Establish a method to receive hepatitis C laboratory data and enter into the hepatitis C system/registry, preferably through an automated ELR system. ELR is the most efficient way to receive these data, especially if the ELR system can automatically enter the hepatitis C records into the surveillance system.
  - » Jurisdictions with an existing ELR system for other conditions can incorporate hepatitis C testing.
  - » If ELR is not possible, work with high volume testers to receive data another way (e.g., periodic flat files).
- Determine whether hepatitis C cases will be updated within the surveillance system/registry as new laboratory reports are received (e.g., case status, patient address, and pregnancy information) or whether only laboratory reports received at the time the case investigation is created will be considered.
- Implement a process to extract data from hepatitis C system/registry, classify case investigations, and transmit to CDC according to procedures for the National Notifiable Diseases Surveillance System.

Investigations

- Document local procedures for case investigations, including defining priority populations (see Section 4.2).
- Conduct case investigations for priority populations where feasible (see Section 4.2). Surveillance activities include but are not limited to reviewing EMRs, communicating with providers and/or health care facilities via phone or facsimile, and interviewing patients to collect demographic, risk, and clinical information and other data deemed necessary.
- Establish a protocol for identifying and investigating health care-associated infections*. Depending on the structure of the health department, this might be conducted separately from hepatitis C surveillance with assistance from health care-association infections staff. Use CDC's health care-associated infection toolkit as a resource: https://www.cdc.gov/hai/outbreaks/outbreaktoolkit.html.
- Establish a protocol for identifying and investigating other unique exposures, including clusters and/or outbreaks of hepatitis C*.

*Some newly reported cases meeting the chronic hepatitis C case definition may reflect asymptomatic acute infections.

Quality Assurance

- Establish a process for data cleaning and standardizing laboratory reports.
- Assess case investigations and laboratory reports for completeness and accuracy.
- Identify and review potential duplicate laboratory reports, patients, and/or case investigations.

Analyses

- Create an annual report, situational analysis, or other data product that can be widely shared with providers, advocates, stakeholders, and other public health professionals.

Policy

- Research existing health code/policy related to hepatitis C reporting and the process for changing such policies (if necessary).
- Identify who should report hepatitis C cases (e.g., health care providers, health care facilities, and/or laboratories).
- Determine what should be reportable. At a minimum, positive anti-HCV, positive NAT for HCV RNA (including qualitative, quantitative, or genotype testing), or a positive test indicating presence of HCV

antigen should be reportable. If possible, pregnancy status and concurrent ALT and total bilirubin results should be reported with positive hepatitis C laboratory results, and negative HCV detection test results should also be reported. Surveillance programs should provide prevention programs with information on people who have positive test outcomes for post-test counseling and referral to treatment and care, as appropriate. At present no HCV antigen tests are approved by the FDA. These tests will be acceptable laboratory criteria, equivalent to HCV RNA testing, when an FDA-approved test becomes available.

Data Sharing

- Research how to obtain access to supplemental sources of data (e.g., data from vital statistics, cancer registry, and HIV registry) to match to the hepatitis C registry.

Enhanced Surveillance

Case Ascertainment and Reporting

- Implement a process for updating cases in the system/registry with potential treatment/cure data to track patients along the hepatitis C cure continuum.
- Use additional data sources to identify cases not previously reported through other means (e.g., pharmacy claims for hepatitis C treatment, hospitalization data, payer records, vital records, and chart review).
- Use additional data sources to supplement data in the system/registry (see Section 5.4). The following are examples of ways to use such data sources:
  - » Conduct vital statistics death registry matches to update vital status and death date.
  - » Conduct vital statistics birth registry matches to update pregnancy information and to link gestational parent-infant pairs within the surveillance system.
  - » Conduct data linkage matches to other disease registries (e.g., HIV and cancer) to find missing information (e.g., race/ethnicity) and to assess and address coinfection and comorbidities.

Investigations

- Conduct chronic hepatitis C case investigations for additional priority populations (see Section 4.2).
- Draft an outbreak response plan that includes jurisdictional actions for hepatitis C clusters and/or outbreaks.
- Establish methods for identifying reinfections (confirm the case was previously treated and cured) to establish reinfection rates and target prevention efforts.
- If personnel and other resources allow, consider in-depth investigation of a random sample of chronic cases to evaluate demographic variables, reason for testing, access and barriers to prevention and treatment services, and other questions of importance for viral hepatitis elimination activities in the jurisdiction. Personnel with expertise in study design, data collection, and analytic skills should develop and oversee these types of in-depth investigations.
- Assure linkage to care, treatment, and harm reduction services for priority populations where resources allow.
- Use detection software (e.g., **SaTScan**) to identify potential hepatitis C clusters and/or outbreaks*.
- Use molecular sequencing (Global Hepatitis Outbreak Surveillance Technology [GHOST]) to establish hepatitis C virus (HCV) transmission linkage for cluster and/or outbreak investigations*.

*Some newly reported cases meeting the chronic hepatitis C case definition may reflect asymptomatic acute infections.

Quality Assurance

- Establish quality assurance processes for chronic hepatitis C case data.
- Implement quality improvement measures to ensure completeness and accuracy of case investigations and interpretation of laboratory reports.
- Establish systems to identify and address decreases in hepatitis C laboratory reporting by test type volume and laboratory that might represent coding or transmission issues.
- Establish systems to identify and address deficiencies in provider reporting (e.g., incomplete or missing hepatitis C reports) that might represent coding or transmission issues.

Analyses

- Create provider-level indicators (e.g., complete reporting, complete diagnostic testing, linkage to care, and treatment initiation) to work with health

plans and health care providers to improve these outcomes.

- Use data linkage matches to other disease databases/registries (e.g., HIV) for analysis of co-infections and implementation and evaluation of data-to-care interventions.
- Use vital statistics birth registry matches for analysis of infants born to HCV-positive gestational parents.
- Use death registry matches to describe hepatitis C-associated mortality.
- Describe trends and disparities in liver cancer incidence and mortality via linkage with jurisdictional cancer registry.
- Identify methods for establishing surveillance-based hepatitis C prevalence estimates.
- Create hepatitis C cure continua, including determining and validating surveillance-based definitions for hepatitis C treatment and cure.
- Describe trends and disparities along the hepatitis C cure continuum (e.g., disparities in screening, viremia, linkage to care, treatment initiation, cure, and reinfection).

Policy

- Use hepatitis C surveillance data (e.g., assessing the proportion of people with anti-HCV positive results and no known HCV RNA result) to support evidence-based health code changes related to testing and reporting (e.g., mandatory reflex HCV RNA testing and reporting of negative HCV detection test results).
- Use surveillance data to assess unmet needs for prevention and harm reduction services, and to support evidence-based health code changes related to expanding access to syringe services programs and other harm reduction services for populations affected by hepatitis C.
- Use analysis of trends and disparities to guide resource allocation and inform public health action, prioritizing those communities most disproportionately affected.

Data Sharing

- Obtain access to supplemental data sources wherever possible and incorporate their usage into routine practices. See Section 5.4 for a description of optional data sources.

4.6.8. Considerations for Hepatitis C Cases who were Transplant Recipients

With the availability of curative treatment for HCV infection, an increasing number of transplant recipients are receiving organs from anti-HCV and HCV-RNA positive donors[110]. This can result in transmission of hepatitis C to the recipient, which is then treated with DAA agents[111]. In some jurisdictions, these expected donor-derived HCV transmissions might represent a significant proportion of new acute HCV infections; therefore, jurisdictions are encouraged to reach out to transplant facilities and discuss public health reporting of expected donor-derived HCV infections.

A listing of transplant facilities in the United States, including facility location and phone number, can be found on the OPTN website[71]. As these patients are already linked to testing and treatment, the infections should be notified to CDC as new acute cases. However, the jurisdiction need not investigate beyond indicating that the infection was donor-derived.

Jurisdictions might also get reports of unexpected donor-derived HCV infection. Unexpected infection occurs rarely when both donor and recipient are HCV RNA negative pre-transplant, usually in situations where the donor was infected (e.g., actively injecting drugs) shortly before demise[66]. When a suspect donor-derived acute hepatitis C case is identified, the transplant center is required to report the infection to OPTN's DTAC that might request assistance from the CDC Office of Blood, Organ and Other Tissues Safety. If CDC accepts the investigation, CDC DVH epidemiologists will work with the laboratory to conduct any testing and reach out to the jurisdiction when that part of the investigation is complete.

Typically, there are two outstanding questions that only the public health jurisdiction can answer: 1) Did the recipient have any behavioral or other risks for hepatitis C and 2) Does the jurisdiction have any ongoing investigations of health care-associated hepatitis C that might be related to this investigation?

Case classification in patients with a documented transplant should consider reports of laboratory test results prior to and post-transplant and potential health care exposures, if suspected. Table 4-3 outlines considerations for hepatitis C cases who were organ transplant recipients.

Table 4-3. Considerations for hepatitis C cases who were organ (or tissue) transplant recipients*

Organ Recipient Pre-Transplant Laboratory Result†	Organ Recipient Post-transplant Laboratory Result†	Case Classification
Positive HCV antibody (anti-HCV) **AND** positive HCV detection test‡	Positive anti-HCV **AND** positive HCV detection test‡	Should not be considered a new case due to organ transplant, but rather an infection documented prior to transplant§. To determine whether this case should be considered newly reported, follow Figure 4-2.
Positive anti-HCV with evidence of cure according to AASLD/IDSA hepatitis C treatment guidelines(92)	Positive anti-HCV **AND** positive HCV detection test‡	Should be classified as an acute infection due to reinfection according to the CDC/CSTE case definition(14) and investigated with three major hypotheses in mind: • donor-derived transmission • transmission related to recipient risk behaviors or exposures • health care-associated transmission CDC's Division of Viral Hepatitis might already have been notified about the investigation and is available for consultation.
Negative anti-HCV **AND** negative HCV detection test‡	Positive anti-HCV **AND** positive HCV detection test‡	Should be classified as an acute infection according to the CDC/CSTE case definition(14) and investigated to identify the source of transmission with 3 major hypotheses in mind: • donor-derived transmission • transmission related to recipient risk behaviors or exposures • health care-associated transmission CDC's Division of Viral Hepatitis might already have been notified about the investigation and is available for consultation.
No prior HCV laboratory results¶		

*It is recommended that donors undergo anti-HCV and HCV RNA testing prior to organ procurement(67). If donors are negative for HCV RNA, transmission is considered "unexpected." Transmission has occurred from donors who were infected/re-infected shortly before death; in this scenario, transmission to the recipient occurs during the "window period"(66).

†Because of the large number of tests performed on recipients, irreproducible positive results are sometimes reported. Investigators should review all results in context. CDC's Division of Viral Hepatitis is available for consultation.

‡The 2020 Public Health Service (PHS) guidelines recommend testing all organ recipients for anti-HCV and HCV RNA pre-transplant and for HCV RNA at 4–5 weeks post-transplant(67).

§If the pre-transplant genotype differs from that observed post-transplant, consider investigating as if the infection is newly acquired.

¶All recipients should be tested pre-transplant for anti-HCV and HCV RNA. If the recipient has not been tested appropriately pre-transplant, consider contacting the transplant center to promote awareness of the 2020 PHS guidelines.

References:

14. Council of State and Territorial Epidemiologists. Position statement 19-ID-06: Revision of the case definition for hepatitis C. Available at: https://cdn.ymaws.com/www.cste.org/resource/resmgr/2019ps/final/19-ID-06_HepatitisC_final_7..pdf. Accessed on January 16, 2020.

92. American Association for the Study of Liver Diseases/Infectious Diseases Society of America. HCV guidance: recommendations for testing, managing, and treating hepatitis C. Available at https://www.hcvguidelines.org/. Accessed January 16, 2020.

Cases of viral hepatitis identified among living organ transplant donors and recipients should be submitted to NNDSS in a standardized way, when possible. The CDC case report forms used for NBS and HL7 transmission both include a reason for testing variable in the core section of the form. For state and territorial HDs transmitting data via NBS or HL7, under the "reason for testing" field, "blood/organ donor screening" should be selected for organ transplant donor cases and "other" should be selected for organ transplant recipient cases

with a specification of "transplant recipient" in the free text under the "other reason for testing" field. For state and territorial HDs transmitting case data via NETSS, there is no field on the case report form to indicate that the case was an organ or tissue transplant donor or recipient.

4.6.9. Monitoring Infection Trends and Disease Outcomes Using a Person-Level Database and Supplemental Data Sources

A person-level surveillance database can support hepatitis C elimination efforts by allowing a jurisdiction to document a person's hepatitis C laboratory testing history, including

- providing information on the number of people at each phase of the hepatitis C cure continuum to identify areas for improvement;
- tracking the number of unique persons living with hepatitis C longitudinally, which can inform more accurate estimates of incidence and prevalence;
- identifying pregnant people tested during prenatal care and perinatally exposed infants born to HCV-infected gestational parents;
- identifying and linking people living with hepatitis C to medical care;
- evaluating the impact of public health and clinical service; and
- matching with secondary data sources (e.g., Vital Statistics, Medicaid, cancer registry, and HIV jurisdictional registries).

Some of these patterns can only be determined for jurisdictions capable of capturing negative HCV RNA test results. Linking a person-level surveillance database to other data sources allows for longitudinal monitoring of disease outcomes and improves completeness of information in the surveillance system[72]. Some jurisdictions have used their surveillance database to identify pregnancy status through routine matching with optional data sources. Supplemental data sources are helpful for understanding the burden of co-morbidities, such as infection with HBV and HIV, by providing cross-sectional data over time and can be used to inform interpretation of prevalence estimates. Section 5.4 describes supplemental data sources to consider.

4.7. Surveillance of Hepatitis C During Pregnancy and Perinatal Hepatitis C

4.7.1. Background

From 2009–2014, the prevalence of hepatitis C among pregnant people in the United States significantly increased by 89%, from 1.8 to 3.4 per 1,000 live births based on maternal HCV infection status reported on birth certificates from NVSS[112]. Additionally, the proportion of infants born to HCV-infected gestational parents increased by 68% nationally from 2011 through 2014[113].

Perinatal hepatitis C became nationally notifiable in 2018[114]. However, case identification of perinatal hepatitis C can be resource-intensive, and implementation of perinatal hepatitis C surveillance is not yet widespread. CDC prioritizes perinatal hepatitis C surveillance to prevent transmission and increase identification of hepatitis C in infants and children born to HCV-positive gestational parents.

To improve the prevention and identification of perinatal hepatitis C and facilitate clinical care for people who are pregnant or postpartum, CDC recommends hepatitis C screening during each pregnancy in settings where the HCV RNA prevalence is ≥0.1% or HCV RNA prevalence is unknown[58,93]. Because most settings are unlikely to have an HCV RNA prevalence as low as 0.1%, hepatitis C screening should be conducted in most settings.

The overall goals of surveillance of hepatitis C during pregnancy are to 1) determine whether pregnant people are currently infected with HCV (as indicated by the presence of HCV RNA) and 2) among HCV-positive people of childbearing age with childbearing potential, identify those who are currently pregnant or have recently delivered a live birth to identify perinatal HCV transmission.

The term "HCV-positive" is used when describing people who are HCV RNA-positive or who are anti-HCV-positive with no evidence of an HCV detection test being performed. Until the HCV detection status is known, surveillance should err on the side of inclusion for perinatal exposures and pregnant people. HCV-positive pregnant people should be linked to care for disease staging and treatment after pregnancy

according to clinical recommendations, as DAAs can cure people of their HCV infection. Not only can curative hepatitis C therapy benefit people, but it can prevent HCV exposures during any future pregnancies.

Treatment during pregnancy is not currently recommended due to limited safety and efficacy data, though clinical trials are ongoing. Children born to HCV-positive gestational parents should be linked to care for appropriate testing to identify potential perinatal HCV transmission.

As resources permit, surveillance of HCV infection during pregnancy should include monitoring each pregnancy as well as assessment of pregnancy status at multiple timepoints and not considering pregnancy to be a one-time event. When feasible, jurisdictions are encouraged to collaborate broadly with other partners addressing SUD in pregnant people to improve access to prenatal care and other services including post-partum treatment for hepatitis C.

The overall goals of perinatal hepatitis C surveillance are to ensure that infants born to HCV-positive gestational parents are identified, appropriately tested for hepatitis C, and linked to care. The additional goals of perinatal hepatitis C surveillance are to

- identify HCV RNA-positive gestational parents not previously identified during pregnancy and link them to care to prevent vertical HCV transmission during any future pregnancies;
- provide data to improve assessment of the burden of perinatal hepatitis C;
- evaluate health outcomes of infected infants;
- evaluate the overall effectiveness of perinatal hepatitis C programs;
- identify the appropriateness of HCV testing among children;
- educate clinicians and guardians on HCV transmission, clinical progression, and treatment; and
- measure the rate of progression to chronic hepatitis C, as determined by a positive HCV detection test result after 36 months of age.

