Chapter 6
Surveillance for Hepatitis C

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Abbreviations

CDC  United States Centers for Disease Control and Prevention
CLD  Chronic liver disease
EHR  Electronic health record
ELR  Electronic laboratory reporting
HCC  Hepatocellular carcinoma
HCV  Hepatitis C virus
HIEs  Health information exchanges
HIT  Health information technology
IDU  Injection drug use
MSM  Men who have sex with men
NHANES  National Health and Nutrition Examination Survey
RIBA  Recombinant immunoblot assay
SVR  Sustained virologic response
U.S.  United States

Core Message  This chapter provides an overview of hepatitis C surveillance methods.
1 Importance and Aims of Hepatitis C Surveillance

Hepatitis C virus (HCV) infection is a common type of chronic blood-borne infection [1]. The World Health Organization estimates that 170 million persons are HCV infected globally [2]. In countries that conduct hepatitis C surveillance, hepatitis C may be required to be reported by laboratories and healthcare providers to health departments.

Hepatitis C surveillance includes acute and chronic hepatitis C cases; however, some countries or local areas may not have the necessary confirmatory laboratory tests to distinguish current (or present) from resolved (or past) HCV infection. Additionally, because the chronic hepatitis C burden is large and conducting follow-up investigation can be labor intensive, some countries and local areas might lack the capacity to investigate and confirm cases. Despite the challenges of conducting hepatitis C surveillance, there is hope for hepatitis C eradication because primary prevention is effective, and secondary transmission and complications are preventable through case management, new effective treatments, and alcohol counseling. Surveillance data are essential to the planning, implementation, and evaluation of public health programs and policies [3].

2 Epidemiology

2.1 Characteristics

Hepatitis C traces back to the mid-1970s, though at the time, the virus was broadly termed “non-A, non-B hepatitis” when serologic tests ruled out hepatitis A or B as the cause of acute hepatitis following a blood transfusion [4]. In 1989, hepatitis C was fully distinguished from non-A, non-B hepatitis [4, 5].

HCV infection may be difficult to measure because 70–85% of HCV-infected persons are asymptomatic. When symptoms are present, they can include jaundice, fever, abdominal pain or discomfort, nausea, vomiting, dark urine, fatigue, joint pain, loss of appetite, and clay-colored stools [6]. For symptomatic HCV-infected individuals, the onset of symptoms usually occurs 6–7 weeks after exposure [7, 8]. For asymptomatic HCV-infected individuals, diagnosis usually occurs incidentally during blood donation screenings and other medical screenings. In the USA, federally supported surveillance captures only a fraction of all acute HCV infections because the identification of acute HCV infection requires the presence of symptoms [9], and the proportion of those with symptoms is relatively small (20–30%) [6]. However, procedures have been developed that account for asymptomatic HCV infections in estimating the total number of reported acute cases (estimation procedures are discussed in Sect. 5.5). Table 6.1 describes the general characteristics of acute and chronic HCV infection.
Table 6.1 Characteristics of acute and chronic hepatitis C virus (HCV) infection

| Characteristic               | Acute hepatitis C                                                                 | Chronic hepatitis C                                                                 |
|-----------------------------|----------------------------------------------------------------------------------|-------------------------------------------------------------------------------------|
| Definition                  | The first 6 months of a new HCV infection                                        | HCV infection persisting past 6 months                                             |
| Burden of disease           | No global estimate available                                                     | 170 million persons worldwide                                                      |
| Persons at risk             | Persons who have percutaneous exposure to HCV-infected blood, e.g., persons who share needles and persons who seek healthcare services in settings where standard precautions and infection control measures are not strictly implemented | About 80 % of persons who are acutely infected with hepatitis C                  |
| Symptoms (if present)       | Jaundice, fever, abdominal pain or discomfort, nausea, vomiting, dark urine, fatigue, joint pain, loss of appetite, and clay-colored stools | Symptoms are usually present in advanced stages: cirrhosis, jaundice, liver failure |
| Rate of spontaneous recovery| 20 %                                                                             | Chronic HCV-infected persons will not recover spontaneously but can achieve a sustained virologic response with treatment |
| Rate of asymptomatic        | 70–85 %                                                                          | Symptoms are usually not present until the advanced stages of liver disease        |
| Laboratory diagnosis        | (1) Antibody to hepatitis C-positive followed by HCV RNA-positive result or genotype result and report of recent risk behavior/factor; (2) positive HCV RNA and documented HCV antibody seroconversion within the past 6 months | (1) Two positive HCV RNA or genotype results performed 6 months apart; (2) antibody to hepatitis C-positive followed by HCV RNA-positive result or genotype result and report of risk behavior/factor occurring more than 6 months prior |
| Mortality                   | 16,000 deaths worldwide in 2010                                                 | 499,000 deaths worldwide in 2010                                                  |
| Progression to chronic infection | Approximately 80 % of acute HCV infections will progress to chronic HCV infection | Not applicable                                                                      |
| Progression to liver cancer | No                                                                               | Yes, the rate of progression is approximately 4–5 % among chronically HCV-infected persons |
| Treatment                   | High rate of sustained virologic response among those treated with ribavirin and/or peginterferon | There are multiple national and regional guidelines for treatment of hepatitis C. The following drugs are currently approved for treatment of hepatitis C: peginterferon and ribavirin, boceprevir, telaprevir, simeprevir, sofosbuvir. Treatment depends on stage of disease and genotype |
| Primary prevention          | Needle exchange programs, standard precaution measures and infection control in healthcare settings, increase awareness of disease | Prevention of acute hepatitis C                                                   |
| Secondary prevention        | Screening for HCV infection                                                      | Hepatitis A and B vaccination                                                      |
| Tertiary prevention         | Some studies have shown that treatment of acute hepatitis C could prevent the progression to chronic disease and provide a cure | Case management, routine medical care, alcohol counseling, treatment                |
2.2 Geographic Distribution

Although the overall estimated global prevalence of past/present HCV infection is high (3%: 170 million persons) [2], there is wide variability in prevalence between geographic regions [10]. Typically, developing countries, such as parts of Africa and Asia, have the highest reported prevalence of >3.5% (Fig. 6.1). In Egypt, for example, 15% of persons aged 15–59 years had evidence of past/present HCV infection [11]. In comparison, more developed countries, such as those in North America, northern and western Europe, and Australia, have a low to moderate reported prevalence (<3.5%) (Fig. 6.1). In the USA, for example, the estimated prevalence of HCV infection is approximately 1.0%, or 2.7 million persons [12]—disproportionately affecting persons who are middle aged [1, 12, 13]. Hepatitis C has at least six distinct genotypes widely distributed across the globe. In the USA, Europe, and Japan, genotypes 1a and 1b are most predominant although genotypes 2a and 2b are also common [14]. Genotype 2c is prevalent in northern Italy while genotype 3a is prevalent among intravenous drug users in Europe and the USA [14]. In North Africa and the Middle East, genotype 4 is predominant while genotypes 5 and 6 are confined to South Africa and Hong Kong [14].
2.3  Mode of Transmission

HCV is primarily transmitted through percutaneous exposure to infected blood [15]. One of the most common ways by which HCV is transmitted is injection drug use (IDU) [1, 2]. In the USA, among persons with acute hepatitis C who responded to questions about IDU, approximately 60 % reported injection of street drugs [16]. From 2007 to 2011, US surveillance data detected a 44 % increase in the hepatitis C incidence [16], which may be due to a rise in injection drug users among young persons [17–19].

