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Hepatitis C virus: An overview for dental healthcare providers

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Abstract

Potential transmission of hepatitis C virus (HCV) in a private dental practice provides a stark reminder that dental healthcare providers (DHCPs) need updated information about this pathogen. As DHCPs will likely treat persons with current infection, training on the science of HCV infection is useful. Furthermore, in the past five years, our understanding of HCV has evolved. The elevated prevalence of chronic HCV infection among “baby boomers” born during 1945–1965 has prompted new national screening guidelines. New therapeutic options are revolutionizing HCV infection. This review summarizes information about the natural history and epidemiology of hepatitis C, describes new CDC screening guidelines and current treatment. In addition it provides an overview of how outbreaks of healthcare-associated HCV are detected and prevented. There are useful references and websites where additional detail is available for those interested in learning more.

Keywords

Hepatitis C; Standard Precautions; injection safety; Healthcare-associated infections

BACKGROUND

Prompted by the potential transmission of hepatitis C virus (HCV) in a private dental practice in 2013,[1] this review brings dental healthcare providers (DHCPs) up-to-date with the natural history and epidemiology, new CDC screening guidelines,[2,3] new treatment, surveillance, and healthcare-associated HCV transmission and prevention options. The review provides useful references and websites where additional detail is available for those interested in learning more.

Even before HCV was identified in the late 1980s, the observation that not all transfusion-associated hepatitis was associated with hepatitis A or B lead to the label ‘non-A, non-B’ hepatitis.[4] Since then, our understanding of the virus and the development of treatments for

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infected persons have evolved rapidly. HCV is an RNA virus with great molecular heterogeneity within and across individuals, since mutations occur frequently during replication. Viral diversity is one of the challenges to vaccine development; others include the lack of a non-primate animal model and the unclear immune responses that lead to viral clearance.[5] There are six major genotypes of HCV with variability by geographic distribution; the majority of isolates (about 85%) in the US are genotype 1a or 1b.[4]

Transmission

HCV is transmitted most efficiently by the parenteral route, and this may occur at even low levels of viral contamination. From 2008–2012 CDC received notice of 15 outbreaks of healthcare associated transmission of HCV in non-dental ambulatory care settings.[6] In general, transmission of infectious agents in healthcare settings can occur from patient to patient (e.g. due to improper injection practices) patient to provider (e.g. from needle sticks), or provider to patient (e.g. during surgery). The risk of transmission depends on factors related to the agent, the host, and the environment. HCV can survive in the environment for 16 hours on a dry surface,[7] in water at low temperatures for up to 5 months,[8] and can be detected in saliva.[9] Disinfectants that inactivate hepatitis B virus will also kill HCV on environmental surfaces,[10] and commercial hand antiseptics are effective at inactivating the virus from hands.[8]

The estimated risk of infection with HCV from a percutaneous injury is about 2%;[11] that is, greater than with HIV, but less than with hepatitis B virus. Standard Precautions[12] for injection safety remain the foundation for prevention of healthcare associated hepatitis infections, with new toolkits and resources available (Table 1).

Before 1992, and the availability of testing to screen blood and blood products, healthcare transmission in the form of blood transfusions was associated with about 15–20% of HCV infections.[13] In the US, injecting drug use is currently the most frequent risk behavior associated with HCV infection.[14,15] Of recent concern are clusters of HCV among young non-urban adults injecting drugs, who often started injecting cheaper heroin when their access to prescription opiods was no longer available.[16,17] Sexual transmission is rare except under high risk sexual practices.[18] Likewise, no infections have been reported associated with commercial tattoos and piercing, but transmission may occur in unregulated environments (e.g., prisons).[19]

Burden of disease

DHCPs can reasonably expect to encounter patients with HCV infection, since about 1.6% of the US population has ever been infected.[20] While about 20% of infections resolve spontaneously,[21] most infected persons develop chronic infection (defined as an HCV-RNA positive test result from plasma or serum). CDC estimated in 2002 that 3.2 million persons (1.3%) in the US were HCV-RNA positive. Prevalence of chronic infection is higher (3.25%) among persons born during 1945–1965.[22] About 60% of dentists are in this cohort (‘baby boomers’)[23] and may have undetected past or current infection themselves; another reason for DHCPs to be knowledgeable about hepatitis C.