4.7.2. Uses of Surveillance Data

Surveillance data on hepatitis C during pregnancy can be used to inform and improve public health interventions in the following ways:

Identifying HCV-positive pregnant people to ensure linkage to hepatitis C-specific care. All HCV-positive people should be evaluated for care and treatment, when clinically indicated, by a medical provider.

Identifying HCV-positive people who are pregnant or who have recently given birth to prioritize testing their infant for hepatitis C. Identification of an HCV-positive pregnant person during or after delivery allows for coordination of case management to ensure appropriate testing of their infant for perinatal HCV transmission. Such early identification of hepatitis C will result in fewer undiagnosed infections in the pediatric and young adult population and creates opportunities for linking infants to care so they can be evaluated for treatment with HCV DAAs at ≥3 years of age.

Monitoring adherence to screening recommendations during pregnancy. To best monitor adherence to AASLD and CDC HCV screening recommendations among pregnant people, surveillance programs should ideally collect negative anti-HCV and negative HCV RNA results. Surveillance can help track changes in hepatitis C incidence among pregnant people or ensure implementation of quality measures to monitor adherence to screening recommendations.

Monitoring trends in disease incidence and prevalence among people of childbearing age with childbearing potential. Knowing the incidence and prevalence of hepatitis C among people who are or have the potential to become pregnant is critical to the control, prevention, and ultimate elimination of HCV infection. Tracking this population with other chronic and acute hepatitis C surveillance data is adequate, but it should be assessed independently from surveillance of the general population.

Perinatal hepatitis C surveillance data can be used to inform and improve public health interventions in the following ways:

Identifying children ≤36 months of age who test positive for anti-HCV and/or positive for HCV RNA. Early identification of children 18–36 months of age who test positive for anti-HCV and/or infants and children 2–36 months of age who test positive for HCV RNA will increase the number diagnosed with hepatitis C in the pediatric and young-adult population. Testing for anti-HCV at <18 months of age is not recommended

as a positive result could be caused by trans-placental maternal anti-HCV. Curative DAA treatment can be provided to children as young as 3 years of age[92]. Early identification is important to ensure access to early treatment.

Monitoring trends in disease incidence among children 2-36 months of age. While perinatal hepatitis C surveillance data should be incorporated into data management systems for acute and chronic hepatitis C, monitoring incidence among children in this age range should close existing gaps in perinatal hepatitis C ascertainment.

Monitoring and evaluating the effectiveness of perinatal hepatitis C programs. The following indicators can be used to monitor and evaluate the effectiveness of perinatal hepatitis C programs:

- The proportion of infants born to HCV-infected gestational parents who are
  - » Tested for hepatitis C and
  - » Tested for hepatitis C according to clinical guidelines.
- The proportion of perinatal hepatitis C cases who
  - » Receive additional testing,
  - » Test HCV RNA negative after 36 months of age,
  - » Test HCV RNA positive after 36 months of age (i.e., reported to CDC as chronic hepatitis C), and
  - » Receive medical evaluation and treatment, if appropriate.

4.7.3. Surveillance Case Definition

No CDC/CSTE surveillance case definition exists for HCV infection during pregnancy. Instead, these cases should be classified in accordance with the CDC/CSTE acute and chronic hepatitis C case definitions. See Section 4.6.3 for the acute and chronic hepatitis C case definitions.

Table 4-4 specifies the surveillance case definition for perinatal hepatitis C, CSTE and CDC in 2018[114,115]. See Appendix C for classification scenarios of cases of perinatal hepatitis C.

Table 4-4. US Centers for Disease Control and Prevention (CDC) and Council of State and Territorial Epidemiologists (CSTE) case definition for perinatal hepatitis C, 2018

Criteria Type	Criteria
Demographic	Diagnosis of hepatitis C in an infant 2–36 months of age
Clinical	Ranges from asymptomatic to fulminant hepatitis
Laboratory*	Child ≤36 months of age with evidence of hepatitis C as shown by the following laboratory results: • **Diagnostic Laboratory Evidence:** HCV detection test: » Positive nucleic acid test (NAT) for HCV RNA (including qualitative, quantitative, or genotype testing) during 2–36 months of age OR » Positive test indicating presence of HCV antigen during 2–36 months of age
Epidemiologic Linkage	• Maternal infection with hepatitis C of any duration, if known **AND** • Not known to have been exposed to hepatitis C via a mechanism other than perinatally (e.g., not acquired via health care)
Case Status	**Classification**
Confirmed Perinatal*	• Has a positive HCV detection test performed during 2–36 months of age **AND** • Is not known to have been exposed to hepatitis C via a mechanism other than perinatally.

*Surveillance programs should provide prevention programs with information on people who have positive test outcomes for post-test counseling and referral to treatment and care, as appropriate. At present no HCV antigen tests are approved by the US Food and Drug Administration (FDA). These tests will be acceptable laboratory criteria, equivalent to HCV RNA testing, when an FDA-approved test becomes available.

Test results prior to 2 months of age should not be used for classification. Cases among children in the specified age range that are known to have been exposed to HCV through a mechanism other than perinatal transmission should also be reported under the 2020 acute and chronic hepatitis C case definition.

HDs should be notified of children with a positive anti-HCV test performed at 18–36 months of age for whom no HCV detection test results have been reported, as this can represent perinatal HCV transmission. However, these cases should not be reported to CDC per the perinatal hepatitis C position statement case definition[115]. HDs might consider classifying these children under a "suspected" or other non-notifiable case classification in their disease surveillance system for tracking and case management to confirm receipt of HCV RNA test results and identify siblings for whom HCV testing may be indicated.

4.7.4. Case Ascertainment

In 2020, CDC published the recommendation that all pregnant people be screened for HCV in settings where the HCV RNA prevalence is ≥0.1% or HCV RNA prevalence is unknown[93], increasing identification of both HCV infection during pregnancy and perinatal hepatitis C. All positive anti-HCV and positive HCV RNA tests should be reported to the responsible public health jurisdiction. See Section 4.4 for additional information on recommended reportable hepatitis C laboratory markers.

Pregnancy status should be considered routinely at multiple timepoints. Examples of timepoints for pregnancy status consideration include

- at the time of every new electronic laboratory report and
- when pregnancy status is provided to the jurisdiction by a laboratory or provider.

Regularly utilizing birth records that are matched to the HCV surveillance registry also can improve case ascertainment.

Determination of pregnancy status for all HCV-positive people who have the potential to become pregnant poses a significant challenge to local HDs, as this activity can potentially strain already limited public health resources. Jurisdictions should explore automated methods for receiving pregnancy status where possible, and if necessary, prioritize a subset of cases for follow-up of pregnancy status. The following are some examples of methods for determining pregnancy status that should be considered and incorporated when resources permit:

- Prioritizing follow-up of HCV-positive laboratory tests that were ordered by prenatal clinics or obstetrics and gynecology (OB/GYN) offices.
- Obtaining pregnancy status when investigations or follow-up is done on people with acute and/or chronic hepatitis C.
- Incorporating pregnancy status reporting within ELR (e.g., via HL7-based laboratory testing codes associated with ordering a prenatal screening panel), electronic medical record (EMR) reporting, and reporting from publicly funded testing sites. ELR messaging can be reviewed and automatically incorporated into data management systems when possible, utilizing analytical software coding to identify new pregnancy reports.
- Utilizing data matching with birth records to identify people who both recently gave birth and represent hepatitis C cases. These matches can be performed at various frequencies to improve timeliness of identification of an HCV-positive person who gave birth.
- Mandating the reporting of pregnancy for those known to be positive or newly tests positive for anti-HCV or HCV RNA, either from the laboratory or provider. Mechanisms for reporting include reporting via REDCap-based forms, electronic health records, facsimile, or electronic laboratory reporting of pregnancy status.

Perinatal hepatitis C surveillance should employ two arms of case ascertainment and case investigation:

- follow-up of infants born to HCV-positive pregnant people and
- follow-up of children ≤36 months of age who have been tested for hepatitis C.

Collectively, these children should be tested appropriately for hepatitis C, and the epidemiologic link with an HCV-positive birth parent should be established where feasible. If screening for hepatitis C does not occur during every pregnancy, there will inevitably be HCV-positive pregnant people whose infections are not reported to the appropriate HD. To ensure identification of all gestational parent-infant

pairs, it is critical to use multiple methods for identifying HCV-positive pregnant people or gestational parents and children ≤36 months of age who have been tested for hepatitis C.

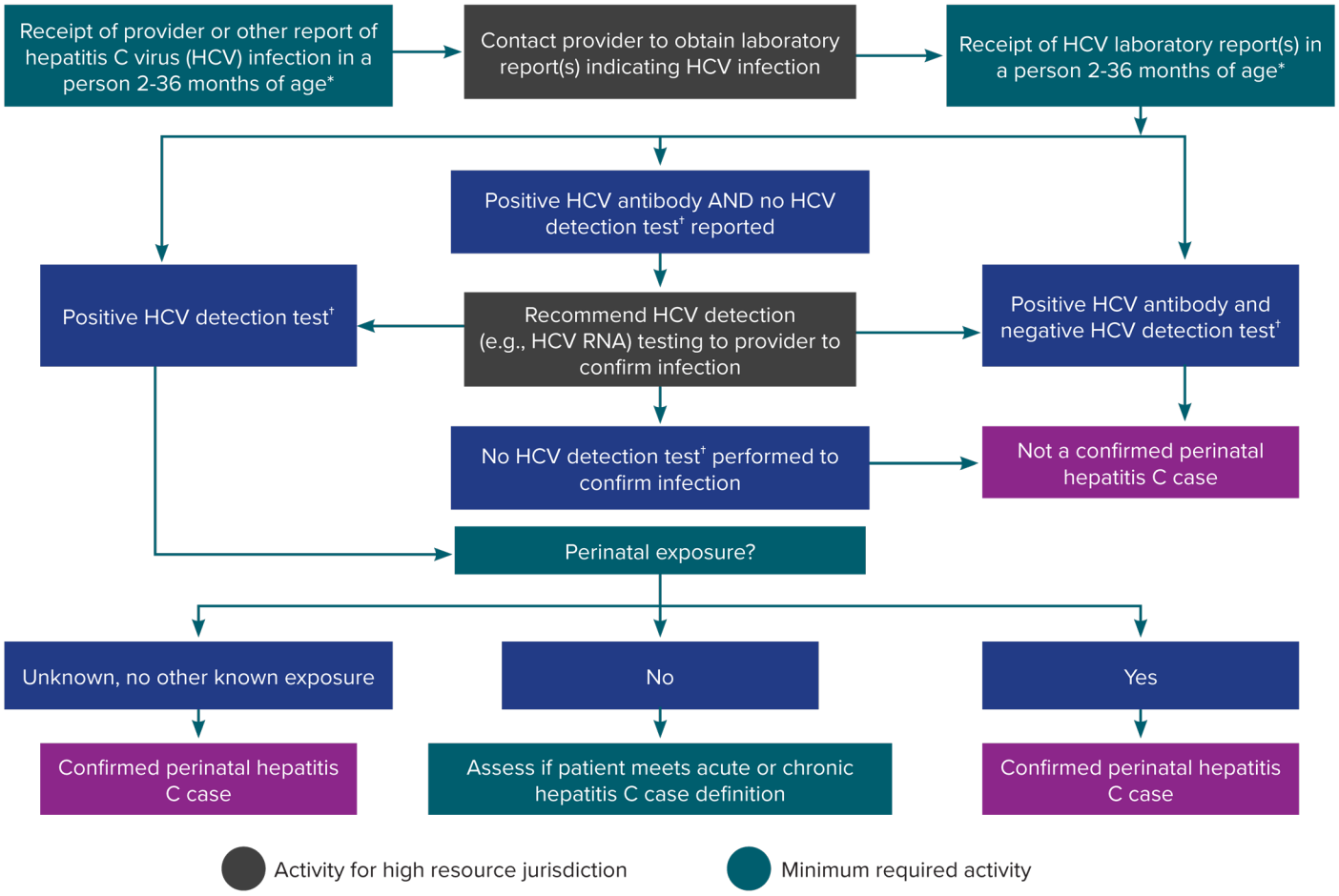
As resources permit, consider that identification during pregnancy does not currently have public health utility in preventing vertical HCV transmission; however, identification of HCV-positive pregnant people can be leveraged to improve treatment outcomes in the post-partum period to prevent subsequent perinatal HCV exposures. Further, earlier identification of HCV-positive pregnant people or gestational parents can improve HCV testing outcomes in their infants and children, allow for timely communication with pediatric providers regarding the exposure and HCV testing recommendations.

To facilitate identification of HCV-infected infants, perinatal hepatitis C surveillance staff should

- develop perinatal hepatitis C programs that have procedures for active tracking and case management of infants born to HCV-infected gestational parents;
- provide case management guidance to health care practitioners and health care organizations that provide care to infants and children;
- conduct follow-up investigation on any anti-HCV-positive infant with no or unknown HCV detection test, including recommending HCV RNA testing to determine whether the infant has hepatitis C and requires linkage to medical care;
- consider measures to facilitate prenatal HCV screening during each pregnancy in settings where the HCV RNA prevalence is ≥0.1% (currently, most settings are unlikely to have an HCV RNA prevalence **as low as** 0.1%) or HCV RNA prevalence is unknown;
- make positive HCV RNA test results in pregnancy a reportable condition;
- establish links with hospitals and infection control practitioners to facilitate reporting of all births to HCV-positive gestational parents;
- consider requirements to document the maternal HCV infection status on the newborn metabolic screening card, hospital discharge summaries, and birth certificate;
- evaluate if HCV RNA testing in the first year of life of all children born to HCV-infected gestational parents serves as a practical method to improve follow-up;
- establish routine reporting as part of HD case management of all HCV-RNA and anti-HCV test results (positive and negative) from infants; and
- routinely match HCV cases reported to the jurisdiction to birth records. (Some jurisdictions have found low sensitivity with vital records matching [i.e., birth records] and would recommend it as a supplementary rather than sole source for case ascertainment.)

Figure 4-3 illustrates a potential approach for perinatal hepatitis C case ascertainment and classification. Specific case ascertainment and classification procedures vary by jurisdiction based on established processes, but should generally follow the scheme below in accordance with the CDC/CSTE Position Statement for the 2018 perinatal hepatitis C case definition[114,115].

Figure 4-3. Process for perinatal hepatitis C case ascertainment and classification



*Test results among infants <2 months of age should not be used for classification. Cases among children ≤36 months of age who are known to have been exposed to HCV through health care or otherwise, and not perinatally, should be reported under the 2020 acute and chronic hepatitis C case definitions.

†HCV detection testing includes nucleic acid testing (NAT) for HCV RNA (including qualitative, quantitative, and genotype testing) or testing indicating the presence of HCV antigen. At present, no HCV antigen tests are approved by the US Food and Drug Administration (FDA). These tests will be acceptable laboratory criteria, equivalent to HCV RNA testing, when an FDA-approved test becomes available.

4.7.5. Case Investigation

The following elements can inform investigation and management of the HCV-infected pregnant person and infant:

Demographic information. For the pregnant person, obtain date of birth, current gender, race, ethnicity, residential address (including zip code), and insurance status. For the infant, obtain the date and place of birth, birth weight, sex, race, ethnicity, and insurance status. The contact information of the legal guardian(s) should also be collected.

Patient and health care provider information. Obtain names of and contact information for the prenatal care provider, infant's health care provider, and parent(s) or legal guardian(s). Information about adoption or foster-care status should also be collected.

Delivery information. Document the expected and actual due dates and delivery facilities.

Diagnostic test results. Obtain documentation of positive HCV test results for both parent and infant. Anti-HCV test results alone do not meet the case definition for perinatal hepatitis C at any age but should still be collected for surveillance and follow-up purposes, including to identify the need for HCV RNA testing of infants exposed at birth.

Clinical features. For the pregnant person, document the presence of jaundice and whether this is a newly acquired infection or of an existing condition. Most infants with hepatitis C are asymptomatic

Epidemiological link. For the infant, confirm birth to an HCV RNA-positive gestational parent and the absence of other potential exposures beyond perinatal.

Reporting information. For all cases, obtain the date reported to health jurisdiction, date of diagnosis, date the investigation was initiated, date of first contact with patient and/or health care provider, and date referred for medical evaluation.

Education and referral for follow-up. Provide education according to national guidelines, to include discussion of perinatal transmission risk, need for appropriate testing for the infant, and current treatment recommendations. No DAAs have been approved for use in pregnancy; AASLD/IDSA guidelines do not recommend treatment during pregnancy[92].

Because stigma against pregnant PWUD could lead to reluctance to seek and continue prenatal care, information collected for public health surveillance should not be used for law enforcement purposes.

Case Investigation Prioritization

Follow-up and investigation of a case of hepatitis C in a pregnant person should occur in pregnancy or as soon as possible thereafter. Successful follow-up might be more likely if contact information is utilized sooner. Further, if treatment as prevention or other interventions are established as standard practice, early identification of HCV-positive pregnant people and timely follow-up will facilitate the prevention of perinatal HCV transmission.