In healthcare settings where standard precautions and infection control measures are less strictly implemented, needle stick injuries and unsafe medical practices are common causes of HCV transmission. In developed countries like the USA, the risk of HCV transmission in healthcare settings has dramatically declined due to the implementation of safe injection and universal infection control practices [20]. Despite the decline, from 2008 to 2012, 16 healthcare-associated hepatitis C outbreaks that resulted in 160 cases of HCV infection were reported to the United States Centers for Disease Control and Prevention (CDC) [21]. Healthcare-associated hepatitis C outbreaks are indicators of failure to implement and strictly adhere to standard precautions and infection control measures. Since the development of the hepatitis C antibody screening test in 1990 and screening of the blood supply for hepatitis C in 1992, HCV transmission from blood transfusions has been greatly reduced in developed countries [22]. In developing countries, this mode of transmission remains significant [22, 23].

HCV also can be transmitted from HIV-coinfected mothers to their infants, and HIV-infected men who have sex with men (MSM) have an increased likelihood of acquiring HCV infection [24]. The risk of HCV transmission among HIV-infected MSM is also increased in the presence of genital ulcerative disease and sexual practices that lead to mucosal trauma [25]. Heterosexual contact among monogamous partners is an unlikely route of transmission [24].

Other demographic groups also are disproportionately affected by hepatitis C, evident by a higher prevalence among those groups. For example, in the USA, the overall hepatitis C antibody prevalence is estimated to be 1.6 %; however, it is 3 % among persons born during 1945–1965 [13]; 5 % among military veterans [26, 27]; 6 % among blacks aged 30–49 years [28]; 14 % among HIV-infected persons [1]; and 23–39 % among the incarcerated [26]. Additionally, some hepatitis C epidemics are fueled by contaminated injection equipment used in mass treatment campaigns, such as schistosomiasis treatment in Egypt during 1960–1980; HCV transmission is still ongoing today [29].

2.4  Complications of Chronic Infection

The burden of hepatitis C, mostly among persons who are undiagnosed and not in care, is evidenced by increasing complications. One such complication is the development and progression of chronic liver disease (CLD). In addition, alcohol use is
independently associated with liver disease progression [13]. Based on representative samples of published reports from at least 1990 and 11 World Health Organization regions, hepatitis C was identified as one of the most common etiologies of CLD throughout most of the world [30] and was associated with 27% of liver cirrhosis and 25% of hepatocellular carcinoma (HCC) [30]. From the same study, death due to HCV infection was identified in approximately 211,000 persons with liver cirrhosis and 155,000 persons with liver cancer [30]. Among US adult residents in two sentinel surveillance sites and one healthcare network site, 64% of newly diagnosed CLD had underlying hepatitis C during 1999–2001 [31]. In the USA, over 15,000 hepatitis C-related deaths occurred in 2007, of which 57% had CLD, including HCC [32].

Although hepatitis C is widely known to increase the risk of dying from liver-related diseases, recent studies have found that HCV infection also increased the risk of dying from non-liver-related diseases [33–35]. In one study, patients with chronic HCV infection had a non-liver-related mortality risk nearly two times higher than uninfected patients [33]. Similarly, in another study, persons who were HCV antibody positive had significantly higher mortality than persons who were HCV antibody negative. Additionally, persons with detectable HCV RNA levels had significantly higher mortality than persons with undetectable RNA levels [34].

2.5 Laboratory Testing

The traditional approach for detecting HCV infection is to screen persons for a history of risk factors and to test those with any identifiable risk factor [36]. While IDU is the most common mode of transmission in developed countries, additional risk factors, including exposure to unsafe blood products and injection practices, are highly prevalent and contribute to significant HCV transmission in developing countries [37]. There are many international recommendations for hepatitis C testing and all have consistency in their recommendation for testing of persons who inject illicit drugs, prior recipients of transfusions or organ transplants, persons with persistently elevated liver enzymes, children born to HCV-infected mothers, and persons exposed to HCV-positive blood in healthcare [38].

Table 6.2 describes the interpretation of hepatitis C test results and corresponding further actions. The initial test is for HCV antibodies, which are detectable approximately 4–10 weeks after exposure [39]. In symptomatic cases, this time period usually occurs at or before the onset of clinical symptoms. The HCV antibody test is positive in acute, chronic, and resolved infections (Table 6.2). Consequently, HCV antibody tests do not have the capacity to distinguish current infection from past, resolved infection [40]. In addition to standard serologic assays, there are also rapid tests to detect HCV antibodies [41]. The availability of standard and rapid assays varies significantly and is dependent on availability of resources [40]. Over the past decade, new generations of standard tests with high sensitivity and specificity have been developed [40, 42]. However, the proportion of
false-positive HCV antibody results is inversely related to the HCV prevalence in that setting [40, 43]. False-negative HCV antibody results also occur, particularly in individuals with severe immunodeficiency [39, 44], but rarely among the general population.

In contrast to HCV antibodies, HCV RNA can detect current infection and is detectable in serum as early as 1–2 weeks after exposure [41]. There are a number of qualitative and quantitative HCV RNA assays [43]. However, these tests are expensive and not widely available. Further, because these tests detect HCV RNA, they are important for differentiating current infection from past, resolved infection [45]. Therefore, both in the clinical practice and in epidemiologic studies, it is important to follow up on every HCV antibody-positive result with an RNA assay [43]. In conditions where the HCV antibody test is likely a false negative, RNA testing may provide the correct diagnosis [43]. For these reasons, quantitative HCV RNA assays and genotype studies are important in the clinical management of chronic HCV infection.

| Test outcome                                      | Interpretation                          | Further actions                                                                 |
|--------------------------------------------------|-----------------------------------------|---------------------------------------------------------------------------------|
| HCV antibody nonreactive                         | No HCV antibody detected                | Sample can be reported as nonreactive for HCV antibody. No further action required. If recent exposure in person tested is suspected, test for HCV RNA \(^a\) |
| HCV antibody reactive                            | Presumptive HCV infection               | A repeatedly reactive result is consistent with current HCV infection, or past HCV infection that has resolved, or biologic false positivity for HCV antibody. Test for HCV RNA to identify current infection |
| HCV antibody reactive, HCV RNA detected          | Current HCV infection                   | Provide person tested with appropriate counseling and link person tested to care and treatment \(^b\) |
| HCV antibody reactive, HCV RNA not detected      | No current HCV infection                | No further action required in most cases. If distinction between true positivity and biologic false positivity for HCV antibody is desired, and if sample is repeatedly reactive in the initial test, test with another HCV antibody assay. In certain situations, follow up with HCV RNA testing and appropriate counseling |