Acute infection is symptomatic in about 50% of cases, fewer (10%) among persons infected through injection drug use.[24] When symptoms are present, these are non-specific and can include jaundice, fever, abdominal pain, malaise, and elevated liver function tests (alanine aminotransferase (ALT) or aspartate aminotransferase (AST)). Many (about 50%) are unaware of their infection status.[25] Among persons with chronic infection, about 15–30% may progress to liver cirrhosis,[13] and of these patients, an estimated 1–3% will develop hepatocellular carcinoma.[26] Currently, HCV is the leading indication for liver transplantation, costing a median of $120,500 per hospitalization.[27] Deaths associated with HCV infection surpassed deaths with HIV infection in 2007.[28]

Screening, Diagnosis, and Treatment

Until 2012, screening for HCV infection was recommended for persons at highest risk of infection (i.e., injection drug users, persons with medical conditions that required dialysis or transfusions, recipients of organs or transfusions before 1992) or with a known exposure to HCV (i.e., children born to HCV-positive women and occupationally exposed persons).[29] Current age-based screening recommendations have recently expanded the recommendation to include a one-time test for all persons born between 1945–1965, with alcohol use screening and referral to care for infected persons.[22]

Diagnosis in public health settings and primary care begins with the detection of antibody against HCV (anti-HCV).[3] Rapid tests are now available with high sensitivity and specificity; these use blood from either a fingerstick capillary or whole blood from venipuncture and provide results in <40 minutes.[30] The majority of anti-HCV tests are immunoassays. Immunoassays can determine whether or not someone has ever been infected with HCV, but only a nucleic acid test to detect HCV-RNA whether a person has current infection.[3] HCV-RNA tests can be qualitative (positive or negative) or quantitative (viral copies/mL). The genotype test is another type of nucleic acid test, which may be performed during evaluation for treatment.[31]

Not all infected persons are diagnosed and treated. Data from a CDC cohort was combined with a nationally representative survey to determine the number of infected persons who have been diagnosed and are receiving appropriate care.[32] Of the estimated 3.2 million US residents currently infected, only about 50% have been diagnosed. Of these, about 32–38% have been referred to care, 7–11% treated, and 5–6% cured. However, new screening recommendations should identify more asymptomatic infections,[2] at a time when there are great improvements in treatment protocols and outcomes.[33]

Until 2011, the standard of care consisted of pegylated interferon plus ribavirin.[26] This regimen required weekly injections, had only about a 50% success rate for genotype 1, and had frequent side effects. Since then, the protease inhibitors telaprevir and boceprevir have been introduced, still in conjunction with interferon and ribavirin, but with greater success rates.[34] In 2013, sofosbuvir, used in the first interferon-free treatment regimens, was submitted for FDA approval. These and other therapies currently in clinical trials are already revolutionizing the treatment of chronic HCV infection.[35]

SURVEILLANCE

Surveillance for HCV in the US

National surveillance is conducted for two discrete HCV events: acute disease and past/present hepatitis C infection (i.e., includes persons with current chronic infection and history of infection). The surveillance case definition for acute disease requires a combination of symptoms and laboratory findings, but for past/present disease, only laboratory findings are required. In 2012, surveillance defined acute HCV infection as illness with 1) discrete onset of symptoms (e.g., nausea, anorexia, fever, malaise, or abdominal pain) and 2) jaundice or elevated serum ALT levels (> 400 IU/L). There is also an option to identify a new seroconversion as an acute case; this requires only one positive test with a previous negative within the past 6 months.[15] With advances in information technology, most health departments have developed electronic, laboratory-initiated reporting to conduct routine surveillance for viral hepatitis cases more efficiently.

Flow of surveillance information

HCV infection is a reportable condition in most states.[14] Providers, facilities and laboratories are usually required to report, but in practice, most cases are identified first from laboratory-initiated reporting. Local and state health departments receive the reports and check to determine whether the case was previously reported or represents a new case.[36] Health departments conduct investigations of reports, depending on available resources, and submit these to CDC weekly (Figure).

When a person with HCV infection is determined to represent a new, acute case, health departments pursue supplemental clinical and demographic data; however, in practice, resources frequently limit the number of cases investigated. Investigators also assess risk factors for infection by identifying exposures during the incubation period (2 weeks – 6 months before symptom onset). Among the potential exposures, health departments collect history of accidental needlestick, outpatient injections, employment in the medical or dental field, hospitalization, surgery, and dental work or oral surgery.