The following situations are considered high-priority for case investigation and follow-up among HCV-positive people of childbearing age with childbearing potential:

- Pregnancy status is unknown
- Co-infected with HIV
- High HCV RNA levels

4.7.6. Case Management

HCV-positive pregnant people should be investigated and followed up in accordance with practices outlined for cases of acute hepatitis C and chronic hepatitis C (see Section 4.6.5). In addition, HCV-positive gestational parents and their infant(s) should be followed through a system that can track case management processes and allow for sharing and/or linking parent and child events. The system should allow each pregnancy to be considered unique and pregnancy-specific data to be captured and maintained. Infants should be monitored in this system at appropriate intervals to ensure appropriate post-birth testing is performed. Viral hepatitis surveillance staff should work with their viral hepatitis prevention coordinator to ensure proper follow-up of infants born to HCV-positive gestational parents.

Perinatal hepatitis C cases should be followed through a minimum of 36 months of age to enable jurisdictions to track spontaneous clearance of infection, progression to chronic infection, clinical evaluation, and treatment/cure. Viral hepatitis prevention coordinators should include information on proper follow-up of these infants in their provider education. HDs should make best efforts to perform some or all the following case-management activities depending on available resources:

- Ensure testing of exposed infants.
  - » Children born to an HCV-positive gestational parent should be tested according to AASLD/IDSA HCV clinical guidelines. Pediatricians should be informed regarding the HCV exposure and testing guidelines, as appropriate.
  - » Children with a positive anti-HCV result prior to 18 months of age should receive HCV RNA testing (if not automatically reflexed).
- Provide parents and caregivers with education regarding the potential for vertical transmission.
  - » Counsel parent(s) or legal guardian(s) about HCV vertical transmission and testing recommendations for their infant.
  - » Provide information on HCV transmission risk to the infant, testing recommendations, and directed medical care.

- Refer HCV-positive people for medical evaluation.
  - » Post-partum HCV curative treatment for HCV-positive gestational parents should be promptly provided by a medical provider according to treatment guidelines, helping reduce disease progression and the risk of future perinatal transmission.
  - » HCV-positive gestational parents should be linked to other services as needed.
  - » Children with a positive HCV RNA result performed at ≥2 months of age or positive anti-HCV result performed ≥18 months of age should be evaluated (by referral or consultation, if appropriate) to
    - › verify the presence of HCV infection and
    - › assess for severity of disease and possible treatment according to current practice guidelines in consultation with, or by referral to, a specialist knowledgeable in this area.

Siblings born to the same gestational parent should be tested if they have not been previously tested, and if positive, reported to CDC according to the appropriate case definition (i.e., children ≥36 months of age should be evaluated based on case definitions for acute and chronic infection).

4.7.7. Case Reporting and National Notification

HCV infection during pregnancy should be a reportable event to the HD. Although no specific NNDSS event exists for HCV infection during pregnancy, CDC recommends classifying these cases as acute or chronic using the appropriate event code (Table 1-2) in accordance with the CDC/CSTE case definitions, and transmitting the pregnancy status to NNDSS for all cases among people of childbearing age with childbearing potential to allow for national tracking. At the jurisdiction-level, there may be a separate classification category specifically for hepatitis C during pregnancy. Cases of perinatal hepatitis C are nationally notifiable to CDC and are submitted using a condition-specific event code (Table 1-2). As more is learned about how jurisdictions are counting and submitting perinatal hepatitis C cases that progress to chronic infection, information in this section will be updated. See Section 4.5 for more information on hepatitis C case reporting and national notification.

5. Additional Information and Resources

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5.1. Classifying Hepatitis C as Acute or Chronic in People with Hepatitis A

5.1.1. Background and Rationale

During person-to-person hepatitis A outbreaks, jurisdictions may receive reports of people with evidence of coinfection of hepatitis A with hepatitis B and hepatitis C. Classification of cases of hepatitis B that are coinfected with hepatitis A is clear because a laboratory marker exists for acute hepatitis B (i.e., anti-HBc IgM); however, for cases of hepatitis C that are coinfected with hepatitis A, it is not always apparent if the HCV infection should be classified as acute or chronic.

The CDC/CSTE hepatitis A case definition, implemented in 2019 (PS 18-ID-07)[116], and the acute and chronic hepatitis C case definitions, implemented in 2020 (PS 19-ID-06)[14], do not explicitly address case classification of hepatitis C in cases associated with hepatitis A coinfection. Because viral hepatitis coinfections occur regardless of whether they are associated with a hepatitis A outbreak, long-term guidance is needed to standardize classification and notification of these cases.

5.1.2. Problem and Next Step

Guidance for determining whether a case with documented clinical information is caused by hepatitis A or acute hepatitis C (or both) is not explicitly included in the CDC/CSTE position statements[1,2]. The following guidance is to be used for cases reported in the 2020 *MMWR* year and beyond.

5.1.3. Considerations for Hepatitis C Case Classification and Notification

Documented HCV Test Conversion

As per the 2020 CDC/ CSTE case definition[107], any documentation of an HCV test conversion from negative to positive within 12 months should be classified as acute hepatitis C, irrespective of signs, symptoms, and other clinical information. An HCV test conversion can either be an anti-HCV test conversion or an HCV detection test conversion. Test conversion definitions are listed in Table 4-2.

Laboratory Results Indicating Early Acute Hepatitis C

Anti-HCV tests have about an 8–11-week window period from HCV exposure to detection of HCV antibodies. HCV RNA is detectable approximately 1–2 weeks after HCV exposure. If HCV RNA is detectable and anti-HCV is undetectable on the same specimen, this could indicate early acute hepatitis C; anti-HCV testing was performed during the window period. This scenario might be more common in settings where HCV testing is regularly performed (e.g., SSP providers and blood or plasma donation centers). In people who are immunocompromised, development of HCV antibodies might be delayed. In immunocompromised people at risk for HCV infection, HCV RNA testing should always be performed to determine current infection, even when the anti-HCV result is negative.

Documentation of Recent IDU Initiation

In the absence of a documented HCV test conversion or other laboratory indicators of acute hepatitis C, cases among co-infected people documented as having recently initiated IDU should be classified as acute. In this context, "recent" is defined as initiating IDU for the first time within 12 months of the first report to public health. This is an optional activity that could be considered for a special project.

Presence of Clinical Criteria in the Absence of Acute Hepatitis C Considerations

Most adults with hepatitis A have signs and symptoms of acute liver injury[117], whereas a much lower percentage (15%–25%) of people with acute hepatitis C present with signs and symptoms[98,99,118]. In the absence of evidence to support acute hepatitis C classification, clinical signs and symptoms might be attributed to hepatitis A in the presence of previously undiagnosed chronic hepatitis C. This rationale is consistent with the 2020 acute hepatitis C case definition, which removes the discrete onset of symptoms as a requirement for classification of acute hepatitis C cases.

In addition, the 2020 acute hepatitis C case definition of the CSTE Hepatitis C Position Statement (PS 19-ID-06) includes a clause under the clinical criteria that states that a more likely diagnosis, such as another viral hepatitis infection (e.g., hepatitis A), should be considered a possible explanation for the presence of clinical criteria before considering that the clinical criteria for acute hepatitis C is met.

5.1.4. Scenarios for Hepatitis C Case Classification and Notification

Table 5-1 describes hepatitis C case classification and notification scenarios when a concurrent hepatitis A diagnosis is present. Because laboratory markers of acute viral hepatitis infection (e.g., anti-HAV IgM, HAV RNA, total bilirubin levels ≥3.0 mg/dL, and peak ALT levels >200 IU/L) can change within a narrow timeframe, the term "concurrently" in this context refers to hepatitis A and hepatitis C-associated laboratory results that were performed on the same specimen or at least within a few days.

Table 5-1. Classification of hepatitis C cases diagnosed concurrently with hepatitis A

Scenario Confirmed hepatitis A* AND…	**Classification**	**Rationale**
Hepatitis C virus (HCV) test conversion* documented	Confirmed acute hepatitis C	Documented HCV test conversion.† Clinical criteria not required to be met for acute hepatitis C case classification. However, because the patient has confirmed hepatitis A, clinical criteria are present.*
• Negative anti-HCV • Positive HCV detection test • HCV test conversion† not documented	Confirmed acute hepatitis C	For the first 8 weeks following exposure to HCV, anti-HCV tests might not detect HCV antibodies.‡,§ HCV RNA is likely detectable ~1–2 weeks after HCV exposure.‡ If HCV RNA is detectable and anti-HCV is not detectable in the same specimen, this could indicate early acute HCV infection.‡ This scenario might be more common in settings where HCV testing is regularly performed (e.g., syringe services providers and blood donation centers).
• Positive anti-HCV (by history or documented) • Positive HCV detection test • HCV test conversion* not documented • Documentation of recent initiation of injection drug use within 12 months of first report to public health	Confirmed acute hepatitis C	The risk of HCV infection associated with injection drug use is strong following onset of injection. However, in the absence of information about recent initiation of injection drug use, this case would be classified as confirmed chronic hepatitis C. See below scenario.
• Positive anti-HCV (by history or documented) • Positive HCV detection test • HCV test conversion† not documented	Confirmed chronic hepatitis C	The 2020 acute hepatitis C case definition, under clinical criteria, states that a more likely diagnosis, such as another viral hepatitis infection (e.g., hepatitis A), should be considered as a possible explanation for the presence of clinical criteria before considering that the clinical criteria for acute hepatitis C is met.
• Positive anti-HCV • No HCV detection test reported • HCV test conversion† not documented	Probable chronic hepatitis C	The 2020 acute hepatitis C case definition, under clinical criteria, states that a more likely diagnosis, such as another viral hepatitis infection (e.g., hepatitis A), should be considered as a possible explanation for the presence of clinical criteria before considering that the clinical criteria for acute hepatitis C is met.

*A case of confirmed hepatitis A, in this context, has evidence of

1) acute hepatitis symptoms (i.e., the abrupt onset of symptoms consistent with acute viral hepatitis [e.g., fever, headache, malaise, anorexia, nausea, vomiting, diarrhea, abdominal pain, or dark urine]), **AND**
2) acute hepatitis signs or laboratory abnormalities (defined as a report of jaundice or peak elevated total bilirubin levels ≥3.0 mg/dL or peak ALT levels >200 IU/L), **AND**
3) anti-HAV IgM positive and/or HAV RNA positive.

†**Anti-HCV test conversion:** 1) documented negative HCV antibody (anti-HCV) test followed by a positive HCV antibody test within 12 months or 2) documented negative HCV detection test followed by a positive anti-HCV test within 12 months.

HCV detection test conversion: 1) documented negative anti-HCV test followed by a positive HCV detection test within 12 months or 2) documented negative HCV detection test in someone without a prior diagnosis of hepatitis C followed by a positive HCV detection test within 12 months.

‡Source of information: https://www.aphl.org/aboutAPHL/publications/Documents/ID-2019Jan-HCV-Test-Result-Interpretation-Guide.pdf

§In people who are immunocompromised, development of HCV antibodies might not occur or be delayed. In people who have risks for HCV infection, HCV detection testing, regardless of HCV antibody status, should always be performed to determine presence or absence of infection.

5.2. Transmitting Multiple Viral Hepatitis Condition Notifications to NNDSS

5.2.1. Background and Rationale

Different scenarios may lead to reports of multiple viral hepatitis condition notifications in the same person. Jurisdictions might receive laboratory reports indicating hepatitis coinfections; additionally, people with perinatal or acute hepatitis B or hepatitis C can develop chronic infection. Capturing these events through surveillance is critical to accurately measure the national burden of hepatitis A, hepatitis B (acute, chronic, and perinatal),

and hepatitis C (acute, chronic, and perinatal) and characterize cases. See Table 1-2 for the complete list of viral hepatitis conditions that are notifiable to CDC.

For jurisdictions using a person-level data transmission mechanism to transmit case-report data (e.g., NBS or HL7), a unique person-specific ID should be transmitted along with each case notification. The same unique person ID should be submitted for all conditions associated with the patient across reporting years. Submission of data in this manner allows for people who have more than one condition notification across time from the same jurisdiction to be grouped together for analyses. Please note that this guidance does not pertain to jurisdictions that are transmitting viral hepatitis cases to NNDSS solely via NETSS, because NETSS is not a person-level system.

5.2.2. Transmission of Multiple Viral Hepatitis Condition Notifications to NNDSS via NBS

Table 5-2 describes the variables that are recommended for transmitting multiple viral hepatitis condition notifications on a person via NBS.

Table 5-2. Person and case identification variables in the National Electronic Disease Surveillance System Base System (NBS)

CDC Variable ID	CDC Variable Name	CDC Variable Type	CDC Question/ Variable Description
DEM197	Person_ local_id	Alphanumeric (<200 characters)	The local ID of the subject/ entity of the case. This is the ID that the state NBS application assigned to the subject when it was entered into NBS.
INV168	Case_ local_id	Alphanumeric (<200 characters)	State-assigned expanded case ID/local record ID in source NBS Master Message.
NOT109/ nbsState Code	NND_ Reporting_ State_Cd	Alphanumeric (<20 characters)	NBS reporting state code.

To transmit multiple viral hepatitis condition notifications on a person via NBS, use the same person local ID (DEM197) for all associated case investigations (INV168). Make sure that all cases are de-duplicated before transmitting to NNDSS.

5.2.3. Transmission of Multiple Viral Hepatitis Condition Notifications to NNDSS via HL7 Case Notification

Table 5-3 describes variables that are recommended for transmitting multiple viral hepatitis condition notifications on a person via HL7 case notification.

Table 5-3. Person and case identification variables via Health Level Seven (HL7) case notification

PHIN Variable	Variable Type	Data Element	Data Element Description
DEM197	Text	Local subject ID	The person local ID associated with the case.
INV168	Text (Alphanumeric <200 characters)	Local record ID	Sending system-assigned local ID of the case with which the subject is associated.
NOT116	Coded value (Alphanumeric <20 characters)	77968-6 National Reporting Jurisdiction	National jurisdiction reporting the notification to CDC.

To transmit multiple viral hepatitis condition notifications on a person via HL7 case notification, use the same person local ID (DEM197) for all associated case investigations (INV168). Make sure that all cases are de-duplicated before transmitting to NNDSS.

5.3. Guidance for Reporting Outbreak Source for Hepatitis A Cases to NNDSS

When transmitting cases of outbreak-associated hepatitis A to NNDSS, it is important to differentiate between cases associated with a common-source (i.e., foodborne or waterborne) versus person-to-person outbreaks.

5.3.1. Data Elements Defining Outbreak Source

Specific reporting fields enable jurisdictions to report outbreak status on hepatitis A cases notified to NNDSS. To indicate that a case of hepatitis A is associated with a person-to-person outbreak (rather than a common source), HDs should use the outbreak variable in the core section. To indicate that a case of hepatitis A is part of a common-source outbreak, HDs are advised to use both the outbreak variable located in the core section and the outbreak variable(s) found in the hepatitis A condition-specific section.

5.3.2. Reporting Outbreak Source to NNDSS via NETSS

Table 5-4 describes the options for indicating the outbreak source for hepatitis A cases notified to NNDSS via NETSS.

Table 5-4. Variables indicating outbreak source for hepatitis A cases notified to the National Notifiable Diseases Surveillance System (NNDSS) via the National Electronic Telecommunications System for Surveillance

CDC Variable Name	Position (Column/ Length)	Description	Coding for Transmission to NNDSS
Outbr (Core Data)	55/1	Outbreak-associated	Indicates whether the case-report was associated with an outbreak. 1 = Case is outbreak-associated 2 = Case is not outbreak-associated 9 = Unknown
Outbreak (Hepatitis-Specific Data)	82/1	Common-source outbreak	Was the patient suspected as being part of a common-source outbreak? 1 = Yes 2 = No 9 = Unknown

To indicate that a hepatitis A case was associated with a person-to-person outbreak, use the following selections:

- Outbreak-associated (core data) = Yes **AND**
- Common-source outbreak (hepatitis A-specific data) = No

To indicate that a hepatitis A case was associated with a common-source (e.g., foodborne or waterborne) outbreak, use the following selections:

- Outbreak-associated (core data) = Yes **AND**
- Common-source outbreak (hepatitis A-specific data) = Yes

5.3.3. Reporting Outbreak Source to NNDSS via NBS

Table 5-5 describes the options for indicating the outbreak source for hepatitis A cases notified to NNDSS via NBS.