Adapted from CDC. Testing for HCV infection: An update of guidance for clinicians and laboratorians. MMWR 2013;62(18)

\(^a\)If HCV RNA testing is not feasible and person tested is not immunocompromised, do follow-up testing for HCV antibody to demonstrate seroconversion. If the person tested is immunocompromised, consider testing for HCV RNA

\(^b\)It is recommended before initiating antiviral therapy to retest for HCV RNA in a subsequent blood sample to confirm HCV RNA positivity

\(^c\)If the person tested is suspected of having HCV exposure within the past 6 months, or has clinical evidence of HCV disease, or if there is concern regarding the handling or storage of the test specimen
Other tests available for hepatitis C detection and diagnosis include the HCV core antigen test [46] and core antigen/antibody tests [47]. These tests are available only in some countries. While the HCV core antigen test is sensitive, will yield results early in the course of infection, and detects active infection [46, 48], the HCV core antigen/antibody test is positive in the presence of either one or both antigen and antibody [47] making it difficult to differentiate between active and resolved infection. Blood donations are screened by testing for HCV RNA and core antigen [49].

Dried blood spot assays are well developed and validated for HIV detection [50]. HCV antibody and RNA testing on a dried blood spot sample are used in research activities whereby a blood draw is not feasible [51, 52]. However, these tests are not well validated and require highly qualified personnel. Therefore, its use is restricted to research use only.

In many sub-Saharan African countries, a high rate of false-positive HCV antibody test results have been reported, even when the latest generation of serologic assays are used [53]. In the majority of HCV antibody-positive samples, the recombinant immunoblot assay (RIBA) yields either a negative or indeterminate result [53]. RIBA is a more specific blood test for detecting HCV antibodies and is sometimes used as a confirmatory test to less specific antibody tests [43]. In the USA, RIBA was phased out in 2013 [41]. Even among RIBA-confirmed HCV antibody-positive samples, the large majority are HCV RNA negative. Such findings have been a challenge for clinical diagnosis, epidemiological studies, and screening of blood products for transfusion. While the cause of the high false positivity is still unknown [54], it raises questions about the best strategy to test for HCV infection in some countries.

### 2.6 Treatment

The goal of treatment for chronic HCV infection is to achieve sustained virologic response (SVR), or cure, currently defined as having an undetectable viral load 24 weeks after the end of treatment [55]. Achieving SVR, in turn, is associated with long-term clearance of the virus and reduced long-term health complications such as cirrhosis, HCC, liver failure, and all-cause mortality [56, 57]. Novel therapies with direct-acting antivirals have demonstrated high virus eradication rates. Persons diagnosed as HCV positive should be medically evaluated and entered into routine care, as appropriate. The evaluation should include confirmation of chronic infection by viral testing including genotype and viral load, an assessment of liver function, stage of liver fibrosis, evidence of liver cancer, and eligibility for treatment [58].

The traditional treatment is pegylated interferon with ribavirin [7]. The duration of treatment is determined by the virologic response, which in turn is associated with the person’s genotype. With pegylated interferon and ribavirin therapy, a 24-week treatment course is recommended for genotypes 2 and 3 and a 48-week
treatment course for other genotypes [7]. Persons with genotypes 2 and 3 who followed this regimen have $\geq 80\%$ SVR rate compared with a 40–50 % SVR rate for persons with genotype 1 [7].

Pegylated interferon and ribavirin is associated with many side effects, requires frequent injections, and has shown low success rates with hepatitis C genotype 1 [59]. In 2011, the United States (US) Food and Drug Administration approved the use of two new protease inhibitors, boceprevir and telaprevir, for the treatment of hepatitis C genotype 1 [7, 59]—the most common genotype reported in the USA. When used in combination with pegylated interferon and ribavirin, boceprevir and telaprevir demonstrated SVR rates of 63–66 % and 69–75 %, respectively [7], a marked increase from traditional standard of care therapy alone.

In November and December 2013, the US Food and Drug Administration approved the use of two new drugs for the treatment of chronic HCV infection, simeprevir and sofosbuvir. These drugs are approved for use in HCV-infected patients with genotypes 1 and 4, which showed $\geq 90\%$ SVR rates in clinical trials [60]. Although treatment is very costly, these are among the new drugs that offer promising hope towards the global eradication of hepatitis C. As new therapies continue to be developed, evidence-based hepatitis C management recommendations are continuously updated to address issues ranging from testing and linkage to care to the optimal treatment regimen in specific patient situations [36].

### 3 Assessment of Priorities

The success of a surveillance system for hepatitis C is dependent on the dedicated resources and established priorities for the surveillance system. For example, if the priority is to measure the overall burden of disease, the design of the system might be to conduct a seroprevalence survey. However, if the objective is to obtain data for case management and evaluation of local area prevention programs, then individual cases should be monitored and records updated over time [61]. Furthermore, the population for which information is needed is an important determinant of surveillance methods. For example, in an enhanced surveillance pilot study in select neighborhoods in England, there were concerns about increases in HCV infection among MSM. Health officials quickly recruited and collected information from certain drug treatment facilities and implemented a surveillance project that provided results that were applied and published in less than a year [62]. In another study, researchers sought to determine which hepatitis C genotypes were circulating among injection drug users in Hungary [63]. They approached needle exchange programs and drug treatment facilities in all health districts and found that HCV strains among injection drug users were very different compared to HCV-infected persons who did not acquire their infections from injecting drugs [63]. The objectives and expected use of the surveillance data also should be tempered with the resources available to conduct the activities.
4 United States Surveillance Methods

4.1 Passive Surveillance

In a population-based passive surveillance system, sources of hepatitis C reports (e.g., hospitals, clinics, laboratories) routinely report cases to health departments [64]. However, in this type of surveillance system, notification may not be timely enough to alert health officials of a potential outbreak. In addition, the data reported are often incomplete because few, if any, incentives are given to the laboratories and healthcare providers to report information [64].

In the USA, as of 2013, acute hepatitis C is reportable in all states and the District of Columbia, and past/present hepatitis C is reportable in 43 states and the District of Columbia. Due to resource constraints, it is oftentimes difficult for health departments to obtain the necessary confirmatory laboratory tests from laboratories or healthcare providers to distinguish current from resolved or past HCV infection. Therefore, these cases are labeled as “past/present hepatitis C.” Under the current national surveillance system, acute and past/present hepatitis C are passively and voluntarily reported on a weekly basis by health departments to a national surveillance network at CDC. The system relies on laboratories and healthcare providers to submit case reports to health departments, as mandated by states. Health departments process case reports to determine that they represent new, unique cases and store data with personal identifiers.

Most laboratory reports and some physician reports are submitted electronically to health departments. However, reporting can be accomplished by fax or telephone, even using toll-free numbers or automated recording devices available at all hours. Time and lack of resources greatly limit such a system to a small percentage of most reportable diseases, but as long as the reporting system and requirements remain unchanged, the changes in incidence may reflect meaningful patterns of disease.