Data from HCV surveillance are used to describe burden of disease and characteristics of infected populations. Reports are disseminated on-line and in scientific venues to guide prevention and plan for healthcare resource needs at the state and national level.[14]

Healthcare-Associated Outbreak Detection and Investigation

It is frequently a telephone call from an astute clinician, who diagnoses HCV infection in a person with no behavioral risk factors or sees an unexpectedly high number of infections in a short period of time (e.g., 2–3 cases in 2 weeks compared to no cases for months), that leads to an investigation.

At the health department, follow-up of potential healthcare transmission of HCV typically begins by confirming whether infection indeed occurred. Then, surveillance investigators assess all potential exposures within the incubation period, including, if appropriate, a relative measure of the risk of healthcare transmission. Once the report is received, health

department officials face many barriers to conducting investigations.[37] If the investigation identifies risky infection control practices, patients potentially exposed during the at-risk time period are notified to seek testing. There have been over 90,000 at-risk persons notified to seek HCV testing associated with the 16 outbreaks reported to CDC from 2008–2012. CDC developed a 'Healthcare Investigation Guide' to support health departments in their efforts to quickly identify transmission of infection and control any unsafe clinical practices (Table 1).

Health department personnel often work in collaboration with CDC during HCV investigations, especially in the area of laboratory support. Genetic sequencing is used to assign virus isolated from different individuals into related clusters by their degree of relatedness.[37] For example, in an investigation of HCV transmission in an endoscopy clinic, molecular characterization confirmed a very high degree of similarity between 2 source patients with chronic HCV infection and 7 patients infected at the clinic.[38] Laboratory analyses are, and must be, conducted and interpreted as a component of a larger epidemiologic investigation.

Reported Healthcare-Associated HCV Outbreaks

From 2008–2012, CDC received notice of 16 outbreaks of healthcare-associated transmission of HCV; 15 of these were in ambulatory care settings.[6] Combined, these outbreaks identified 160 outbreak-associated, confirmed infections. Five of these outbreaks were likely associated with syringe reuse, three were associated with drug diversion (i.e., when a prescription medication is used by an infected healthcare worker with subsequent contamination of the medication vial or syringe), six were in hemodialysis settings, and in one outbreak, there were no identified lapses in infection control observed during the investigation. Currently, the Oklahoma Health Department is collaborating with CDC in investigating the first potential transmission of HCV in a dental setting, specifically in an oral surgery practice. Further detail is available on-line.[1] CDC maintains an updated list of viral hepatitis outbreaks associated with healthcare, as well as links to toolkits for investigation of healthcare-associated infections, on an easy to remember website: "CDC.gov/hepatitis/Outbreaks."[39]

Because of the long incubation period (up to 6 months) and typically asymptomatic course of acute HCV infection, many are missed by routine surveillance. Therefore it is likely that only a fraction of such outbreaks that occurred have been detected. Asymptomatic infections frequently go undetected for many years, leading to under-reporting of cases to the health department and difficulty in identifying a healthcare encounter where transmission may have taken place. Furthermore, even persons with HCV-related symptoms might not recognize them and seek medical attention, or the clinician might not suspect HCV infection. Even if diagnosed, HCV infections might not be reported to the health department because clinicians might not understand when, how or what to report. Personnel, resource and legal barriers may prevent state and local health departments from thoroughly investigating clusters and reporting to CDC.[37] There is also under-recognition of the potential for healthcare as a risk factor for viral hepatitis transmission, so the numbers reported to CDC likely underestimate the number of outbreak-associated cases and the number of at-risk persons notified for

screening. CDC has developed numerous tools and questionnaires to support health departments in investigating potential outbreaks of healthcare-associated infections.[39,40]

PREVENTION

There is currently no vaccine for primary prevention of hepatitis C. Standard Precautions remain the foundation to protect against transmission of HCV and other infectious agents during patient care in the dental setting. Original infection control guidelines for dental offices were published in 2003,[41] and these are the same basic principles and evidence base for all outpatient settings. In 2011, CDC developed a new tool outlining the minimum expectations for safe care in outpatient settings. The tool is a document that packages basic information as a general reference, from which more detailed documents can be accessed quickly and easily.[42]

Standard Precautions for dental and other outpatient settings are summarized in Table 2. These include hand hygiene, proper use of personal protective equipment (i.e., gloves, mask, gowns), safe handling of sharps and injection practices, environmental cleaning, proper use of medical equipment and drugs (e.g., reusable vs. single-use), and respiratory hygiene/cough etiquette (i.e., use of measures to contain respiratory secretions of symptomatic persons and education of healthcare workers to prevent spread of respiratory secretions). CDC provides many resources for DHCPs (Table 1) including continuing education training for healthcare providers and materials to train staff in infection control.