Table 5-5. Variables indicating outbreak source for hepatitis A cases notified to the National Notifiable Diseases Surveillance System (NNDSS) via the National Electronic Disease Surveillance System Base System (NBS)

NBS ID	NBS Label	Description	Coding for Transmission to NNDSS
INV150	OUTBREAK	Outbreak-associated	Indicates whether the case-report was associated with an outbreak. 1 = Case is outbreak-associated 2 = Case is not outbreak-associated 9 = Unknown
HEP143	AOUTBREAK	Common-source outbreak	Was the patient suspected as being part of a common-source foodborne or water borne outbreak? 1 = Yes 2 = No

To indicate that a hepatitis A case was associated with a person-to-person outbreak, use the following selections:

- INV150 = Yes **AND**
- HEP143 = No

To indicate that a hepatitis A case was associated with a common-source (e.g., foodborne or waterborne) outbreak, use the following selections:

- INV150 = Yes **AND**
- HEP143 = Yes

5.3.4. Reporting Outbreak Status to NNDSS via HL7 Case Notification

Table 5-6 describes the options for indicating the outbreak source for hepatitis A cases notified to NNDSS via HL7 case notification.

Table 5-6. Variables indicating outbreak source for hepatitis A cases notified to the National Notifiable Diseases Surveillance System via Health Level Seven case notification

PHIN Variable	OBX 3.1 Identifier	Data Element Name	Data Element Description
INV150	77980-1	Case outbreak indicator	Indicates whether the case report was associated with an outbreak.
INV618	INV618	Common-source outbreak	Is the subject suspected as being part of a common-source outbreak?
INV609	INV609	Foodborne outbreak; infected food handler	If yes, was the outbreak associated with an infected food handler?
INV610	INV610	Foodborne outbreak; not an infected food handler	If yes, was the outbreak not associated with an infected food handler?
INV612	INV612	Waterborne outbreak	If yes, was the outbreak waterborne?

Table 5-7 describes the selections that should be used to indicate the outbreak source for hepatitis A cases notified to NNDSS via HL7 case notification.

Table 5-7. Selections for variables indicating outbreak source for hepatitis A cases notified to the National Notifiable Diseases Surveillance System via Health Level Seven case notification

Hepatitis A Outbreak Scenario	Variable Selections				
	77980-1	INV618	INV609	INV610	INV612
Person-to-person outbreak	Yes	No	No	No	No
Foodborne outbreak, infected food handler	Yes	Yes	Yes	No	No
Foodborne outbreak, not infected food handler	Yes	Yes	No	Yes	No
Waterborne outbreak	Yes	Yes	No	No	Yes

5.4. Optional Data Sources to Supplement Viral Hepatitis Surveillance Systems

Supplementary data sources can be used to augment case surveillance data. For example, certain sources can provide information on progression of chronic infection to advanced liver disease or cancer; births to people of childbearing age with childbearing potential with HBV and HCV infection; deaths among patients; and data for missing demographic, risk, and vaccination status needed for completing case reports.

Even without linkage to case reports, supplementary data sources can be used to assess the extent of disease burden associated with viral hepatitis; track trends in risk behaviors or exposures and awareness of infection, and access to treatment; and monitor the impact of prevention and control programs or elimination plans. Some supplementary data sources provide information at the jurisdiction level, others provide only national level data*, and some provide both. Cost to jurisdictions also varies, with some data sources being free or low cost and others requiring substantial investment or a licensing fee, particularly data previously collected or compiled from multiple data providing organizations. Collaborations with universities, public health institutes, and other partners with capacity and experience in using these other data sources can be advantageous when a HD's resources are insufficient to support in-house use of one or more of these data sources.

*National data sources are noted to aid jurisdiction-level viral hepatitis epidemiologists in interpretation of published findings, not for analytic purposes.

Each type of data source and each specific source has unique strengths and limitations, making each one more suitable for certain uses and less suitable for others. None is a perfect substitute for another, so they should be viewed as a portfolio that can be used to provide a more complete overview of the burden of viral hepatitis in a jurisdiction. Awareness of these data sources and their uses is especially important before deciding to undertake additional data collection efforts and for prioritizing use of other supplementary data sources.

Table 5-8 lists some data sources that might be helpful in improving the understanding of the viral hepatitis burden in a jurisdiction.

Table 5-8. Supplementary data sources

Data Source	Representativeness	May Be Able to Link to Surveillance Data?	Additional Information
Registry/Surveillance System Data			
Accurint/LexisNexis	Jurisdiction-specific	No	https://www.accurint.com
Birth Certificates	National-level and jurisdiction-specific	Yes	https://www.cdc.gov/nchs/nvss/births.htm
Birth Defects Registry	Jurisdiction-specific	Yes	https://www.cdc.gov/ncbddd/birthdefects/data.html
Cancer Registry	National-level and jurisdiction-specific	Yes	https://www.cdc.gov/cancer/npcr/index.htm
Commercial Laboratory	US population-based	No (standalone system)	https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6606113/
Death Certificates	National-level and jurisdiction-specific	Yes	https://www.cdc.gov/nchs/nvss/deaths.htm
Enhanced HIV/AIDS Reporting System (eHARS)	National-level and jurisdiction-specific	Yes	https://www.cdc.gov/hiv/library/reports/hiv-surveillance.html
Immunization Registry	Jurisdiction-specific	Yes	https://www.cdc.gov/vaccines/programs/iis/index.html
National Death Index (NDI)	National-level and jurisdiction-specific	Yes	https://www.cdc.gov/nchs/ndi/index.htm
Ryan White Eligibility System (RWES)	National-level and jurisdiction-specific	Yes	https://hab.hrsa.gov/data/data-reports
Jurisdiction-specific Infectious Disease Surveillance Databases (e.g., HIV, STI, Tuberculosis Case Surveillance)	Jurisdiction-specific	Yes	
Jurisdiction-specific Non-infectious Disease Surveillance Databases (e.g., Cancer Registry and Injury Prevention)	Jurisdiction-specific	Yes	
Social Security Death Master File (SSDMF)	National-level and jurisdiction-specific	Yes	https://dmf.ntis.gov
Jurisdictional Corrections Information Systems	Jurisdiction-specific	Yes	

Data Source	Representativeness	May Be Able to Link to Surveillance Data?	Additional Information
Health Care Systems Data			
AIDS Drug Assistance Programs (ADAP)	Jurisdiction-specific	Yes	https://adap.directory
All-payers/Insurance Claims	Jurisdiction-specific	Yes	https://www.ahrq.gov/data/apcd/index.html https://www.cms.gov/OpenPayments/Explore-the-Data/Data-Overview
Electronic Medical Records (EMR) or Electronic Health Records (EHR)	Jurisdiction-specific	Yes	https://www.cancer.gov/publications/dictionaries/cancer-terms/def/electronic-medical-record
Electronic Case Reporting (eCR)	Jurisdiction-specific pilot study	Yes	https://www.cdc.gov/ecr/index.html
Hospital Discharge Databases	Jurisdiction-specific	Yes	https://www.cdc.gov/nchs/nhds/index.htm
Healthcare Cost and Utilization Project (HCUP)	National-level	No (standalone system)	https://www.hcup-us.ahrq.gov/overview.jsp
Pharmacy Claims	US-population-based	Yes	https://www.ajmc.com/journals/supplement/2019/burden-chronic-hepatitis-c/assessing-burden-illness-chronic-hepatitis-impact-antiviral-healthcare-costs-medicaid
Syndromic Surveillance for Injection Drug-Related Complaints, Non-Fatal Drug Overdoses	Jurisdiction-specific	Dependent on capabilities of surveillance system	https://www.cdc.gov/nssp/overview.html
Survey Data			
Behavioral Risk Factor Surveillance System (BRFSS)	Jurisdiction-specific	No (standalone system)	https://www.cdc.gov/brfss/index.html
Medical Monitoring Project (MMP) (e.g., HCV in medical chart review portion)	Jurisdiction-specific	Yes	https://www.cdc.gov/hiv/statistics/systems/mmp/index.html
National Health and Nutrition Examination Survey (NHANES)	National-level	No (standalone system)	https://www.cdc.gov/nchs/nhanes/index.htm
National HIV Behavioral Surveillance (HCV testing during IDU cycle)	Jurisdiction-specific	No (standalone system)	https://www.cdc.gov/hiv/statistics/systems/nhbs/index.html
National Health Interview Survey	National-level	No (standalone system)	https://www.cdc.gov/nchs/nhis/index.htm

Table 5-9 describes the usefulness of select data sources that might supplement case ascertainment, investigation, characterization, and for monitoring of infection trends and disease-related outcomes. Some data sources are more useful for certain purposes than others.

Table 5-9. Use of supplementary data sources for case ascertainment, investigation, characterization, and for monitoring of infection trends and disease-related outcomes

Data Source	Usefulness
Birth Certificates	Birth certificate data can be matched with surveillance data to identify infants born to gestational parents who are positive for hepatitis B and hepatitis C. Some jurisdictions' birth certificates also have indicators of a history of maternal hepatitis B and hepatitis C, which can help identify unreported cases, although the quality of these variables should be validated prior to use for case ascertainment. For hepatitis B, matching birth certificates to gestational parent-infant pairs in the Perinatal Hepatitis B Prevention Program and/or hepatitis B registry or database may be used to assess appropriate hepatitis B testing, and the administration of hepatitis B immunoglobulin and hepatitis B vaccine.
Death Certificates	Death certificate data can be used to identify people reported with viral hepatitis as the underlying or contributing cause of death. This information is stored in both text form and in ICD-10 codes. Though viral hepatitis infections are often underreported on death certificates, crossmatches between viral hepatitis surveillance data and death certificates can identify deaths among people known to have viral hepatitis and can characterize trends in mortality among affected populations.
All-payers/ Insurance Claims	These databases have information regarding specific medical claims and reimbursements (e.g., Medicaid data). When identifiable, viral hepatitis surveillance staff can match viral hepatitis surveillance data to these data sources to identify unreported cases and learn about case-specific viral hepatitis-related health care visits or costs and prescribed medications. If the database cannot be matched to viral hepatitis surveillance data, it can be used as a standalone system to a) provide estimates of viral hepatitis-related health care visits, prescriptions, and costs and b) assist in constructing the care and cure continuum in the jurisdiction.
Hospital Discharge Databases	Hospital discharge databases are maintained by many jurisdictions and contain data about hospital admissions. The databases generally contain inpatient records; other types of records (e.g., emergency department visits) are available in some jurisdictions. Some conditions, like endocarditis, are suggestive of risk behaviors (e.g., injection drug use) for viral hepatitis. Identifying the distribution of such conditions, such as data regarding the prevalence of injection drug use, can be used to inform hospitals of the need to test for viral hepatitis. Matching viral hepatitis surveillance data with hospital discharge databases can also help monitor disease severity, specifics of treatment, and cost of hospitalizations among specific populations.
Electronic Medical and Health Records (EHRs)	EHRs can be used to obtain additional patient data for case ascertainment, investigation, and classification (e.g., review negative laboratory results to clarify infection status, test results for other types of viral and non-viral hepatitis, and collect risk history). These data can also be used for identifying unreported cases in facilities that have data mining capabilities. EHRs can also potentially be used to identify missing data elements from known cases (e.g., race/ethnicity) through electronic case reporting, although EHR data quality and completeness varies depending on how data are stored.
Supplementary Laboratory Data	In addition to the positive viral hepatitis laboratory results that are routinely received by jurisdictions, some jurisdictions also receive non-positive laboratory results (e.g., undetectable HBV DNA and undetectable HCV RNA results). If available, viral hepatitis surveillance staff can use these data to identify acute cases by test conversion, differentiate between acute hepatitis B and hepatitis B reactivation, identify hepatitis C reinfection, determine if a laboratory result is likely false-positive, estimate hepatitis B and hepatitis C treatment coverage in their jurisdiction, and detect the prevalence of viral suppression in certain communities. Staff can use these data to clarify whether a positive HBV DNA or HCV RNA is in a chronic case, a reinfection (hepatitis C), a reactivation (hepatitis B), or possibly represents treatment failure. In addition, pregnancy status can be added to laboratory reports to encourage timely reporting of hepatitis B and hepatitis C in pregnancy.
Jurisdiction-specific Infectious Disease Surveillance Databases	Viral hepatitis surveillance data can be matched to other infectious disease surveillance databases (e.g., HIV, sexually transmitted infections, and tuberculosis) to obtain additional patient data for case investigation and classification. Matching viral hepatitis surveillance data with those for other infectious diseases can also be used to monitor rates of coinfection and inform data-to-care interventions.
Jurisdiction-specific Non-infectious Disease Surveillance Databases	Non-infectious disease surveillance data for related conditions can also be matched to viral hepatitis databases. For example, matching hepatitis B and hepatitis C databases to cancer registries or other chronic disease surveillance databases can be used to identify the prevalence of these outcomes among patients with chronic hepatitis B and hepatitis C. Data from injury prevention records can also be used to better characterize the intersecting epidemics of infectious diseases, opioid, methamphetamine, and other drug use disorder, and to inform the development of integrated public health interventions for people who use drugs.

If a jurisdiction decides to use medical claims or death certificate data to supplement their viral hepatitis surveillance data, International Statistical Classification of Diseases and Related Health Problems, Tenth Revision (ICD-10) codes are used in these data sources to categorize hepatitis A, hepatitis B, and hepatitis C diagnoses and causes of death. Table 5-10 lists the ICD-10 codes.

Table 5-10. International Statistical Classification of Diseases and Related Health Problems, Tenth Revision (ICD-10) codes for hepatitis A, hepatitis B, and hepatitis C for clinical diagnosis and cause of death coding

Condition	ICD-10 Codes
Hepatitis A	B15
Hepatitis B	B16, B17.0, B18.0, and B18.1
Hepatitis C	B17.1 and B18.2

Source: World Health Organization. ICD-10 Version: 2019. Available at: https://icd.who.int/browse10/2019/en#/. Accessed on May 20, 2021.

5.5. CDC Training Resources for Disease Investigation Specialists

Passport to Partner Services is a national training program that provides education materials and resources for disease investigation specialists (DIS) and other providers of partner services at no cost to the registrant[119]. This training program was developed by CDC's Division of HIV/AIDS Prevention and Division of STD Prevention in collaboration with the National Network of STD/HIV Prevention Training Centers. The training consists of two components: self-study online modules and in-person, classroom-based training. Passport to Partner Services provides training for conducting surveillance activities, including case investigation that, although it is specific to HIV and STIs, the concepts can be applied to viral hepatitis case investigation. Staff who are interested in taking the training can register by visiting the Passport to Partner Services website and following registration instructions.

DIS who perform viral hepatitis case investigations do not need to participate in the entire course, as not all material is relevant. The focus areas that are most applicable for viral hepatitis case investigation are:

- Introduction to partner services,
- Communication skills,
- Interviewing,
- Field investigation and notification, and
- Referrals and linkage to care.

5.6. CDC DVH Technical Assistance for Viral Hepatitis Surveillance

The Surveillance Team within DVH is responsible for viral hepatitis surveillance at the national level. The team works directly with viral hepatitis surveillance programs within state, territorial, and local HDs to ensure standardization of methodologies, including surveillance definitions and processes. The collaborative goal is to develop, implement, evaluate, and improve viral hepatitis surveillance to support and evaluate prevention policies and programs.

The Surveillance Team includes epidemiologists and statisticians with expertise in surveillance. Epidemiologists provide consultation in epidemiology, surveillance, study design, questionnaire design and development, data collection, epidemiologic methodology, data analyses, data interpretation, and information technology. Statisticians provide consultation in sample and study design, data standardization, data analyses, and statistical methodology. DVH's Surveillance Team provides HDs with technical assistance (TA) to evaluate state, territorial, and local programs to highlight strengths and identify areas for improvement; to outline goals and objectives and define activities that facilitate achievement of such goals and objectives; and identify and recommend resources to help programs address areas for improvement.

The team also works with partner organizations to address surveillance-related issues. For example, the Surveillance Team collaborates with CSTE members

to develop surveillance case definitions for nationally notifiable viral hepatitis conditions. Other partners work with DVH and the Surveillance Team to identify and address surveillance issues that impact specific populations (e.g., Asian Americans, African Americans, PWUD, and specific age groups).

The Epidemiology Research Team within DVH includes medical epidemiologists who work with the Surveillance Team to ensure that clinical aspects of viral hepatitis are included in all decisions. Medical epidemiologists also provide expert clinical consultation directly and indirectly to state and local programs.

TA is provided by e-mail, telephone, site visits, periodic group trainings during conferences, and webinars.

5.7. NASTAD HepTAC: Online TA and Capacity Building Center

In 2018, NASTAD was awarded funding through a CDC DVH cooperative agreement to provide TA to viral hepatitis prevention and surveillance programs within state and local HDs. In 2019, NASTAD introduced HepTAC, an online system that provides TA and capacity building for HD viral hepatitis programs[120]. The primary goals of HepTAC are to build jurisdiction-level technical expertise and enhance HD capacity to support viral hepatitis prevention, control, and elimination activities[120]. Goals are accomplished through collaborative activities, including conference calls, webinars, workgroups, bi-monthly newsletters, an online resource bank, and a discussion board. Success stories are shared, and mentorships and courses are offered in the following tracks:

1. Hepatitis program infrastructure and workforce;
2. Community engagement and strategic planning;
3. Harm reduction and prevention;
4. Epidemiology and surveillance;
5. Testing and linkage to care;
6. Care and treatment;
7. Stigma and health equity; and
8. Elimination[120].