The advantage of a case reporting system is that there is an organized system of reporting and tabulating cases at both the local and national level. Also, at the local level, individuals are identified for intervention. However, case-reporting systems also have a number of disadvantages, including the following: (1) not all cases are reported despite legal requirements, primarily because of the lack of both symptoms and resources; (2) the variability in reporting from one jurisdiction to another; and (3) the lack of hepatitis C laboratory tests that distinguish between acute and chronic HCV infection.

Due to the large volume of past/present hepatitis C case reports and the resource-intensive process of identifying and classifying a case, chronic hepatitis C is grossly underreported in the USA. Current estimates indicate 2.2–3.2 million persons chronically infected with HCV [12].

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4.2 Active Surveillance

Active surveillance requires health departments to contact sources of hepatitis C reports at regular intervals and request specific information for case reports [64]. Reporting frequency is monitored and data on epidemiologic features, such as complications of infections, which would not otherwise be collected through passive surveillance, are obtained. In addition, the data are reported in a more timely fashion than in a passive system. However, unlike passive surveillance, active surveillance is expensive and resource intensive.

4.3 Enhanced Surveillance

CDC provides additional funding to support enhanced surveillance programs. These programs conduct follow-up investigation on cases to obtain additional information, including information about risk behaviors and/or exposures. As a result, data are more complete than passive surveillance. These additional data allow the surveillance infrastructure to answer discrete surveillance and research questions. From 1982 through 2006, the Sentinel Counties Study of Acute Viral Hepatitis enrolled all acute viral hepatitis patients in six county/city health departments in the USA [65]. From this project, funded sites collected data about cases of acute viral hepatitis from hospitals, healthcare providers, and other agencies and patient care sources. These data were used to describe the incidence of acute viral hepatitis [66], characterize individual cases, and identify and describe risk behaviors/exposures. From 2005 through 2011, CDC funded seven sites to conduct enhanced viral hepatitis surveillance throughout major US cities and states. Because of additional resources, completeness of reporting significantly improved in the enhanced surveillance sites [67].

4.4 Analysis of Specimens/Supplementary Data Sources

In the USA, there are existing data from other sources to augment hepatitis C surveillance data. For example, cancer registries have information on HCC [68]. Vital statistics generally include information on the number of deaths for which hepatitis C was listed among causes of death and calculating trends in HCV infection as a cause of death relative to other causes is useful [32]. Healthcare administrative data are available electronically and may be a useful source of data as well. Events available from administrative data include diagnosis, procedure codes, and cost information to examine the economic impact of hepatitis C [69].

Currently, CDC uses data from a variety of sources to further understand the burden of chronic HCV infection; characterize persons who receive treatment;
describe treatments, results of treatment, and sequelae of disease; and characterize those who die with and as a consequence of hepatitis C:

(a) **Vital Statistics:** The oldest form of surveillance in the USA is mortality registration. Registration of death, using a death certificate, is legally required in the USA. As a result, virtually all deaths are included in the registries. Cause of death listed on the death certificate is dependent on the presence/absence of a physician or family member who is knowledgeable about the health of the deceased, severity of disease, complexity of the disease, associated illnesses, and whether or not an autopsy or diagnostic laboratory testing was performed. Death certificates are completed by funeral directors based on information from attending physicians, medical examiners, coroners, and family members. Death certificates are filed in vital statistics offices within each state and the District of Columbia. States share information from death certificates with CDC through the National Vital Statistics System, which then produces public-use mortality files containing death information with cause of death coded in accordance with the International Classification of Disease, Tenth Revision [70]. These data are used to determine the national burden of mortality associated with specific diseases, including viral hepatitis. A recent analyses of these mortality data from 1999 through 2007 indicated that the hepatitis C mortality rate exceeded the HIV mortality rate in 2007 [32].

(b) **Surveys:** Health surveys are used for a variety of reasons, including augmenting our understanding of viral hepatitis from surveillance. Currently, the CDC uses several national surveys, which may include seroprevalence data, to describe and understand hepatitis C-related prevalence, hospitalizations, treatments, and development of CLD. For example, the National Health and Nutrition Examination Survey (NHANES) has provided valuable seroprevalence data on hepatitis A [71], hepatitis B [72], and hepatitis C [12] that are representative of the US noninstitutionalized civilian population [73]. The National Ambulatory Medical Care Survey and the National Hospital Ambulatory Medical Care Survey use a national sample of visits from nonfederal employed office-based physicians who provide direct patient care and from emergency departments and outpatient department of noninstitutional general and short-stay hospitals, respectively, to obtain information about the use and provision of ambulatory medical care services, including viral hepatitis-related visits [74], in these settings. The National Hospital Discharge Survey was a nationally representative survey conducted from 1965-2010 that provided information from patients of non-federal, short-stay hospitals in the USA about the characteristics of these patients, conditions for which they were treated, cost of treatment, and a number of other public health topics of interest. The National Hospital Care Survey is a new survey which links the inpatient data that was collected by the National Hospital Discharge Survey with the emergency department, outpatient department, and ambulatory surgery center data collected by the National Hospital Ambulatory Medical Care Survey. Together, these population-based surveys provide a wealth of readily available data that are already in electronic format. As a result, they can be relatively inexpensive sources of useful information in addition to that obtained from surveillance.
5 Sequence in Case-Based Surveillance Processes

5.1 Sequential Flow of Case Data for Hepatitis C Surveillance to CDC

CDC uses message mapping guides to standardize the data transmitted for all notifiable diseases monitored by health departments transmitted to the national surveillance network. States report basic demographic, clinical, and risk information on cases of notifiable conditions to the national surveillance network. The CDC Division of Viral Hepatitis retrieves data from servers once a week. These data are used to detect outbreaks, flag cases requiring immediate public health follow-up, and perform data quality checks. Viral hepatitis data are summarized in annual surveillance reports and are made available to the public on the CDC Division of Viral Hepatitis website [75].

5.2 Case Definitions in the USA, Europe, and Australia

Cases of notifiable conditions must meet standard case definitions. In the USA, these case definitions are developed and updated in collaboration with the Council of State and Territorial Epidemiologists and CDC. The 2012 hepatitis C surveillance case definitions require a combination of symptoms and laboratory findings for acute disease and laboratory findings only for past/present hepatitis C [9]. Because the clinical characteristics are the same for acute hepatitis A, B, and C, laboratory testing is needed to identify the specific viral cause of illness. For both acute and past/present hepatitis C cases, laboratory findings include a positive antibody to hepatitis C virus screening test, nucleic acid test for HCV RNA, and genotype testing. A special definition is applied to identify new seroconversions that require only one positive test and a previous negative test within the past 6 months [9].