Injection Safety

Safe injection practices are a part of Standard Precautions. Most HCV transmissions in outpatient healthcare settings have been attributed to syringe reuse or other practices that led to contamination of the solution or medication intended to be injected[43] (e.g., fentanyl, propofol). Medications should never be administered to more than one patient using the same syringe, even if the needle is changed. In other words, medication vials should not be entered with a used syringe or needle. Single-use vials should never be used for more than one patient.[43]

Post-exposure Management of Exposed Healthcare Workers

If, despite prevention efforts, a needlestick or other exposure to HCV occurs, it is important to have a protocol to follow. Briefly, CDC's recommended follow-up[11] of exposed healthcare workers consists of baseline HCV antibody testing of both the exposed healthcare worker and the source patient. In addition, the healthcare worker should have a baseline assessment of ALT activity. Follow-up testing of the exposed healthcare worker should be performed (e.g., at 4–6 months). HCV-RNA may also be tested at 4–6 weeks if earlier diagnosis is desired. Immunoglobulin is not recommended for post-exposure protection.[11]

Recent recommendations for the management of hepatitis B infected healthcare workers did not address the issue of HCV-infected healthcare workers.[44] However, The Society for Healthcare Epidemiology of America (SHEA) recommends that HCV infected healthcare workers with high circulating viral burden ($\geq 10^4$ genome equivalents/mL) follow certain precautions and abstain from performing certain invasive procedures. According to SHEA

guidelines, HCV-infected HCWs with $<10^4$ genome equivalents/mL of circulating virus should have routine follow up with a personal physician and maintain consultation with an infection control expert to ensure appropriate infection control practices are used.[45]

Oversight of Infection Control Practices

In hospitals and some outpatient healthcare settings the Centers for Medicare and Medicaid Services (CMS) require periodic reports of quality measures from many types of facilities receiving reimbursement for services (e.g., ambulatory surgical centers, hemodialysis facilities). CMS routinely conducts audits and surveys of facilities through regional offices. CDC collaborates with CMS because both agencies are concerned with patient safety and preventing healthcare-associated infections (e.g., coverage with vaccination for hepatitis B among hemodialysis patients and healthcare workers). For example, CDC developed an infection control audit tool to help ambulatory surgical centers prepare for CMS audits. Importantly, facilities that demonstrate adherence to CDC infection control guidelines receive CMS financial incentives. Currently, no such oversight exists for monitoring infection control practices in dental settings.

Summary

The first investigation of HCV transmission in a dental setting serves as a reminder to educate DHCPs about hepatitis C. An estimated 3.2 million persons have chronic HCV infection in the US, most are asymptomatic. HCV transmission in healthcare settings is preventable by the use of Standard Precautions, including injection safety. New tools are available to support health departments in conducting investigations, and for providers to easily access to information on infection control. Because DHCPs will likely treat persons with current or past infection, training on the evolving science of HCV infection could be of substantial value.

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The findings and conclusions in this report are those of the authors and do not necessarily represent the official position of the Centers for Disease Control and Prevention/the Agency for Toxic Substances and Disease Registry.

Abbreviations

ALT	Alanine aminotransferase
AST	Aspartate aminotransferase
CDC	Centers for Disease Control and Prevention
CMS	Centers for Medicare and Medicaid Services
DHCP	dental healthcare providers
HCV	Hepatitis C virus

HIV	Human immunodeficiency virus
RNA	Ribonucleic acid
SHEA	The Society for Healthcare Epidemiology of America