One-on-one viral hepatitis surveillance and prevention TA is provided by logging in to HepTAC's Online Technical Assistance Platform (OnTAP) and submitting an inquiry[121].

6. Appendices

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Appendix A. Glossary

42 Code of Federal Regulations (CFR) Part 2: A federal regulation that protects the confidentiality of substance use disorder client records with no exemption for public health access without specific consent.

Acute viral hepatitis: The early stage of a viral infection of the liver caused by one of five different hepatitis viruses (A, B, C, D, or E). Signs and symptoms of early (or acute) viral hepatitis include yellowing of the skin or eyes (jaundice), abdominal pain, vomiting, nausea, diarrhea, malaise, grey-colored stools, and dark urine. For hepatitis B, hepatitis C, hepatitis D, and hepatitis E, acute infection can lead to chronic infection.

Case status: The classification of the condition utilizing the Centers for Disease Control and Prevention (CDC)/Council of State and Territorial Epidemiologists (CSTE) viral hepatitis case definitions (i.e., confirmed, probable, and not a case).

Chronic viral hepatitis: A long-term illness that occurs when a hepatitis virus infection persists. Chronic hepatitis can last a lifetime and lead to serious liver problems, including liver cirrhosis and liver cancer.

Coinfection: Simultaneous infection with two or more separate pathogens.

Condition: In regard to viral hepatitis, the type of infection and situation (e.g., hepatitis A, acute hepatitis B, chronic hepatitis B, perinatal hepatitis B, hepatitis B during pregnancy, acute hepatitis C, chronic hepatitis C, perinatal hepatitis C, and hepatitis C during pregnancy).

Event: A paper or electronic laboratory report, or an occurrence of disease or reportable condition.

Event code: A standardized, unique code that is assigned to each disease or condition to simplify storage and retrieval of information about cases transmitted to the National Notifiable Diseases Surveillance System (NNDSS).

Event date: A variable in the National Notifiable Diseases Surveillance System generated by the Center for Surveillance, Epidemiology, and Laboratory Services that is based on a hierarchy of dates. In decreasing order of specificity, these are date of disease/symptom onset, date of specimen collection/diagnosis, date of laboratory result receipt, date of first report to health department, and state/territory or MMWR report date.

Field-based or community-based staff: Terms used to describe health department staff (such as disease intervention specialists or DIS) who conduct patient and provider interviews.

HBV-infected: People who are positive for hepatitis B surface antigen (HBsAg) and/or hepatitis B virus deoxyribonucleic acid (HBV DNA).

HCV detection test: A nucleic acid test (NAT) for hepatitis C virus (HCV) ribonucleic acid (RNA) may be qualitative, quantitative, or done for genotype testing, or a test indicating the presence of HCV antigen. At present, no HCV antigen tests are approved by the US Food and Drug Administration (FDA). When these tests become available, they will serve as acceptable laboratory criteria for active infection, equivalent to HCV RNA testing.

HCV-positive: People who are either: 1) positive for HCV RNA; or 2) positive for HCV antibody with no evidence of an HCV RNA test being conducted. Until the HCV RNA status is known, out of caution, cases should be considered HCV-positive for perinatal HCV exposures and pregnant people.

Hepatitis A: A vaccine-preventable, communicable disease of the liver caused by the hepatitis A virus (HAV) and usually transmitted person-to-person through the fecal-oral route or consumption of contaminated food or water. Hepatitis A is a self-limited disease that does not result in chronic infection.

Hepatitis B: A vaccine-preventable, communicable disease of the liver caused by HBV and transmitted when blood, semen, or another body fluid from an infected person enters the body of someone who is not infected, including from parent to child at birth. Hepatitis B can be a short-term illness, but for others, it can become a long-term, chronic infection. The likelihood of chronic infection is inversely associated with age at infection.

Hepatitis C: A communicable disease of the liver caused by HCV transmitted when blood from an infected person enters the body of someone who is not infected, including from parent to child at birth. Hepatitis C can be a short-term illness, but for approximately three fourths of people who become infected, it can become a long-term, chronic infection.

HIPAA Privacy Rule 45 CFR 164.512(b): A federal privacy rule that allows public health authorities and others responsible for protecting the public's health and safety to collect and receive protected health information without patient authorization for the purpose of preventing and/or controlling disease, injury or disability, including the conducting of public health surveillance, public health investigations, and public health interventions.

Investigation start date: The date a case investigation was opened.

Laboratory report: A paper or electronic laboratory report entered within a jurisdiction's surveillance system.

Medication assisted treatment (MAT): Medication assisted treatment is the use of opioid substitution medication for opioid use disorder (MOUD) in conjunction with a variety of behavioral support interventions. See also medication for opioid use disorder.

Medication for opioid use disorder (MOUD): Any licensed medication such as methadone, buprenorphine or naltrexone used for treatment of opioid use disorder. For information on MOUD, visit the Substance Abuse and Mental Health Services Administration (SAMHSA) and the Providers Clinical Support System websites.

NNDSS Modernization Initiative: A multi-year initiative under the CDC Surveillance Strategy that aims to enhance the ability of NNDSS to provide more comprehensive, timely, and higher quality data for public health decision making. The NNDSS Modernization Initiative involves collaboration with disease-specific programs at CDC and health departments to develop disease-specific data elements for new message mapping guides (MMGs) for Health Level 7 (HL7)-formatted disease case notification. CDC is increasing the robustness of the NNDSS technological infrastructure so that it is based on interoperable, standardized data and exchange mechanisms.

Notifiable: The conditions that CSTE recommends state and territorial health departments perform surveillance upon and notify to CDC.

Opioid use disorder: Substance use disorder involving opioid medications. See substance use disorder.

Pregnant person, person of childbearing age with childbearing potential, and gestational parent: Terminology used to describe a parent who is pregnant, has the potential to become pregnant, or has physically given birth, regardless of gender.

Print criteria: The standards under which CDC can publish case information, as determined by CSTE and CDC and listed in CSTE's Position Statements.

Reportable: The conditions that are required to be reported to the local, state or territorial health department.

Substance use disorder: A medical condition of addiction in which a person is compelled by physiological dependence on a legal or illegal drug. For more information, review the consumer version of the Merck Manual on substance use disorders.

Surveillance case definition: Criteria defined in CSTE's Position Statements to provide uniform case ascertainment, case classification, and consistent national notification of nationally notifiable conditions.

Superinfection: A second infection that occurs in addition to an existing infection.

Suspected hepatitis A and/or B vaccine failure: Occurs when a person who has completed the hepatitis A and/or hepatitis B vaccine series according to the appropriate immunization schedule becomes infected >30 days after vaccine series completion.

Sustained virologic response: Occurs when a person's HCV infection is considered to be cured when HCV RNA is undetectable in the blood at or after 12 weeks following treatment completion.

Syringe services program (SSP): A community-based facility, mobile unit, or other organized program whose mission includes distribution of sterile paraphernalia for injection of drugs and safe disposal of used paraphernalia without stigma or judgement. Paraphernalia includes syringes, needles, cookers and all other needed supplies for injection of drugs. Comprehensive SSPs include not only distribution and safe disposal of injection supplies, but multiple other services needed by people who inject drugs including, but not limited to, naloxone distribution and training; vaccination for hepatitis A and hepatitis B; testing and treatment or linkage to treatment for HBV, HCV, HIV, and sexually transmitted infections; pre-exposure prophylaxis for HIV; treatment or linkage to treatment for substance use disorder; and patient-centered reproductive health care, including access to long-acting reversible contraceptives. For more information, visit the CDC website on SSPs.

Window period: The period of time after a person is infected with a communicable disease but before laboratory eveidence (e.g., antibodies) of infection is detectable on testing. During the window period, a patient's antibody test will be negative even though the patient is infected.

Appendix B. Description of Hepatitis A, Hepatitis B, and Hepatitis C Laboratory Markers

Viral Hepatitide	Laboratory Marker	Description
Hepatitis A	Immunoglobulin M antibody to hepatitis A virus (anti-HAV IgM)	Indicates hepatitis A virus (HAV) infection. On average, appears approximately 5–10 days before the onset of clinical symptoms and can circulate for up to 6 months in the bloodstream following infection.
	Immunoglobulin G antibody to hepatitis A virus (anti-HAV IgG)	Indicates recovery from HAV infection, past infection, or vaccine-induced immunity. Remains in serum for life-long protection.
	Total hepatitis A virus antibody (total anti-HAV)	Indicates current HAV infection (if also positive for anti-HAV IgM) or immunity to hepatitis A from past infection or vaccination (negative for anti-HAV IgM). Consists of both IgM and IgG class antibodies.
	Hepatitis A virus ribonucleic acid (HAV RNA)	Indicates current HAV infection. During an outbreak, people might be tested for the presence of HAV RNA, and if detectable, HAV may be genotyped for specific strain of virus. HAV RNA is the most sensitive and specific indicator of current infection, and if quantified, correlates with levels of HAV in serum or plasma, measured in IU/mL.
	HAV genotype	Categorizes the specific HAV genetic strain with which a person is infected. When a genotype is determined, it indicates detection of current HAV infection.
Hepatitis B	Hepatitis B surface antigen (HBsAg)	Indicates current hepatitis B virus (HBV) infection. Also indicates chronic hepatitis B in those who are positive for HBsAg for ≥6 months.
	IgM antibody to hepa-titis B core antigen (anti-HBc IgM)	Indicates acute HBV infection.
	Total hepatitis B core antibody (total anti-HBc)	Indicates current hepatitis B (in someone with a positive HBsAg) or past hepatitis B (in someone with a negative HBsAg). On average, appears approximately 5 weeks post HBV exposure. Consists of both IgM and IgG class antibodies. After approximately 6 months, anti-HBc IgM becomes undetectable, whereas anti-HBc IgG persists indefinitely.
	Hepatitis B surface antibody (anti-HBs)	Indicates recovery and immunity from hepatitis B. Anti-HBs is also detected in people who develop immunity through hepatitis B vaccination. According to the World Health Organization, anti-HBs levels ≥10mIU/mL indicate adequate immunity.
	Hepatitis B virus de-oxyribonucleic acid (HBV DNA)	Indicates chronic hepatitis B in those with detectable HBV DNA for ≥6 months and occult hepatitis B and HBsAg mutant infection in those who test positive but are negative for HBsAg. It is the most sensitive and specific indicator of current infection, and if quantified, correlates with levels of HBV in serum or plasma, measured in IU/mL.
	HBV genotype	Categorizes the specific HBV genetic strain with which a person is infected, which can affect the natural history of chronic infection. When a genotype is determined, it indicates current detection of HBV infection.
	Hepatitis B envelope antigen (HBeAg)	Indicates current infection. The presence of HBeAg indicates that the virus is replicating, and the infected person is likely to have high levels of HBV DNA.
	Hepatitis B envelope antibody (anti-HBe)	Spontaneous conversion from e antigen positivity to e antibody positivity (a change known as “seroconversion”) develops after resolution of acute infection and can occur spontaneously in the evolution of chronic infection. Seroconversion also may happen among HBeAg-positive, chronically infected people after they receive treatment. This marker is not used in hepatitis B surveillance case classification.

Viral Hepatitide	Laboratory Marker	Description
Hepatitis C	HCV antibody (anti-HCV)	Indicates current hepatitis C [in someone with a positive hepatitis C virus (HCV) detection test] or past HCV infection (in someone with a negative HCV detection test). On average, becomes detectable by current HCV immunoassay tests approximately 8–11 weeks post HCV exposure.
	Hepatitis C virus ribo-nucleic acid (HCV RNA)	Indicates current HCV infection. Also indicates chronic hepatitis C in those who have detectable HCV RNA for ≥6 months. On aver-age, HCV RNA becomes detectable approximately 1–2 weeks post HCV exposure. HCV RNA represents the most sensitive and specific indicator of current infection, and if quantified, correlates with levels of HCV in serum or plasma, measured in IU/mL.
	HCV core antigen	Indicates current HCV infection. Also indicates chronic HCV infec-tion in those who are positive for HCV core antigen for ≥6 months. Can be used as an alternative to HCV RNA as an indicator of active infection. No HCV core antigen tests have approved by the US Food and Drug Administration (FDA). When these tests become available, they will serve as acceptable laboratory criteria for active infection, equivalent to HCV RNA testing.
	HCV genotype	Categorizes the specific HCV genetic strain, which can affect the natural history of chronic infection. When a genotype is determined, it indicates current HCV infection.

Appendix C. Classification Scenarios for Cases of Hepatitis A, Hepatitis B, and Hepatitis C

Cases of hepatitis A; acute, chronic, and perinatal hepatitis B; and acute, chronic, and perinatal hepatitis C should be classified in accordance with their respective CDC/CSTE surveillance case definition. The scenarios provided in the following tables can serve as guidance for classification of these cases. Technical assistance is available for more complex scenarios by contacting the assigned regional CDC DVH technical assistance team.

Classification Scenarios for Cases of Hepatitis A

Scenario 1: A primary care provider reported a case of hepatitis A. The patient had a positive anti-HAV IgM test result, and the provider reported abdominal pain, dark urine, and nausea. Liver function tests show a total bilirubin level of 6.2 mg/dL, and there is not a more likely diagnosis than hepatitis A. You were not able to find this patient in the surveillance system.

Case Classification Criteria	Scenario	Rationale for Classification
Does this meet the laboratory or epidemiologic linkage criterion?		
Lab criterion 1: anti-HAV IgM	Positive	**Needs to meet at least 1:** ☑ Positive anti-HAV IgM ☐ Positive HAV RNA ☐ Epi-linked
Lab criterion 2: HAV RNA	Unknown	
Epidemiologic linkage: Contact with lab-confirmed hepatitis A case during exposure period	Unknown	
Does this meet all 3 clinical criteria?		
Clinical criterion 1: Jaundice or peak elevated total bilirubin ≥3.0 mg/dL or peak elevated ALT >200 IU/L	Present	**Needs to meet all 3 unless lab criterion 2 is met:** ☑ Jaundice or elevated total bilirubin or elevated ALT ☑ Acutely symptomatic ☑ Absence of more likely diagnosis
Clinical criterion 2: Distinct episode of symptoms consistent with acute viral hepatitis	Present	
Clinical criterion 3: Alternate, more likely diagnosis	Absent	
Is this a new event?		
Is the patient newly reported (i.e., not a relapse case)?	Yes	**Needs to be newly reported event:** ☑ Newly reported
Classification: This patient meets the classification criteria for confirmed hepatitis A.		

Scenario 2: The HD received a positive HAV RNA laboratory result from a local plasma donation center. The patient does not have a more likely diagnosis than hepatitis A, and the donor was not located in the surveillance system.

Case Classification Criteria	Scenario	Rationale for Classification
Does this meet the laboratory or epidemiologic linkage criterion?		
Lab criterion 1: anti-HAV IgM	Unknown	**Needs to meet at least 1:** ☐ Positive anti-HAV IgM ☑ Positive HAV RNA ☐ Epi-linked
Lab criterion 2: HAV RNA	Positive	
Epidemiologic linkage: Contact with lab-confirmed hepatitis A case during exposure period	Unknown	
Does this meet all 3 clinical criteria?		
Clinical criterion 1: Jaundice or peak elevated total bilirubin ≥3.0 mg/dL or peak elevated ALT >200 IU/L	Not needed	**Needs to meet all 3 unless lab criterion 2 is met:** ☐ Jaundice or elevated total bilirubin or elevated ALT ☐ Acutely symptomatic ☑ Absence of more likely diagnosis
Clinical criterion 2: Distinct episode of symptoms consistent with acute viral hepatitis	Not needed	
Clinical criterion 3: Alternate, more likely diagnosis	Absent	
Is this a new event?		
Is the patient newly reported (i.e., not a relapse case)?	Yes	**Needs to be newly reported event:** ☑ Newly reported
Classification: This patient meets the classification criteria for confirmed hepatitis A.		

Scenario 3: The HD received an electronic laboratory report from a hospital for a patient who is positive for anti-HAV IgM. After speaking with the infection preventionist, the surveillance staff member learned that the patient has symptoms of vomiting, abdominal pain, and weakness. Liver function tests show an ALT level of 1,347 IU/L, and there is a diagnosis of acetaminophen toxicity.

Case Classification Criteria	Scenario	Rationale for Classification
Does this meet the laboratory or epidemiologic linkage criterion?		
Lab criterion 1: anti-HAV IgM	Present	**Needs to meet at least 1:** ☑ Positive anti-HAV IgM ☐ Positive HAV RNA ☐ Epi-linked
Lab criterion 2: HAV RNA	Unknown	
Epidemiologic linkage: Contact with lab-confirmed hepatitis A case during exposure period	Unknown	
Does this meet all 3 clinical criteria?		
Clinical criterion 1: Jaundice or peak elevated total bilirubin ≥3.0 mg/dL or peak elevated ALT >200 IU/L	Present	**Needs to meet all 3 unless lab criterion 2 is met:** ☑ Jaundice or elevated total bilirubin or elevated ALT ☑ Acutely symptomatic ☐ Absence of more likely diagnosis
Clinical criterion 2: Distinct episode of symptoms consistent with acute viral hepatitis	Present	
Clinical criterion 3: Alternate, more likely diagnosis	Present	
Is this a new event?		
Is the patient newly reported (i.e., not a relapse case)?	Yes	**Needs to be newly reported event:** ☑ Newly reported
Classification: This patient does not meet the classification criteria for confirmed hepatitis A.		