In 2012, the European Union decided not to require clinical signs/symptoms for a confirmed case. Instead, at least one laboratory finding (RNA, core antigen, or antibody) in a person aged >18 months represents a confirmed case. The definition classifies an acute hepatitis C case as one that has a seroconversion within 12 months or has detected either RNA or core antigen but is antibody negative. A chronic case is defined as two samples positive for RNA or core antigen detected at least 12 months apart [76]. In Australia, case reports supplement other sources of information on HCV infection. A confirmed case in Australia requires laboratory evidence of either an antibody or nucleic acid test (either genotype or RNA) in a person aged at least 24 months, and who does not meet the criteria for a newly acquired case; that is, there is no evidence that the infection was acquired in the 24 months before diagnosis [77].
5.3 Follow-Up Investigation and Case Management

A hepatitis C case report is usually initiated with a positive antibody test, which can indicate either acute or chronic infection. After checking the surveillance database to determine whether the potential case was previously reported and had other epidemiologic or laboratory information, health departments can either attempt follow-up investigation or wait for future laboratory information to be received. Follow-up might require contacting the case patient’s provider to determine whether symptoms of hepatitis were present. Together with information that the case was not previously reported suggests a newly reported acute hepatitis C case. Follow-up with the case patient and/or the healthcare provider is required to obtain additional epidemiologic data. Cases might be divided into groups of interest, such as persons aged <30 years that may indicate IDU [78] or adults aged >65 years that may indicate transmission in healthcare and extended care facilities. Prioritizing groups of interest reduces the number of cases to be investigated, which makes the task more achievable. Basic demographic, clinical, and risk information are collected using a standard case report form (Fig. 6.2). This information is needed to confirm the classification, determine the most likely source of infection, and limit further transmission [79].

5.4 Uses of Surveillance Data in the USA

The uses of surveillance data vary depending on the public health agency’s need for the data. In general, at the national level, surveillance data are used to understand the burden of disease, inform local partners of disease clusters or outbreaks within and across jurisdictions, identify high-risk populations, and inform, prioritize, and evaluate prevention activities. At the local level, surveillance data are used to identify the most likely mode of transmission in the community to limit further transmission, detect and control local outbreaks, improve outreach services, and provide appropriate case management including screening and linking infected persons into care and counseling. Additionally, hepatitis C surveillance data can be matched with other disease registries, such as HIV, in order to integrate medical services for each individual and further understand disease burden. Surveillance data can also be used to evaluate the quality of care, including implementation of hepatitis A and B vaccine recommendations, among HCV-infected patients. Hepatitis A and B vaccine history can be obtained through follow-up investigation of cases and can be used to improve vaccine coverage rates.
Viral hepatitis case report form

**DEMOGRAPHIC INFORMATION**

- **Race** (check all that apply): [ ] Asian, [ ] African American, [ ] White, [ ] Native Hawaiian or Pacific Islander, [ ] Other Race, specify ____________________________, [ ] Other/Unknown
- **Sex**: [ ] Male, [ ] Female
- **Date of Birth**: [ ] 1/1/1945 - 4/30/1965
- **Place of Birth**: [ ] USA, [ ] Other
- **AGE**: ______ (years) (0 = 0yrs, 99 = Unknown)
- **Race**: Hispanic: [ ] Yes, [ ] No

**CLINICAL & DIAGNOSTIC DATA**

- **Reason for Testing**: (check all that apply)
  - [ ] Viral hepatitis
  - [ ] Screening for asymptomatic patient with reported risk factors
  - [ ] Screening for asymptomatic patient with no risk factors

- **Methods**: [ ] Enzyme-Linked Immunosorbent Assay (ELISA), [ ] Radioimmunoassay (RIA), [ ] Immunofluorescence (IF), [ ] Immunodiffusion (ID), [ ] Other

**CLINICAL Data**

| Evidence | Yes | No | Unknown |
|----------|-----|----|---------|
| Patient symptoms? | | | |
| If yes, onset date: | | | |
| At diagnosis, was the patient: | | | |
| Hospitalized for hepatitis? | | | |
| Was the patient pregnant? | | | |
| Date of death: | | | |
| Did the patient have hepatitis? | | | |
| Was the patient aware they had viral hepatitis prior to lab testing? | | | |
| Does the patient have a provider of care for hepatitis? | | | |
| Does the patient have diabetes? | | | |
| Diabetes diagnosis date: | | | |

**LIVER ENZYME LEVELS AT TIME OF DIAGNOSIS**

- **ALT (GGT) Result**: Upper limit normal ____________
- **Date of ALT result**: ____________
- **AST (GGT) Result**: Upper limit normal ____________
- **Date of AST result**: ____________

**DIAGNOSIS**: (check all that apply)

- [ ] Acute hepatitis A
- [ ] Acute hepatitis B
- [ ] Acute hepatitis C
- [ ] Chronic HBV infection
- [ ] Perinatal HBV infection
- [ ] Acute hepatitis D
- [ ] Acute hepatitis E
- [ ] HCV infection (Past or Present)

**The following questions should be asked for every case of viral hepatitis**

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**Fig. 6.2 Viral hepatitis case report form**
### Patient History — Acute Hepatitis A

**Case ID:**

| Question                                                                 | Yes | No | Unk |
|--------------------------------------------------------------------------|-----|----|-----|
| During the 2-6 weeks prior to onset of symptoms—                        |     |    |     |
| Was the patient a contact of a person with confirmed or suspected hepatitis A virus infection? |     |    |     |
| If yes, was the contact (check one)                                      |     |    |     |
| • household member (non-sexual)                                          |     |    |     |
| • sex partner                                                            |     |    |     |
| • child cared for by this patient                                        |     |    |     |
| • babysitter of this patient                                             |     |    |     |
| • playmate                                                               |     |    |     |
| • other                                                                  |     |    |     |
| Was the patient                                                          |     |    |     |
| • a child or employee in a day care center, nursery, or preschool?       |     |    |     |
| • a household contact of a child or employee in a day care center, nursery or preschool? |     |    |     |
| If yes for either of these, was there an identified hepatitis A case in the child care facility? |     |    |     |
| What is the sexual preference of the patient?                            |     |    |     |
| 0 Heterosexual 1 Homosexual 2 Bisexual 3 Unknown                           |     |    |     |
| Please ask both of the following questions regardless of the patient's gender. |     |    |     |
| In the 2-6 weeks before symptom onset how many male sex partners did the patient have? |     |    |     |
| female sex partners did the patient have?                                |     |    |     |
| In the 2-6 weeks before symptom onset                                    |     |    |     |
| Did the patient inject drugs not prescribed by a doctor?                 |     |    |     |
| Did the patient use street drugs but not inject?                         |     |    |     |
| Did the patient travel or live outside of the U.S.A. or Canada?          |     |    |     |
| If yes, where?                                                           |     |    |     |
| 1 ) ______________________________________ 2 ) ___________________________ |     |    |     |
| (Country) 3 ) _________________________________________________________ |     |    |     |
| What was the principle reason for travel? 0 Business 1 New Immigrant 2 Other 3 Unknown |     |    |     |
| In the X months prior to symptom onset did anyone in the patient's household travel outside of the U.S.A. or Canada? |     |    |     |
| If yes, where?                                                           |     |    |     |
| 1 ) ______________________________________ 2 ) ___________________________ |     |    |     |
| (Country) 3 ) _________________________________________________________ |     |    |     |
| Is the patient suspected as being part of a common-source outbreak?      |     |    |     |
| If yes, was the outbreak                                                  |     |    |     |
| Foodborne — associated with an infected food handler                     |     |    |     |
| Foodborne — NOT associated with an infected food handler                 |     |    |     |
| Specify food item                                                        |     |    |     |
| Waterborne                                                               |     |    |     |
| Source not identified                                                     |     |    |     |
| Was the patient employed as a food handler during the TWO WEEKS prior to onset of symptoms or while ill? |     |    |     |