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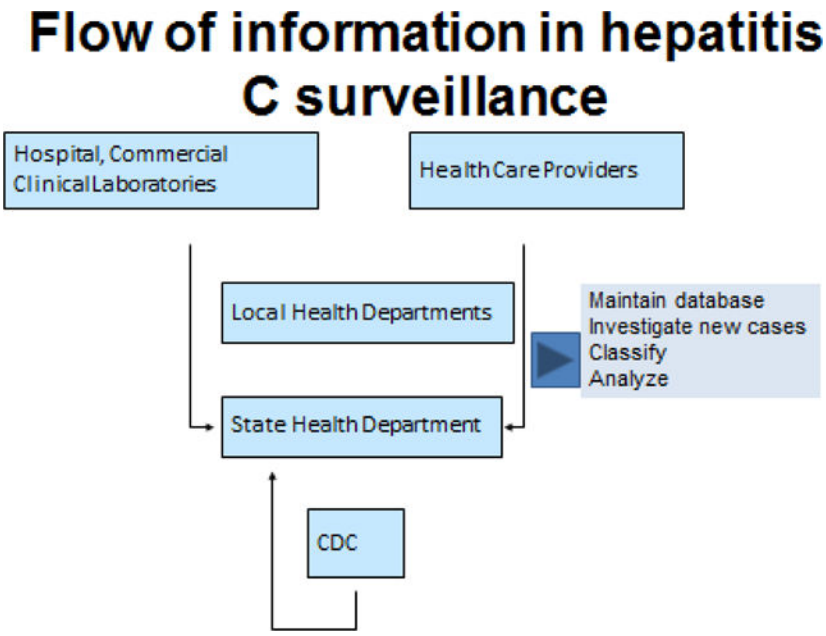

Figure.

Table 1

Resources for dental healthcare practitioners to learn more about hepatitis and other infections that can be transmitted during healthcare services.

Resource	Location	Description
Outbreak investigations in the US notified to CDC	http://www.cdc.gov/hepatitis/Outbreaks/HealthcareHepOutbreakTable	Listing of investigations of healthcare transmission of hepatitis B or C, including links to references.
Injection safety	www.cdc.gov/injectionsafety	Continuing education, slides, campaign materials.
Outpatient guide and checklist	www.cdc.gov/HAI/settings/outpatient-settings.html	Integrates information from other sources to prevent infections in ambulatory care settings.
Guidelines and recommendations for preventing healthcare associated infections	http://www.cdc.gov/HAI/prevent/prevent_pubs.html	Links to detailed documents for infection control including hand hygiene and standard precautions.
Healthcare Investigation Guide	www.cdc.gov/hepatitis/Outbreaks/HealthcareInvestigationGuide.html	Step by step approach to investigate possible healthcare transmission of hepatitis B and C, intended for State and local health departments.

Table 2

Summary of Standard Precautions to prevent transmission of infectious agents during patient care in outpatient settings

Component	Recommendations
Hand hygiene	After touching blood, body fluids, secretions, excretions, contaminated items; immediately after removing gloves; between patient contacts
Personal protective equipment (PPE)	
Gloves	For touching blood, body fluids, secretions, excretions, contaminated items; for touching mucous membranes and nonintact skin
Mask, eye protection, face shield	During procedures and patient-care activities likely to generate splashes or sprays of blood, body fluids, secretions
Gown	During procedures and patient-care activities when contact of clothing/exposed skin with blood/body fluids, secretions, and excretions is anticipated
Soiled patient-care equipment	Handle in a manner that prevents transfer of microorganisms to others and to the environment; wear gloves if visibly contaminated; perform hand hygiene
Environmental infection control	Develop procedures for routine care, cleaning, and disinfection of environmental surfaces, especially frequently touched surfaces in patient-care areas
Textiles (linen and laundry)	Handle in a manner that prevents transfer of microorganisms to others and to the environment
Needles and other sharps	Do not recap, bend, break, or hand-manipulate used needles; use safety features when available; place used sharps in puncture-resistant container
Injection safety	Never administer medications from the same syringe to more than one patient; do not enter a medication vial with a used needle or syringe; never use single-dose vials for more than one patient; follow proper infection control practices during administration of injected medications
Respiratory hygiene/cough etiquette (source containment of infectious respiratory secretions in symptomatic patients, beginning at initial point of encounter)	Instruct symptomatic persons to cover mouth/nose when sneezing/coughing; use tissues and dispose in no-touch receptacle; observe hand hygiene after soiling of hands with respiratory secretions; wear surgical mask if tolerated or maintain spatial separation, > 3 feet if possible