Classification Scenarios for Cases of Acute Hepatitis B

Scenario 1: A primary care provider contacted the HD to report a positive HBsAg test result from a person 49 years of age. The patient's anti-HBc IgM status is unknown. The patient has jaundice, abdominal pain, dark urine, and nausea. Liver function tests show an ALT level of 453 IU/L. This patient was not found in the surveillance system as an acute or chronic hepatitis B case.

Case Classification Criteria	Scenario	Rationale for Classification
Does this meet age criterion?		
Age criterion: >24 months of age (or mode of exposure is not perinatal if ≤24 months of age)	49 years of age	**Needs to meet age criterion:** ☑ Age criterion
Does this meet laboratory criteria?		
Lab criterion 1: HBsAg	Positive	**Needs to meet lab criteria 1 and 2 (if case is not an HBsAg test conversion):** ☑ Positive HBsAg ☑ Positive or unknown anti-HBc IgM ☐ Documented HBsAg test conversion
Lab criterion 2: anti-HBc IgM	Not done	
Lab criterion 3: HBsAg test conversion from negative to positive within 6 months*	Not documented	
Does this meet clinical criteria?		
Clinical criterion 1: Jaundice or peak elevated ALT >100 IU/L	Present	**Need to meet both criteria unless HBsAg test conversion criterion is met:** ☑ Jaundice or elevated ALT ☑ Acutely symptomatic
Clinical criterion 2: Distinct episode of symptoms consistent with acute viral hepatitis	Present	
Is this a new event?		
New event criterion: Is the patient newly reported?	Yes	**Needs to be newly reported event:** ☑ Newly reported
Classification: This patient meets the classification criteria for confirmed acute hepatitis B.		

*Negative HBsAg laboratory test within 6 months prior to a positive test for either HBsAg, HBeAg, or HBV DNA (including qualitative, quantitative, or genotype).

Scenario 2: The HD received a positive HBsAg laboratory result from a regular donor 52 years of age at a local plasma donation center in June. The patient had a previous negative HBsAg laboratory result in February.

Case Classification Criteria	Scenario	Rationale for Classification
Does this meet age criterion?		
Age criterion: >24 months of age (or mode of exposure is not perinatal if ≤24 months of age)	52 years of age	**Needs to meet age criterion:** ☑ Age criterion
Does this meet laboratory criteria?		
Lab criterion 1: HBsAg	Positive	**Needs to meet lab criteria 1 and 2 (if case is not an HBsAg test conversion):** ☑ Positive HBsAg ☑ Positive or unknown anti-HBc IgM ☑ Documented HBsAg test conversion
Lab criterion 2: anti-HBc IgM	Not done	
Lab criterion 3: HBsAg test conversion from negative to positive within 6 months*	Documented	
Does this meet clinical criteria?		
Clinical criterion 1: Jaundice or peak elevated ALT >100 IU/L	Not needed	**Needs to meet both criteria unless HBsAg test conversion criterion is met:** ☐ Jaundice or elevated ALT ☐ Acutely symptomatic
Clinical criterion 2: Distinct episode of symptoms consistent with acute viral hepatitis	Not needed	
Is this a new event?		
New event criterion: Is the patient newly reported?	Yes	**Needs to be newly reported event:** ☑ Newly reported
Classification: This patient meets the classification criteria for confirmed acute hepatitis B.		

*Negative HBsAg laboratory test within 6 months prior to a positive test for either HBsAg, HBeAg, or HBV DNA (including qualitative, quantitative, or genotype).

Scenario 3: The HD received a positive HBsAg laboratory result and a positive anti-HBc IgM laboratory result on a person 37 years of age. Liver function tests show an ALT level of 226 IU/L. The patient has abdominal pain and nausea. The patient was not an acute or chronic hepatitis B case in the surveillance system.

Case Classification Criteria	Scenario	Rationale for Classification
Does this meet age criterion?		
Age criterion: >24 months of age (or mode of exposure is not perinatal if ≤24 months of age)	37 years of age	**Needs to meet age criterion:** ☑ Age criterion
Does this meet laboratory criteria?		
Lab criterion 1: HBsAg	Positive	**Needs to meet lab criteria 1 and 2 (if case is not an HBsAg test conversion):** ☑ Positive HBsAg ☑ Positive or unknown anti-HBc IgM ☐ Documented HBsAg test conversion
Lab criterion 2: anti-HBc IgM	Positive	
Lab criterion 3: HBsAg test conversion from negative to positive within 6 months*	Not documented	
Does this meet clinical criteria?		
Clinical criterion 1: Jaundice or peak elevated ALT >100 IU/L	Present	**Needs to meet both criteria unless HBsAg test conversion criterion is met:** ☑ Jaundice or elevated ALT ☑ Acutely symptomatic
Clinical criterion 2: Distinct episode of symptoms consistent with acute viral hepatitis	Present	
Is this a new event?		
New event criterion: Is the patient newly reported?	Yes	**Needs to be newly reported event:** ☑ Newly reported
Classification: This patient meets the classification criteria for confirmed acute hepatitis B.		

*Negative HBsAg laboratory test within 6 months prior to a positive test for either HBsAg, HBeAg, or HBV DNA (including qualitative, quantitative, or genotype).

Scenario 4: The HD received a positive anti-HBc IgM laboratory result. The surveillance staff contacted the ordering provider and determined that the patient tested negative for HBsAg. The patient does not have symptoms consistent with acute viral hepatitis, and liver function tests are normal. The patient is 38 years of age. The patient was not an acute or chronic hepatitis B case in the surveillance system.

Case Classification Criteria	Scenario	Rationale for Classification
Does this meet age criterion?		
Age criterion: >24 months of age (or mode of exposure is not perinatal if ≤24 months of age)	38 years of age	**Needs to meet age criterion:** ☑ Age criterion
Does this meet laboratory criteria?		
Lab criterion 1: HBsAg	Negative	**Needs to meet lab criteria 1 and 2 (if case is not an HBsAg test conversion):** ☐ Positive HBsAg ☑ Positive or unknown anti-HBc IgM ☐ Documented HBsAg test conversion
Lab criterion 2: anti-HBc IgM	Positive	
Lab criterion 3: HBsAg test conversion from negative to positive within 6 months*	Not documented	
Does this meet clinical criteria?		
Clinical criterion 1: Jaundice or peak elevated ALT >100 IU/L	No	**Needs to meet both criteria unless HBsAg test conversion criterion is met:** ☐ Jaundice or elevated ALT ☐ Acutely symptomatic
Clinical criterion 2: Distinct episode of symptoms consistent with acute viral hepatitis	No	
Is this a new event?		
New event criterion: Is the patient newly reported?	Yes	**Needs to be newly reported event:** ☑ Newly reported
Classification: This patient does not meet the classification criteria for confirmed acute hepatitis B. The positive anti-HBc IgM result is likely false-positive.		

*Negative HBsAg laboratory test within 6 months prior to a positive test for either HBsAg, HBeAg, or HBV DNA (including qualitative, quantitative, or genotype).

Classification Scenarios for Cases of Chronic Hepatitis B

Scenario 1: The HD received a positive HBV DNA laboratory result on a person 28 years of age. The patient was an existing acute hepatitis B case in the HD's surveillance system from a previous year (i.e., a positive HBsAg laboratory result with met clinical criteria).

Case Classification Criteria	Scenario	Rationale for Classification
Does this meet age criterion?		
Age criterion: >24 months of age (or mode of exposure is not perinatal if ≤24 months of age)	28 years of age	**Needs to meet age criterion:** ☑ Age criterion
Does this case have diagnostic laboratory evidence?		
Lab criterion 1: Negative anti-HBc IgM **and** positive for HBsAg, HBV DNA, or HBeAg	Not documented	**Confirmed if meets 1 diagnostic lab criterion:** ☐ Negative anti-HBc IgM **and** positive for HBsAg, HBV DNA, or HBeAg ☑ Positive for any combination of the following tests 2 times at least 6 months apart: HBsAg, HBV DNA, or HBeAg
Lab criterion 2: Positive for any combination of the following tests 2 times at least 6 months apart: HBsAg, HBV DNA, or HBeAg	Documented (Positive HBsAg followed by positive HBV DNA)	
Does this case have presumptive laboratory evidence?		
Lab criterion 1: A single positive HBsAg, HBV DNA, or HBeAg test (and does not meet the case definition for acute hepatitis B)	No	**Probable if meets presumptive lab criterion:** ☐ Single positive HBsAg, HBV DNA or HBeAg (and does not meet the case definition for acute hepatitis B)
Is this a new event?		
New event criterion 1: Is the patient newly reported?	No	**Needs to meet 1 new event criterion:** ☐ Newly reported ☑ If previously reported acute event, the event occurred in a prior MMWR year
New event criterion 2: Does the patient have an acute hepatitis B event in the surveillance system from a previous MMWR year?	Yes	
Classification: This patient meets the classification criteria for confirmed chronic hepatitis B.		

Scenario 2: The HD received a positive HBsAg laboratory result on a person 42 years of age. The anti-HBc IgM result was unknown. The case report form filled out by the provider did not indicate that the patient had any clinical signs or symptoms of acute viral hepatitis. The patient was not an acute or chronic hepatitis B case in the surveillance system.

Case Classification Criteria	Scenario	Rationale for Classification
Does this meet age criterion?		
Age criterion: >24 months of age (or mode of exposure is not perinatal if ≤24 months of age)	42 years of age	**Needs to meet age criterion:** ☑ Age criterion
Does this case have diagnostic laboratory evidence?		
Lab criterion 1: Negative anti-HBc IgM **and** positive for HBsAg, HBV DNA, or HBeAg	Not documented (anti-HBc IgM result unknown)	**Confirmed if meets 1 diagnostic lab criterion:** ☐ Negative anti-HBc IgM **and** positive for HBsAg, HBV DNA, or HBeAg ☐ Positive for any combination of the following tests 2 times at least 6 months apart: HBsAg, HBV DNA, or HBeAg
Lab criterion 2: Positive for any combination of the following tests 2 times at least 6 months apart: HBsAg, HBV DNA, or HBeAg	Not documented	
Does this case have presumptive laboratory evidence?		
Lab criterion 1: A single positive HBsAg, HBV DNA, or HBeAg test (and does not meet the case definition for acute hepatitis B)	Yes	**Probable if meets presumptive lab criterion:** ☑ Single positive HBsAg, HBV DNA or HBeAg (and does not meet the case definition for acute hepatitis B)
Is this a new event?		
New event criterion 1: Is the patient newly reported?	Yes	**Needs to meet 1 new event criterion:** ☑ Newly reported ☐ If previously reported acute event, the event occurred in a prior MMWR year
New event criterion 2: Does the patient have an acute hepatitis B event in the surveillance system from a previous MMWR year?	No	
Classification: This patient meets the classification criteria for probable chronic hepatitis B.		

Scenario 3: The surveillance staff member was later able to contact the provider of the patient from Scenario 2 and obtained the anti-HBc IgM result, which was negative and had the same specimen collection date as the positive HBsAg result.

Case Classification Criteria	Scenario	Rationale for Classification
Does this meet age criterion?		
Age criterion: >24 months of age (or mode of exposure is not perinatal if ≤24 months of age)	42 years of age	**Needs to meet age criterion:** ☑ Age criterion
Does this case have diagnostic laboratory evidence?		
Lab criterion 1: Negative anti-HBc IgM **and** positive for HBsAg, HBV DNA, or HBeAg	Documented	**Confirmed if meets 1 diagnostic lab criterion:** ☑ Negative anti-HBc IgM **and** positive for HBsAg, HBV DNA, or HBeAg ☐ Positive for any combination of the following tests 2 times at least 6 months apart: HBsAg, HBV DNA, or HBeAg
Lab criterion 2: Positive for any combination of the following tests 2 times at least 6 months apart: HBsAg, HBV DNA, or HBeAg	Not documented	
Does this case have presumptive laboratory evidence?		
Lab criterion 1: A single positive HBsAg, HBV DNA, or HBeAg test (and does not meet the case definition for acute hepatitis B)	No	**Probable if meets presumptive lab criterion:** ☐ Single positive HBsAg, HBV DNA or HBeAg (and does not meet the case definition for acute hepatitis B)
Is this a new event?		
New event criterion 1: Is the patient newly reported?	Yes	**Needs to meet 1 new event criterion:** ☑ Newly reported ☐ If previously reported acute event, the event occurred in a prior MMWR year
New event criterion 2: Does the patient have an acute hepatitis B event in the surveillance system from a previous MMWR year?	No	
Classification: This patient meets the classification criteria for confirmed chronic hepatitis B. Reclassify the case and update the case notification from probable chronic hepatitis B to confirmed chronic hepatitis B.		

Classification Scenarios for Cases of Perinatal Hepatitis B

Scenario 1: A provider contacted the HD to report a positive HBsAg test result in an infant 12 months of age. The infant's gestational parent was positive for HBsAg at the time of delivery, and the birth occurred at a local hospital. The infant's anti-HBs result, also performed at 12 months of age as part of PVST, was negative. The infant could not be matched with an existing case of hepatitis B in the surveillance system.

Case Classification Criteria	Scenario	Rationale for Classification
Does this meet demographic criteria?		
Demographic criterion 1: 1–24 months of age	12 months of age	**Needs to meet both demographic criteria:** ☑ 1–24 months of age ☑ Birth occurred in the United States
Demographic criterion 2: Birth occurred in the United States	Documented	
Does this meet epidemiologic linkage criterion?		
Epidemiologic linkage criterion: Birth to an HBV-infected gestational parent	Documented	**Confirmed if case meets epidemiologic linkage criterion; probable if case does not meet epidemiologic linkage criterion:** ☑ Epidemiologic linkage criterion
Does this meet at least 1 laboratory criterion?		
Lab criterion 1: HBsAg during 1–24 months of age	Positive	**Needs to meet at least 1 lab criterion:** ☑ Positive HBsAg during 1–24 months of age ☐ Positive HBeAg during 9–24 months of age ☐ Positive HBV DNA during 9–24 months of age
Lab criterion 2: HBeAg during 9–24 months of age	Unknown	
Lab criterion 3: HBV DNA during 9–24 months of age	Unknown	
Is this a new event?		
New event criterion: Is the patient newly reported?	Yes	**Needs to be newly reported event:** ☑ Newly reported
Classification: This patient meets the classification criteria for confirmed perinatal hepatitis B.		

Scenario 2: A provider contacted the HD to report a positive HBsAg test result in an infant 9 months of age. The test was performed 2 months after receipt of the last dose of hepatitis B vaccine, and the birth occurred at a local hospital. Information could not be obtained on the gestational parent's HBsAg or HBV DNA status at the time of delivery. The infant could not be matched with an existing case of hepatitis B in the surveillance system.

Case Classification Criteria	Scenario	Rationale for Classification
Does this meet demographic criteria?		
Demographic criterion 1: 1–24 months of age	9 months of age	**Needs to meet both demographic criteria:** ☑ 1–24 months of age ☑ Birth occurred in the United States
Demographic criterion 2: Birth occurred in the United States	Documented	
Does this meet epidemiologic linkage criterion?		
Epidemiologic linkage criterion: Birth to an HBV-infected gestational parent	Unknown	**Confirmed if case meets epidemiologic linkage criterion; probable if case does not meet epidemiologic linkage criterion:** ☐ Epidemiologic linkage criterion
Does this meet at least 1 laboratory criterion?		
Lab criterion 1: HBsAg during 1–24 months of age	Positive	**Needs to meet at least 1 lab criterion:** ☑ Positive HBsAg during 1–24 months of age ☐ Positive HBeAg during 9–24 months of age ☐ Positive HBV DNA during 9–24 months of age
Lab criterion 2: HBeAg during 9–24 months of age	Unknown	
Lab criterion 3: HBV DNA during 9–24 months of age	Unknown	
Is this a new event?		
New event criterion: Is the patient newly reported?	Yes	**Needs to be newly reported event:** ☑ Newly reported
Classification: This patient meets the classification criteria for probable perinatal hepatitis B. This case may be reclassified as confirmed perinatal hepatitis B if the gestational parent's HBsAg or HBV DNA status is verified to be positive.		

Scenario 3: The HD received a positive HBV DNA laboratory result on a child 18 months of age who recently immigrated to the United States. Through follow-up investigation, it was determined that the gestational parent has chronic hepatitis B. The infant could not be matched with an existing case of hepatitis B in the surveillance system.