### Vaccination History

| Question | Yes | No | Unk |
|----------|-----|----|-----|
| • Has the patient ever received the hepatitis A vaccine? |     |    |     |
| If yes, how many doses? |     |    |     |
| Specify dose 1 > 2 |     |    |     |
| • In what year was the last dose received? |     |    |     |
| If yes, when was the last dose received? |     |    |     |

---

Fig. 6.2 (continued)
### Patient History — Acute Hepatitis B

| Case ID: ____________________________ | Yes | No | Unk |
|--------------------------------------|-----|----|-----|

#### Surveillance for Hepatitis C

**Fig. 6.2 (continued)**

**6 Surveillance for Hepatitis C**

| During the 6 weeks – 6 months prior to onset of symptoms: | Yes | No | Unk |
|----------------------------------------------------------|-----|----|-----|
| Condom or other contraceptive device.......................... | ☐   | ☐  | ☐  |
| No contraceptive.................................................... | ☐   | ☐  | ☐  |

**Did the patient:**
- undergo hemodialysis? ........................................... ☐  ☐  ☐
- have an accident or puncture with a needle or other object contaminated with blood? ......... ☐  ☐  ☐
- receive any IV infusions and/or injections in the last 12 months? .......................................... ☐  ☐  ☐
- have any other exposure to someone else’s blood? ................................................................. ☐  ☐  ☐

**During the 6 weeks – 6 months prior to onset of symptoms:**
- Did the patient receive a tattoo? .................................. ☐  ☐  ☐
- Where was the tattooing performed? (select all that apply): ☐  ☐  ☐
  - commercial parlor/club
  - correctional facility
  - other

**Did the patient ever receive hepatitis B vaccine?............. ☐  ☐  ☐
- If yes, how many shots? ........................................... ☐  ☐  ☐
- If in what year was the last shot received? .................... ☐  ☐  ☐

**Was the patient tested for antibody to HBsAg (anti-HBs) within 1-2 months after the last dose?......... ☐  ☐  ☐
- If yes, was the result 1 unit/mL? ................................. ☐  ☐  ☐

**What is the sexual preference of the patient?**
- Heterosexual  ☐
- Homosexual  ☐
- Bi/sexual  ☐
- Unknown  ☐

**Ask both of the following questions regardless of the patient’s gender:**
- In the 6 months before symptom onset, how many male sex partners did the patient have? ........... ☐  ☐  ☐  ☐  ☐
- In the 6 months before symptom onset, how many female sex partners did the patient have? ........... ☐  ☐  ☐  ☐  ☐

**Was the patient EVER treated for a sexually-transmitted disease?........................................... ☐  ☐  ☐
- If yes, in what year was the most recent treatment? ............................... ☐  ☐  ☐

**During the 6 weeks – 6 months prior to onset of symptoms:**
- inject drugs not prescribed by a doctor? ...................... ☐  ☐  ☐
- use street drugs but not inject? ................................. ☐  ☐  ☐
- Did the patient have any part of their body pierced (other than ear)? ...................................... ☐  ☐  ☐
- Where was the piercing performed? (select all that apply):
  - commercial parlor/club
  - correctional facility
  - other

**Did the patient have dental work or oral surgery?........... ☐  ☐  ☐
- Did the patient have surgery other than oral surgery? .................................................. ☐  ☐  ☐

**Was the patient (check all that apply):**
- hospitalized.......................................................... ☐  ☐  ☐
- a resident of a long-term care facility? ............................. ☐  ☐  ☐
- incarcerated for longer than 24 hours................................... ☐  ☐  ☐
- if yes, what type of facility (check all that apply):
  - prison
  - jail
  - juvenile facility

**During his/her lifetime, was the patient EVER incarcerated for longer than 6 months? ................... ☐  ☐  ☐
- If yes, what year was the most recent incarceration? ...... ☐  ☐  ☐

**Did patient have a negative HBsAg test within 6 months prior to positive test? ......................... ☐  ☐  ☐
- Verified test date: .................................................. ☐  ☐  ☐

**Was the patient tested for hepatitis D?......................... ☐  ☐  ☐
- Did patient have a co-infection with hepatitis D? .......... ☐  ☐  ☐
### Perinatal Hepatitis B Virus Infection

**Case ID:**

| RACE OF MOTHER: | ETHNICITY OF MOTHER: |
|-----------------|-----------------------|
| Amer Ind or Alaska Native | Hispanic: |
| Black or African American | Non-Hispanic: |
| White | Other/Unknown: |
| Unknown | |

| Other Race, specify: | |

| Was Mother born outside of United States? | Yes | No | Unk |
|-----------------------------------------|-----|----|-----|

| Was the Mother confirmed HBlAg positive prior to or at time of delivery? | Yes | No | Unk |
|----------------------------------------------------------------------------|-----|----|-----|
| * If no, was the mother confirmed HBsAg positive after delivery? | Yes | No | Unk |

| Date of earliest HBsAg positive test result | M | D | Y | Y | Y | Y | Y | Y |

| How many doses of hepatitis B vaccine did the child receive? | 0 | 1 | 2 | 3* |
|-------------------------------------------------------------|---|---|---|----|
| * Wren? | Yes | No | Unk |
| * Dose 1 | Yes | No | Unk |
| * Dose 2 | Yes | No | Unk |
| * Dose 3 | Yes | No | Unk |

| Did the child receive hepatitis B immune globulin (HBlG)? | Yes | No | Unk |
|----------------------------------------------------------|-----|----|-----|
| * If yes, on what date did the child receive HBlG? | | | |

---

**Fig. 6.2** (continued)
### Patient History — Acute Hepatitis C

**Case ID:**

| During the 2 weeks – 6 months prior to onset of symptoms was the patient a contact of a person with confirmed or suspected acute or chronic hepatitis C virus infection? | Yes | No | Unk |
| --- | --- | --- | --- |
| If yes, type of contact  
  - Sexual  
  - Household (non-sexual)  
  - Other: | | | |

| During the 2 weeks – 6 months prior to onset of symptoms  
  - Undergo hemodialysis?  
  - Have an accidental stick or puncture with a needle or other object contaminated with blood?  
  - Receive blood or blood products (transfusion)?  
  - If yes, where?  
  - Receive any IV infusions and/or injections in the outpatient setting?  
  - Have other exposure to someone else’s blood?  
  - Specify: | Yes | No | Unk |

| During the 2 weeks – 6 months prior to onset of symptoms  
  - Was the patient employed in a medical or dental field involving direct contact with human blood?  
  - If yes, frequency of direct blood contact?  
  - Was the patient employed as a public safety worker (firefighter, law enforcement or correctional officer) having direct contact with human blood?  
  - If yes, frequency of direct blood contact?  
  - Was the patient receive a tattoo?  
  - Where was the tattooing performed? (select all that apply)  
  - Commercial parlor/ink  
  - Correctional facility  
  - Other | Yes | No | Unk |

| During the 2 weeks – 6 months prior to onset of symptoms  
  - Did the patient have any part of their body pierced other than ear?  
  - Where was the piercing performed? (select all that apply)  
  - Commercial piercing shop  
  - Correctional facility  
  - Other | Yes | No | Unk |

| During the 2 weeks – 6 months prior to onset of symptoms  
  - Did the patient have dental work or oral surgery?  
  - Did the patient have surgery (other than oral surgery)? | Yes | No | Unk |

| During this other lifetime, was the patient EVER incarcerated for longer than 6 months? | Yes | No | Unk |

**Fig. 6.2 (continued)**
5.5 **Estimation of Hepatitis C Incidence in the USA**

Most HCV infections are not captured through surveillance because many of these infections are asymptomatic. Estimation methodologies are used to account for underreporting of asymptomatic hepatitis C infections. The methodology employed by the CDC to estimate the incidence of HCV infections in the USA was revised in 2011. This methodology uses a simple probability model to estimate all new hepatitis C infections that occur in the USA during a calendar year [80].
Under this model, the estimated number of acute HCV infections in the USA is the number of reported confirmed acute hepatitis C cases multiplied by the joint probability that acute HCV-infected persons who would have developed symptoms, sought healthcare tests, and been reported to health officials [80]. CDC conducted a meta-analysis of peer-reviewed studies to inform the three parameters [80]. However, more sophisticated models informed by representative and comprehensive studies are needed to best estimate acute HCV infections in the USA.

5.6 Security and Confidentiality

While hepatitis C surveillance data can serve many useful public health purposes, these data must be collected, stored, shared, and used in a way that protects the identity of infected individuals [81]. Countries with a well-established hepatitis C surveillance system may have data security and confidentiality policies and procedures in place while countries that are still developing their surveillance system may not. In general, there are guiding principles [82] that can be followed by all countries in order to guarantee security and confidentiality of public health data. These principles are summarized below:

- Data collection and use policies should respect the rights of individuals and community groups and minimize undue burden.
- Program officials should be active, responsible stewards of public health data.
- Programs should:
  - Require that public health data be acquired, used, disclosed, and stored for legitimate public health purposes
  - Collect the minimum amount of personally identifiable information necessary to conduct public health activities
  - Have strong policies to protect the privacy and security of personally identifiable data
  - Have policies and procedures to ensure the quality of any data they collect or use
  - Have the obligation to use and disseminate summary data to relevant stakeholders in a timely manner
  - Have public health data maintained in a secure environment and transmitted through secure methods
  - Share data for legitimate public health purposes and establish data-use agreements to facilitate sharing data in a timely manner
  - Minimize the number of persons and entities granted access to identifiable data
6 Limitations and Challenges of Surveillance

6.1 Distinguishing Acute and Chronic HCV Infection

Many countries do not distinguish between acute and chronic HCV infection and use a case definition based on HCV antibody results alone [76]. For example, in a survey of countries, the European Centre for Disease Prevention and Control found that Germany, the Netherlands, Sweden, England and Wales, and Scotland were enumerating hepatitis C cases based on an antibody test alone [76].

Jaundice may be a practical method for conducting viral hepatitis surveillance in areas where laboratory testing is not routinely included in healthcare visits. For example, in a surveillance system developed to measure the frequency of hepatitis E in northern Uganda, epidemiologists implemented a system originally designed for malaria surveillance [83]. Upon presentation of a person with jaundice to one of the facilities where providers were trained, providers completed a brief case report form, and collected a specimen that was then sent to a central laboratory [83]. At a centralized location, the information from the case report forms and the laboratory results were processed and analyzed to determine the frequency of the different etiologies of jaundice [83].

6.2 Underreporting

Even with the technological advances made in the areas of health information in the USA, the surveillance of hepatitis C continues to be hampered by underreporting, misclassification of cases, and need for more complete data since hepatitis C reporting to the national surveillance network is voluntary. In the USA, CDC estimates that for every reported case of acute hepatitis C, another 12 infections go unreported [80]. There are many reasons why hepatitis C is underreported in the USA. First, HCV infections can only be considered acute if symptoms are present or there is a documented seroconversion. However, 70–85 % of HCV-infected individuals are asymptomatic; about one-half are unaware of their infection [84]. Second, a large percentage of HCV-infected persons may lack access to healthcare services and are thus not reported to health departments. In addition, many states lack the funding needed to conduct enhanced surveillance and do not have the capacity to develop a surveillance system capable of receiving and processing the large number of positive HCV antibody laboratory reports. The number of hepatitis C cases annually reported to health departments often outpaces the amount of resources on hand to fully conduct follow-up investigations to determine if the newly reported case is acute. For these reasons, identifying hepatitis C cases is challenging.
6.3 **Resources**

Case-based hepatitis C surveillance is a resource-intensive process. Because of many low-resource settings and competing priorities to dedicate the majority of resources to surveillance for acute and effectively preventable conditions, hepatitis C surveillance is often not well developed. As a result, many health departments do not have the capacity to fully investigate every newly reported hepatitis C case. The inability to depend solely on serologic testing to identify acute hepatitis C cases combined with the inability to fully investigate all newly reported cases often leads to the inability to determine if hepatitis C cases are confirmed; these cases instead have a case status label of “probable,” “suspect,” or “unknown.” Unconfirmed cases may never be tested or investigated to determine if they are currently infected [85]. An important decision should be made about the specific objectives and needs for hepatitis C surveillance data such that resources can be used most efficiently and effectively.

6.4 **Laboratory Issues**

Although a number of highly sensitive and specific rapid tests are available in order to accurately and quickly identify HCV-infected persons and link them to the appropriate care, these tests are often not available in resource-limited settings. The barriers for correctly identifying HCV-infected persons include the lack of simple laboratory assays, need for additional confirmatory testing, and lack of a test for delineating acute from chronic infection.

7 **Future Directions**

7.1 **Health Information Technology**

Health information technology (HIT) provides the tools necessary for healthcare providers to better manage patient care through the secure electronic exchange of health information [86]. In a fragmented healthcare system such as that in the USA where multiple healthcare providers are making individual healthcare decisions on the same patient, benefits of the widespread use of HIT include improved quality of healthcare, significantly reduced medical errors, decreased healthcare costs, increased administrative efficiencies, decreased paperwork, and expanded access to affordable healthcare [86, 87]. For example, in 2004, the Massachusetts eHealth Collaborative was formed to establish an electronic health record (EHR) system that would improve the quality, efficiency, and safety of patient care in Massachusetts [88]. By August 2007, nearly 600 physicians participating in the initiative were using EHRs [89].
Historically, a series of critical events which occurred during the late 1990s and early 2000s drew concerns regarding the ability of the USA to respond effectively to acts of bioterrorism and natural epidemics while continuing to protect the health of the nation. These events included the anthrax attacks; destruction of the World Trade Center and the attack on the Pentagon; and emerging disease epidemics such as SARS, avian influenza, and West Nile virus [90]. Having a national system with medical and health information on its citizens would be critical. In response, on April 27, 2004, the president of the USA signed Executive Order 12225, which created the Office of the National Coordinator of Health Information Technology, the principal federal entity charged with supporting the widespread meaningful use of HIT and coordinating efforts to implement and use a nationwide interoperable and secure health information exchange system [90].