Case Classification Criteria	Scenario	Rationale for Classification
Does this meet demographic criteria?		
Demographic criterion 1: 1–24 months of age	18 months of age	**Needs to meet both demographic criteria:** ☑ 1–24 months of age ☐ Birth occurred in the United States
Demographic criterion 2: Birth occurred in the United States	No	
Does this meet epidemiologic linkage criterion?		
Epidemiologic linkage criterion: Birth to an HBV-infected gestational parent	Documented	**Confirmed if case meets epidemiologic linkage criterion; probable if case does not meet epidemiologic linkage criterion:** ☑ Epidemiologic linkage criterion
Does this meet at least 1 laboratory criterion?		
Lab criterion 1: HBsAg during 1–24 months of age	Unknown	**Needs to meet at least 1 lab criterion:** ☐ Positive HBsAg during 1–24 months of age ☐ Positive HBeAg during 9–24 months of age ☑ Positive HBV DNA during 9–24 months of age
Lab criterion 2: HBeAg during 9–24 months of age	Unknown	
Lab criterion 3: HBV DNA during 9–24 months of age	Positive	
Is this a new event?		
New event criterion: Is the patient newly reported?	Yes	**Needs to be newly reported event:** ☑ Newly reported
Classification: This patient does not meet the classification criteria for either confirmed or probable perinatal hepatitis B. Children 1–24 months of age whose birth location was unknown or occurred outside of the United States should be classified under the acute or chronic hepatitis B case definition, even if other criteria categories were met.		

Classification Scenarios for Cases of Acute Hepatitis C

Scenario 1: A primary care provider reported a positive HCV RNA test result in a person 24 years of age. Liver function tests show a peak ALT level of 236 IU/L, but jaundice is not present. There is not a more likely diagnosis than acute hepatitis C. The patient could not be matched with an existing acute or chronic case of hepatitis C in the surveillance system.

Case Classification Criteria	Scenario	Rationale for Classification
Does this meet age criterion?		
Age criterion: >36 months of age (or mode of exposure is not perinatal if 2–36 months of age)	24 years of age	**Needs to meet age criterion:** ☑ Age criterion
Does this meet laboratory criteria?		
Confirmatory lab criterion: HCV detection* test (i.e., HCV RNA, HCV genotype, or HCV antigen)	Positive	**Confirmed if meets confirmatory or test conversion lab criterion; probable if meets only presumptive lab criterion:** ☑ Positive HCV detection test ☐ Positive HCV antibody test ☐ HCV antibody or HCV detection test conversion
Presumptive lab criterion: HCV antibody test	Unknown	
Test conversion lab criterion: HCV antibody or HCV detection* test conversion from negative to positive within 12 months	Not documented	
Does this meet clinical criteria?		
Clinical criterion 1: Jaundice or peak elevated total bilirubin ≥3.0 mg/dL or peak elevated ALT >200 IU/L	Present	**Needs to meet both criteria unless anti-HCV or HCV detection test conversion criterion is met:** ☑ Jaundice or peak elevated total bilirubin or peak elevated ALT ☑ Absence of more likely diagnosis
Clinical criterion 2: Alternate, more likely diagnosis	Absent	
Is this a new event?		
New event criterion 1: Is the patient newly reported?	Yes	**Needs to meet 1 new event criterion†:** ☑ Newly reported ☐ Evidence of reinfection
New event criterion 2: Does the patient have an existing acute or chronic hepatitis C event with evidence of reinfection?	No	
Classification: This patient meets the classification criteria for confirmed acute hepatitis C.		

*HCV detection tests include a nucleic acid test (NAT) for HCV RNA (including qualitative, quantitative, or genotype testing) or a test indicating the presence of HCV antigen. At present, no HCV antigen tests are approved by the US Food and Drug Administration (FDA). These tests will be acceptable laboratory criteria, equivalent to HCV RNA testing, when an FDA-approved test becomes available.

†Some jurisdictions are creating a local condition specific for reinfection as opposed to creating a new acute condition to maintain a deduplicated registry.

Scenario 2: The HD received a positive anti-HCV laboratory result from an SSP in December on a person 39 years of age. The HD collects negative hepatitis C (anti-HCV and HCV detection) laboratory results. The patient had a previous negative anti-HCV laboratory result in February.

Case Classification Criteria	Scenario	Rationale for Classification
Does this meet age criterion?		
Age criterion: >36 months of age (or mode of exposure is not perinatal if 2–36 months of age)	39 years of age	**Needs to meet age criterion:** ☑ Age criterion
Does this meet laboratory criteria?		
Confirmatory lab criterion: HCV detection* test (i.e., HCV RNA, HCV genotype, or HCV antigen)	Unknown	**Confirmed if meets confirmatory or test conversion lab criterion; probable if meets only presumptive lab criterion:** ☐ Positive HCV detection test ☑ Positive HCV antibody test ☑ HCV antibody or HCV detection test conversion
Presumptive lab criterion: HCV antibody test	Positive	
Test conversion lab criterion: HCV antibody or HCV detection* test conversion from negative to positive within 12 months	Documented	
Does this meet clinical criteria?		
Clinical criterion 1: Jaundice or peak elevated total bilirubin ≥3.0 mg/dL or peak elevated ALT >200 IU/L	Unknown	**Needs to meet both criteria unless anti-HCV or HCV detection test conversion criterion is met:** ☐ Jaundice or peak elevated total bilirubin or peak elevated ALT ☐ Absence of more likely diagnosis
Clinical criterion 2: Alternate, more likely diagnosis	Not required	
Is this a new event?		
New event criterion 1: Is the patient newly reported?	Yes	**Needs to meet 1 new event criterion†:** ☑ Newly reported ☐ Evidence of reinfection
New event criterion 2: Does the patient have an existing acute or chronic hepatitis C event with evidence of reinfection?	No	
Classification: This patient meets the classification criteria for confirmed acute hepatitis C.		

*HCV detection tests include a nucleic acid test (NAT) for HCV RNA (including qualitative, quantitative, or genotype testing) or a test indicating the presence of HCV antigen. At present, no HCV antigen tests are approved by the US Food and Drug Administration (FDA). These tests will be acceptable laboratory criteria, equivalent to HCV RNA testing, when an FDA-approved test becomes available.

†Some jurisdictions are creating a local condition specific for reinfection as opposed to creating a new acute condition to maintain a deduplicated registry.

Scenario 3: In September, the HD received a positive HCV RNA laboratory result on a person 42 years of age. Three months later, the HD received another positive HCV RNA laboratory result on the same person. The HD collects negative hepatitis C (anti-HCV and HCV detection) laboratory results. The patient was matched with an existing chronic hepatitis C case from a previous year, and there are two subsequent negative HCV RNA laboratory results 3 months apart, indicating a cleared HCV infection.

Case Classification Criteria	Scenario	Rationale for Classification
Does this meet age criterion?		
Age criterion: >36 months of age (or mode of exposure is not perinatal if 2–36 months of age)	42 years of age	**Needs to meet age criterion:** ☑ Age criterion
Does this meet laboratory criteria?		
Confirmatory lab criterion: HCV detection* test (i.e., HCV RNA, HCV genotype, or HCV antigen)	Positive	**Confirmed if meets confirmatory or test conversion lab criterion; probable if meets only presumptive lab criterion:** ☑ Positive HCV detection test ☑ Positive HCV antibody test ☑ HCV antibody or HCV detection test conversion
Presumptive lab criterion: HCV antibody test	Positive	
Test conversion lab criterion: HCV antibody or HCV detection* test conversion from negative to positive within 12 months	Documented	
Does this meet clinical criteria?		
Clinical criterion 1: Jaundice or peak elevated total bilirubin ≥3.0 mg/dL or peak elevated ALT >200 IU/L	Unknown	**Needs to meet both criteria unless anti-HCV or HCV detection test conversion criterion is met:** ☐ Jaundice or peak elevated total bilirubin or peak elevated ALT ☐ Absence of more likely diagnosis
Clinical criterion 2: Alternate, more likely diagnosis	Unknown	
Is this a new event?		
New event criterion 1: Is the patient newly reported?	No	**Needs to meet 1 new event criterion†:** ☐ Newly reported ☑ Evidence of reinfection
New event criterion 2: Does the patient have an existing acute or chronic hepatitis C event with evidence of reinfection?	Yes	
Classification: This patient meets the classification criteria for confirmed acute hepatitis C†.		

*HCV detection tests include a nucleic acid test (NAT) for HCV RNA (including qualitative, quantitative, or genotype testing) or a test indicating the presence of HCV antigen. At present, no HCV antigen tests are approved by the US Food and Drug Administration (FDA). These tests will be acceptable laboratory criteria, equivalent to HCV RNA testing, when an FDA-approved test becomes available.

†Some jurisdictions are creating a local condition specific for reinfection as opposed to creating a new acute condition to maintain a deduplicated registry.

Scenario 4: The HD received a positive anti-HCV laboratory result on a person 20 years of age. The person's HCV RNA status is unknown. Through provider follow-up, it was determined that the patient presented with nausea, fatigue, and jaundice; the peak ALT level was 642 IU/L. There is not a more likely diagnosis than acute hepatitis C. This patient could not be matched with an existing acute or chronic case of hepatitis C in the surveillance system.

Case Classification Criteria	Scenario	Rationale for Classification
Does this meet age criterion?		
Age criterion: >36 months of age (or mode of exposure is not perinatal if 2–36 months of age)	20 years of age	**Needs to meet age criterion:** ☑ Age criterion
Does this meet laboratory criteria?		
Confirmatory lab criterion: HCV detection* test (i.e., HCV RNA, HCV genotype, or HCV antigen)	Unknown	**Confirmed if meets confirmatory or test conversion lab criterion; probable if meets only presumptive lab criterion:** ☐ Positive HCV detection test ☑ Positive HCV antibody test ☐ HCV antibody or HCV detection test conversion
Presumptive lab criterion: HCV antibody test	Positive	
Test conversion lab criterion: HCV antibody or HCV detectiona test conversion from negative to positive within 12 months	Not documented	
Does this meet clinical criteria?		
Clinical criterion 1: Jaundice or peak elevated total bilirubin ≥3.0 mg/dL or peak elevated ALT >200 IU/L	Present	**Needs to meet both criteria unless anti-HCV or HCV detection test conversion criterion is met:** ☑ Jaundice or peak elevated total bilirubin or peak elevated ALT ☑ Absence of more likely diagnosis
Clinical criterion 2: Alternate, more likely diagnosis	Absent	
Is this a new event?		
New event criterion 1: : Is the patient newly reported?	Yes	**Needs to meet 1 new event criterion†:** ☑ Newly reported ☐ Evidence of reinfection
New event criterion 2: Does the patient have an existing acute or chronic hepatitis C event with evidence of reinfection?	No	
Classification: This patient meets the classification criteria for probable acute hepatitis C.		

*HCV detection tests include a nucleic acid test (NAT) for HCV RNA (including qualitative, quantitative, or genotype testing) or a test indicating the presence of HCV antigen. At present, no HCV antigen tests are approved by the US Food and Drug Administration (FDA). These tests will be acceptable laboratory criteria, equivalent to HCV RNA testing, when an FDA-approved test becomes available.

†Some jurisdictions are creating a local condition specific for reinfection as opposed to creating a new acute condition to maintain a deduplicated registry.

Classification Scenarios for Cases of Chronic Hepatitis C

Scenario 1: The HD received a laboratory result on a person 62 years of age who has a positive anti-HCV result and a positive HCV RNA result. Total bilirubin level was 0.2 mg/dL, and ALT was 22 IU/L. The patient could not be matched with an existing acute or chronic case of hepatitis C in the surveillance system.

Case Classification Criteria	Scenario	Rationale for Classification
Does this meet age criterion?		
Age criterion: >36 months of age (or mode of exposure is not perinatal if 2–36 months of age)	62 years of age	**Needs to meet age criterion:** ☑ Age criterion
Does this meet laboratory criteria?		
Confirmatory laboratory evidence: HCV detection* test (i.e., HCV RNA, HCV genotype, or HCV antigen)	Positive	**Confirmed if meets confirmed lab case classification criteria; probable if meets probable lab case classification criteria:** ☑ Positive HCV detection test and has no documentation of HCV antibody or HCV detection test conversion within 12 months ☐ Positive HCV antibody test, does not have HCV detection test reported, and has no documentation of HCV antibody or HCV detection test conversion within 12 months
Presumptive laboratory evidence: HCV antibody test	Positive	
Does this meet clinical criteria?		
Clinical criteria: Jaundice or peak elevated total bilirubin ≥3.0 mg/dL or peak elevated ALT >200 IU/L and the absence of a more likely diagnosis	No	**Does not meet or has no report of clinical criteria:** ☐ Jaundice or peak elevated total bilirubin or peak elevated ALT and the absence of a more likely diagnosis
Is this a new event?		
New event criterion 1: Is the patient newly reported?	Yes	**Needs to meet 1 new event criterion:** ☑ Newly reported ☐ If previously reported acute event, the event occurred in a prior MMWR year and >1 year after acute onset
New event criterion 2: Does the patient have an acute hepatitis C event in the surveillance system in a previous MMWR year and ≥1 year after acute onset?	No	
Classification: This patient meets the classification criteria for confirmed chronic hepatitis C.		

*HCV detection tests include a nucleic acid test (NAT) for HCV RNA (including qualitative, quantitative, or genotype testing) or a test indicating the presence of HCV antigen. At present, no HCV antigen tests are approved by the US Food and Drug Administration (FDA). These tests will be acceptable laboratory criteria, equivalent to HCV RNA testing, when an FDA-approved test becomes available.

Scenario 2: The HD received an HCV genotype laboratory result on a person 38 years of age. The patient was matched to an existing acute hepatitis C case in your jurisdiction's surveillance system from 18 months prior (i.e., positive HCV antibody with positive reflexed HCV RNA).

Case Classification Criteria	Scenario	Rationale for Classification
Does this meet age criterion?		
Age criterion: >36 months of age (or mode of exposure is not perinatal if 2–36 months of age)	38 years of age	**Needs to meet age criterion:** ☑ Age criterion
Does this meet laboratory criteria?		
Confirmatory laboratory evidence: HCV detection* test (i.e., HCV RNA, HCV genotype, or HCV antigen)	Positive	**Confirmed if meets confirmed lab case classification criteria; probable if meets probable lab case classification criteria:** ☑ Positive HCV detection test and has no documentation of HCV antibody or HCV detection test conversion within 12 months ☐ Positive HCV antibody test, does not have HCV detection test reported, and has no documentation of HCV antibody or HCV detection test conversion within 12 months
Presumptive laboratory evidence: HCV antibody test	Positive	
Does this meet clinical criteria?		
Clinical criteria: Jaundice or peak elevated total bilirubin ≥3.0 mg/dL or peak elevated ALT >200 IU/L and the absence of a more likely diagnosis	No	**Does not meet or has no report of clinical criteria:** ☐ Jaundice or peak elevated total bilirubin or peak elevated ALT and the absence of a more likely diagnosis
Is this a new event?		
New event criterion 1: Is the patient newly reported?	No	**Needs to meet 1 new event criterion:** ☐ Newly reported ☑ If previously reported acute event, the event occurred in a prior MMWR year and >1 year after acute onset
New event criterion 2: Does the patient have an acute hepatitis C event in the surveillance system in a previous MMWR year and ≥1 year after acute onset?	Yes	
Classification: This patient meets the classification criteria for confirmed chronic hepatitis C.		

*HCV detection tests include a nucleic acid test (NAT) for HCV RNA (including qualitative, quantitative, or genotype testing) or a test indicating the presence of HCV antigen. At present, no HCV antigen tests are approved by the US Food and Drug Administration (FDA). These tests will be acceptable laboratory criteria, equivalent to HCV RNA testing, when an FDA-approved test becomes available.

Scenario 3: The HD received a positive anti-HCV laboratory result on a person 38 years of age from an SSP. Upon contacting the SSP, it was learned that the patient did not show up to the referring provider for HCV RNA follow-up testing. Liver function tests were not available. This patient could not be matched with an existing acute or chronic case of hepatitis C in the surveillance system.

Case Classification Criteria	Scenario	Rationale for Classification
Does this meet age criterion?		
Age criterion: >36 months of age (or mode of exposure is not perinatal if 2–36 months of age)	38 years of age	**Needs to meet age criterion:** ☑ Age criterion
Does this meet laboratory criteria?		
Confirmatory laboratory evidence: HCV detection* test (i.e., HCV RNA, HCV genotype, or HCV antigen)	Unknown	**Confirmed if meets confirmed lab case classification criteria; probable if meets probable lab case classification criteria:** ☐ Positive HCV detection test and has no documentation of HCV antibody or HCV detection test conversion within 12 months ☑ Positive HCV antibody test, does not have HCV detection test reported, and has no documentation of HCV antibody or HCV detection test conversion within 12 months
Presumptive laboratory evidence: HCV antibody test	Positive	
Does this meet clinical criteria?		
Clinical criteria: Jaundice or peak elevated total bilirubin ≥3.0 mg/dL or peak elevated ALT >200 IU/L and the absence of a more likely diagnosis	Unknown	**Does not meet or has no report of clinical criteria:** ☐ Jaundice or peak elevated total bilirubin or peak elevated ALT and the absence of a more likely diagnosis
Is this a new event?		
New event criterion 1: Is the patient newly reported?	Yes	**Needs to meet 1 new event criterion:** ☑ Newly reported ☐ If previously reported acute event, the event occurred in a prior MMWR year and >1 year after acute onset
New event criterion 2: Does the patient have an acute hepatitis C event in the surveillance system in a previous MMWR year and ≥1 year after acute onset?	No	
Classification: This patient meets the classification criteria for probable chronic hepatitis C. If resources permit, staff who are coordinating linkage-to-cure activities should follow-up with the patient to offer referral to care, follow-up testing, and other services, as needed.		

*HCV detection tests include a nucleic acid test (NAT) for HCV RNA (including qualitative, quantitative, or genotype testing) or a test indicating the presence of HCV antigen. At present, no HCV antigen tests are approved by the US Food and Drug Administration (FDA). These tests will be acceptable laboratory criteria, equivalent to HCV RNA testing, when an FDA-approved test becomes available.

Scenario 4: The HD received a positive anti-HCV laboratory result and a positive HCV RNA laboratory result on a pregnant person 25 years of age. Liver function tests were not elevated. The patient could not be matched with an existing acute or chronic case of hepatitis C in the surveillance system.

Case Classification Criteria	Scenario	Rationale for Classification
Does this meet age criterion?		
Age criterion: >36 months of age (or mode of exposure is not perinatal if 2–36 months of age)	25 years of age	**Needs to meet age criterion:** ☑ Age criterion
Does this meet laboratory criteria?		
Confirmatory laboratory evidence: HCV detection* test (i.e., HCV RNA, HCV genotype, or HCV antigen)	Positive	**Confirmed if meets confirmed lab case classification criteria; probable if meets probable lab case classification criteria:** ☑ Positive HCV detection test and has no documentation of HCV antibody or HCV detection test conversion within 12 months ☐ Positive HCV antibody test, does not have HCV detection test reported, and has no documentation of HCV antibody or HCV detection test conversion within 12 months
Presumptive laboratory evidence: HCV antibody test	Positive	
Does this meet clinical criteria?		
Clinical criteria: Jaundice or peak elevated total bilirubin ≥3.0 mg/dL or peak elevated ALT >200 IU/L and the absence of a more likely diagnosis	No	**Does not meet or has no report of clinical criteria:** ☐ Jaundice or peak elevated total bilirubin or peak elevated ALT and the absence of a more likely diagnosis
Is this a new event?		
New event criterion 1: Is the patient newly reported?	Yes	**Needs to meet 1 new event criterion:** ☑ Newly reported ☐ If previously reported acute event, the event occurred in a prior MMWR year and >1 year after acute onset
New event criterion 2: Does the patient have an acute hepatitis C event in the surveillance system in a previous MMWR year and ≥1 year after acute onset?	No	
Classification: This patient meets the classification criteria for confirmed chronic hepatitis C. Depending on local protocols, a jurisdiction might additionally open a perinatal hepatitis C case investigation record with a non-notifiable classification such as 'suspected' as a reminder in the system that the infant's HCV infection test results will need be obtained. The infant's HCV detection test results performed during 2–36 months of age will determine whether the infant will be classified as confirmed perinatal hepatitis C.		

*HCV detection tests include a nucleic acid test (NAT) for HCV RNA (including qualitative, quantitative, or genotype testing) or a test indicating the presence of HCV antigen. At present, no HCV antigen tests are approved by the US Food and Drug Administration (FDA). These tests will be acceptable laboratory criteria, equivalent to HCV RNA testing, when an FDA-approved test becomes available.

Classification Scenarios for Cases of Perinatal Hepatitis C

Scenario 1: A provider contacted the HD to report a positive HCV RNA test result in a child 6 months of age. Through birth certificate matching, the gestational parent was reported as a chronic hepatitis C case in the surveillance system. No evidence of another likely mode of transmission exists other than perinatal. The child is not an existing hepatitis C case in the surveillance system.

Case Classification Criteria	Scenario	Rationale for Classification
Does this meet age criterion?		
Age criterion: 2–36 months of age	6 months of age	**Needs to meet age criterion:** ☑ 2–36 months of age
Does this meet the epidemiologic linkage criterion?		
Epidemiologic linkage criterion: Not known to have been exposed to hepatitis C via a mechanism other than perinatal	Documented	**Needs to meet epidemiologic linkage criterion:** ☑ Epidemiologic linkage criteria
Does this meet the laboratory criterion?		
Laboratory criterion: HCV detection* test (i.e., HCV RNA, HCV genotype, or HCV antigen) during 2–36 months of age	Positive	**Needs to meet laboratory criterion:** ☑ Positive HCV detection test during 2–36 months of age
Is this a new event?		
New event criterion: Is the patient newly reported?	Yes	**Needs to be newly reported event:** ☑ Newly reported
Classification: This patient meets the classification criteria for confirmed perinatal hepatitis C.		

*HCV detection tests include a nucleic acid test (NAT) for HCV RNA (including qualitative, quantitative, or genotype testing) or a test indicating the presence of HCV antigen. At present, no HCV antigen tests are approved by the US Food and Drug Administration (FDA). These tests will be acceptable laboratory criteria, equivalent to HCV RNA testing, when an FDA-approved test becomes available.

Scenario 2: The HD received a positive anti-HCV laboratory result on a child 24 months of age. Through follow-up with the ordering provider, the gestational parent's information was obtained. The gestational parent is a confirmed chronic hepatitis C case in the surveillance system. The HCV detection status of the child is unknown, and the gestational parent was lost to follow-up. The child could not be matched to an existing hepatitis C case in the surveillance system.

Case Classification Criteria	Scenario	Rationale for Classification
Does this meet age criterion?		
Age criterion: 2–36 months of age	24 months of age	Needs to meet age criterion: ☑ 2–36 months of age
Does this meet the epidemiologic linkage criterion?		
Epidemiologic linkage criterion: Not known to have been exposed to hepatitis C via a mechanism other than perinatal	Documented	Needs to meet epidemiologic linkage criterion: ☑ Epidemiologic linkage criteria
Does this meet the laboratory criterion?		
Laboratory criterion: HCV detection* test (i.e., HCV RNA, HCV genotype, or HCV antigen) during 2–36 months of age	Unknown	Needs to meet laboratory criterion: ☐ Positive HCV detection test during 2–36 months of age
Is this a new event?		
New event criterion: Is the patient newly reported?	Yes	Needs to be newly reported event: ☑ Newly reported
Classification: This patient does not meet the classification criteria for confirmed perinatal hepatitis C. Though there is laboratory evidence of perinatal exposure (i.e., positive anti-HCV result 18–36 months of age), HCV detection is needed for confirmation. HDs might consider classifying the patient as 'suspected' as a way to hold the patient in the surveillance system for receipt of the HCV detection test result.		

*HCV detection tests include a nucleic acid test (NAT) for HCV RNA (including qualitative, quantitative, or genotype testing) or a test indicating the presence of HCV antigen. At present, no HCV antigen tests are approved by the US Food and Drug Administration (FDA). These tests will be acceptable laboratory criteria, equivalent to HCV RNA testing, when an FDA-approved test becomes available.

Scenario 3: The HD received a positive anti-HCV laboratory result on a child 24 months of age. Through follow-up with the ordering provider, the gestational parent's information was obtained. The gestational parent is a confirmed chronic hepatitis C case in the surveillance system. Upon further investigation, the HCV RNA status of the child is negative. The child could not be matched to an existing hepatitis C case in the surveillance system.

Case Classification Criteria	Scenario	Rationale for Classification
Does this meet age criterion?		
Age criterion: 2–36 months of age	24 months of age	Needs to meet age criterion: ☑ 2–36 months of age
Does this meet the epidemiologic linkage criterion?		
Epidemiologic linkage criterion: Not known to have been exposed to hepatitis C via a mechanism other than perinatal	Documented	Needs to meet epidemiologic linkage criterion: ☑ Epidemiologic linkage criteria
Does this meet the laboratory criterion?		
Laboratory criterion: HCV detection* test (i.e., HCV RNA, HCV genotype, or HCV antigen) during 2–36 months of age	Negative	Needs to meet laboratory criterion: ☐ Positive HCV detection test during 2–36 months of age
Is this a new event?		
New event criterion: Is the patient newly reported?	Yes	Needs to be newly reported event: ☑ Newly reported
Classification: This patient does not meet the classification criteria for confirmed perinatal hepatitis C.		

*HCV detection tests include a nucleic acid test (NAT) for HCV RNA (including qualitative, quantitative, or genotype testing) or a test indicating the presence of HCV antigen. At present, no HCV antigen tests are approved by the US Food and Drug Administration (FDA). These tests will be acceptable laboratory criteria, equivalent to HCV RNA testing, when an FDA-approved test becomes available.

Appendix D. Hepatitis B Surface Antigen Testing Sequence

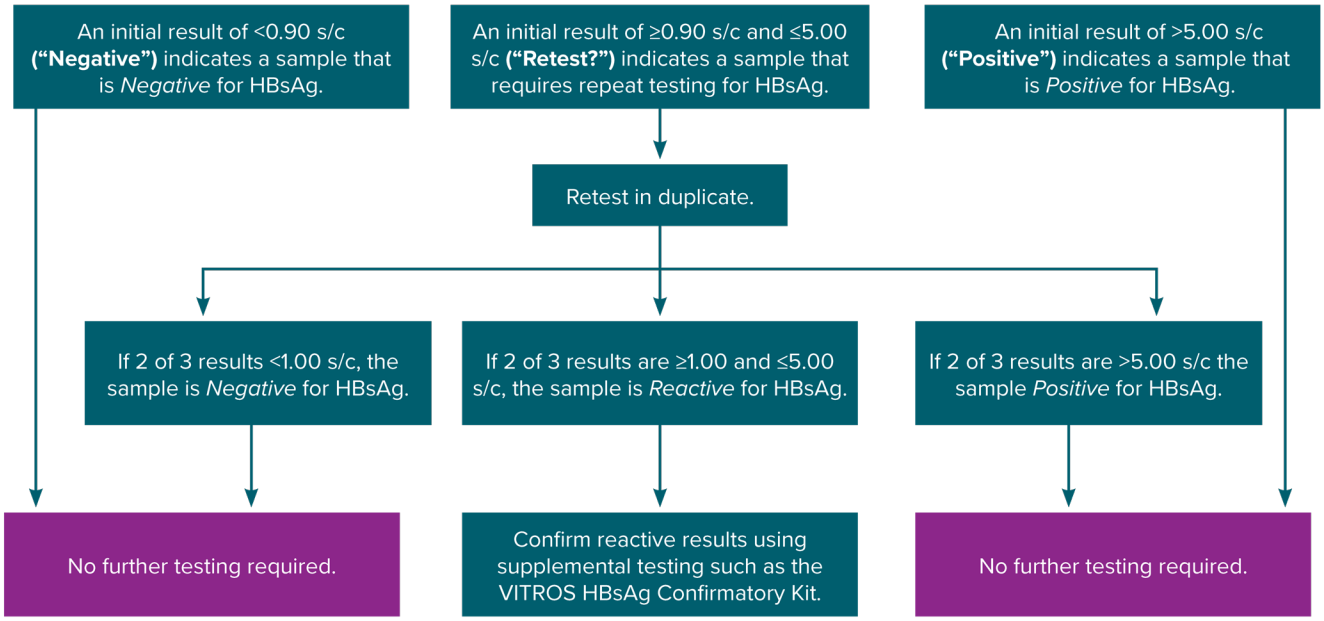
All HBsAg testing of patients in the United States should be performed in accordance with Clinical Laboratory Improvement Amendments (CLIA) regulations. The need for additional repeat testing is determined by the signal-to-cutoff (s/c) value during initial HBsAg screening. Confirmatory (e.g., neutralization) testing is required for samples that have that s/c values falling within a specified range for two of three retests, in accordance with the instructions for use provided with the initial HBsAg test assay.

Figure 6-1 illustrates the HBsAg testing algorithm for the Ortho VITROS HBsAg initial assay. For this assay, a s/c value <0.90 from initial HBsAg testing is considered negative, and a s/c value >5.00 is considered positive. S/c values that are <0.90 or >5.00 do not require retesting or additional confirmatory testing, as these are considered clear negative and clear positive, respectively. However, specimens for HBsAg testing ordered on pregnant people might be automatically reflexed to confirmatory testing by some laboratories regardless of the s/c value of the initial test.

A s/c value in the range of 0.90–5.00 on an initial HBsAg test (representing the "gray zone") indicates the need for retesting, as these could represent samples that are false-positive, low-positive, or have a very high concentration of HBsAg interfering with the test. If the s/c values for two of three repeat tests are less than 1.00, the sample is considered negative. If the s/c values for two of three repeat tests are >5.00, the sample is considered positive. Samples that are considered negative or positive upon repeat testing do not require further testing. Other assays do not use a gray zone or use a different gray zone range to determine the need for repeat testing.

If the s/c values for two of three results are in the range of 1.00–5.00, the sample is considered reactive, and supplemental confirmatory (e.g., neutralization) testing should be performed.

Figure 6-1. Testing algorithm for the Ortho VITROS hepatitis B surface antigen initial assay



Obtained from https://www.utmb.edu/policies_and_procedures/IHOP/Supporting_Documents/IHOP%20-%2009.13.15%20-%20Serological%20Testing%20for%20Syphilis,%20Hepatitis%20B,%20and%20HIV%20during%20Pregnancy%20and%20Delivery%20(HBsAg_Screening).pdf.

In the neutralization test, used as a confirmatory test, specific antibodies are used to bind to HBsAg and when HBsAg is the actual cause of an initial test positive, the amount of HBsAg detected in a repeat assay will be reduced. The final HBsAg qualitative confirmatory result is based on the s/c and % neutralization of the sample as defined in the instructions for use of the confirmatory assay. For example, a confirmed HBsAg positive by the HBsAg Confirmatory Kit by Ortho's Vitros Immunodiagnostic Products is an undiluted or diluted specimen with s/c ≥0.8 and neutralization of ≥50% reduction in signal on assay[122].

The Instructions for Use insert that accompanies the HBsAg confirmatory test kit includes more specific information on testing algorithm and result interpretations. Specimens that should receive HBsAg confirmatory testing, but were not confirmed, or specimens that were negative or indeterminate upon confirmatory HBsAg testing should not be considered positive for HBsAg. If an HD is frequently receiving unconfirmed HBsAg positive results that meet criteria to have been subject to confirmatory testing, the informatics staff at the HD should be consulted and/or the reporting laboratory contacted to clarify testing practices and reporting requirements.

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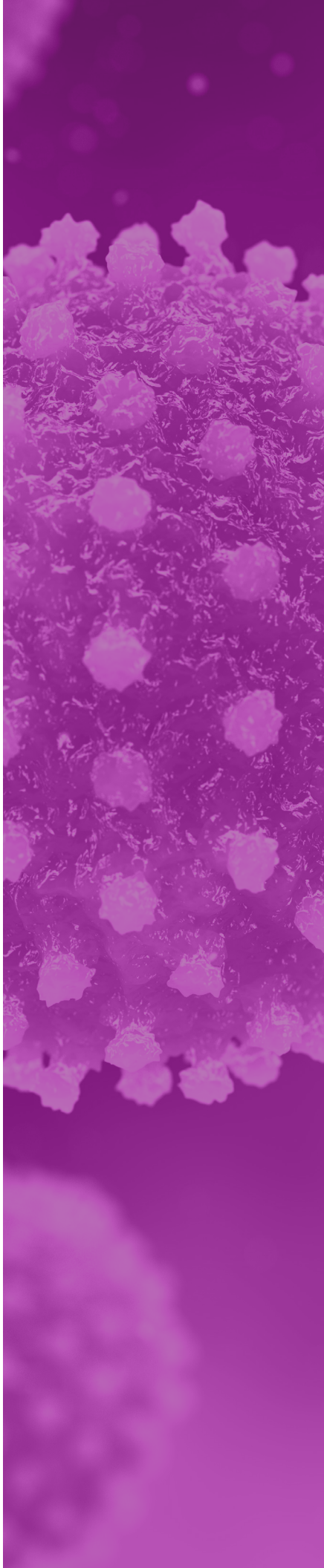

Viral Hepatitis Surveillance and Case Management: Guidance for State, Territorial, and Local Health Departments is prepared by the Centers for Disease Control and Prevention (CDC) and is available free of charge in electronic format from CDC's Division of Viral Hepatitis website at https://www.cdc.gov/hepatitis/statistics/GuidelinesAndForms.htm. Address inquiries to dvh_foa@cdc.gov.

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