7.1.1 Electronic Integration

Ideally, electronic sources of data on HCV infections would have some standardization allowing easy aggregation, supplementation, and analyses. In the USA, with the exception of 16 states, viral hepatitis surveillance systems are neither integrated nor interoperable to produce a singular national electronic surveillance system. Such a system would help to prevent the spread of viral hepatitis and help understand the relationship between viral hepatitis and comorbidities [91]. Hepatitis C surveillance can be greatly improved by expanding health information exchanges (HIEs) and electronic laboratory reporting (ELR).

Where electronic medical records are not integrated, separate data streams can be used to identify persons with HCV infection, for example, using pharmacy records that list antiviral medications specific for hepatitis C [60].

7.1.2 Health Information Exchanges

The framework for a nationwide health information network that connects independent but interoperable public health data systems dates back to 2004 [92]. A key goal of a nationwide health information network is to create an electronic system that can accurately and in a timely fashion exchange patient health information while following security and other protection protocols [93]. HIEs facilitate information flow across various healthcare delivery systems including hospitals, healthcare provider groups, insurers, and government agencies, and are characterized by formal agreements and technologies that facilitate the electronic movement of health-related information [94]. In the USA, funding by the CDC and other public health agencies have supported the development of HIEs and a nationwide health information network [95, 96].

The ability of HIEs to strengthen patient safety through improving laboratory result processing, diagnoses, treatment modalities, and communication between pro-
providers and patients has magnified the potential uses for HIEs. Despite the potential uses of HIEs and the great amount of progress that has occurred over the past 10 years, resource constraints prevent widespread implementation of HIEs [97, 98].

### 7.1.3 Electronic Laboratory Reporting

In the USA, electronic laboratory reporting is conducted by the automated transmission of laboratory test results of notifiable diseases from commercial, public health, and hospital laboratories to health departments through a laboratory information management system. The goal of ELR for reporting of hepatitis C is to improve the accuracy, timeliness, and completeness by reducing the number of laboratory reports that are manually entered by health departments. When using ELR, laboratories export data from their information systems in a standard file format and electronically transmit it to their health departments through the laboratory information management system.

Prior to the advances in ELR technology in the USA, manual data entry of paper laboratory reports was the standard procedure for collecting data on viral hepatitis infections. However, manual data entry of paper laboratory reports is both labor intensive and costly. ELR has been shown to identify almost three times as many hepatitis C cases as the traditional paper-based method, and, on average, identified those cases nearly 5.5 days earlier than the conventional method [99].

Although ELR shows promising hope for timely and accurate laboratory reporting, there are challenges. First, these systems report only data listed on laboratory reports and do not contain the clinical information required to confirm a hepatitis C case. Secondly, these systems do not report any enhanced epidemiologic data including risk behaviors/exposures, hepatitis A and B vaccination history, and pregnancy status. These additional components are obtained through enhanced follow-up investigation with the provider and patient. Because of the overwhelming burden of past/present hepatitis C laboratory reports that are submitted to health departments, follow-up investigations are often an enormous endeavor, and for highly populated areas such as New York State, only a sample of total past/present hepatitis C reports can be followed. Additionally, complex ELR algorithms that are either inept or inefficient often lead to incorrect detection of new viral hepatitis cases [99].

### 7.2 Lessons Learned from Enhanced Surveillance in the USA

From 2005 through 2011, the CDC funded seven health departments to conduct enhanced hepatitis C surveillance throughout the USA. Experiences from this collaboration suggest that certain elements are critical to the success of conducting complete, useful surveillance:

(a) **Electronic infrastructure to receive and process hepatitis C laboratory reports.**

Most clinical laboratories have the capacity to report tests associated with all
notifiable diseases in an electronic format to the health departments. However, because laboratories lack a standardized system and health departments vary in their capacity to receive and process electronic information, the large number of hepatitis C reports easily overwhelmed their systems. The lesson learned was that health departments needed to invest in electronic data systems that allowed significant numbers of test results to be received, de-duplicated to result in patient-level information, and then processed to determine electronically whether the patient had been reported previously or was a new case [100].

(b) Funding for staff at health departments to conduct follow-up investigation. Because of limited human resources, it became clear that attempting to follow-up on all de-duplicated cases was not feasible. The solution to this problem was to conduct follow-up investigation on a random sample of cases. In most sites, sampling was conducted prospectively on recently reported cases, allowing a 3-month waiting period to ensure that providers had notified patients of their test results. The goal in most sites was to sample $\geq 10\%$ of reported cases and to obtain supplemental information from the healthcare provider associated with the positive test result.

(c) Flexibility of data collection instruments and data entry and storage systems. Previously, information on mode of transmission was considered desirable, but more helpful to prevention was the identification of which individuals were linked to care. Several health departments had the flexibility to pilot new information items including whether the individual had seen a healthcare provider for hepatitis-related care, and whether they had ever been treated for hepatitis C.

(d) Secure and standardized transmission of data to a central office. Difficulties with the larger electronic system for notifiable diseases resulted in the use of an independent, secure transfer protocol mechanism to receive electronic data from sites.

(e) Capacity to conduct analyses at the central office. The application of standardized case definitions was complicated at the local level by subjective interpretations and applications of the definition. Data collected on all positive HCV antibody tests allows surveillance programs to understand the population testing positive, and not only those who have the additional confirmatory testing requirements to meet the case definition (e.g., RIBA, RNA). Therefore, a best practice is to receive all data elements and observations health departments are able to collect and send them to a central office. Then, standardized selection criteria can be applied prior to data analyses. For example, the current US hepatitis C case definition requires a confirmatory antibody test; however, understanding the frequency with which persons test positive and are then not reported to have a follow-up test is useful for prevention [85].

7.3 Conclusions

Hepatitis C surveillance can yield useful information for understanding burden of disease, preventing outbreaks, identifying high-risk populations, and planning and evaluating prevention activities. However, careful consideration of objectives should
be balanced with available resources. The current US hepatitis C surveillance system forms the backbone of surveillance and provides incidence data. Enhanced surveillance activities provide additional risk and exposure information on cases. To describe the complete spectrum of HCV disease, HCV-related information from additional sources of data, including population-based surveys, is used. As healthcare services evolve in their application of informatics, surveillance of HCV infection can take advantage of the events generated from HCV-related medical encounters in electronic medical records. Testing data from laboratories could be used to monitor the implementation of screening recommendations, and results from nucleic acid tests could be useful to distinguish between current present and resolved or past HCV infection.

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