HCV infection as an emerging sexually transmitted disease

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Hepatitis C virus (HCV) infection is the most common chronic bloodborne infection in the United States.[1] According to the Centers for Disease Control and Prevention (CDC), there were an estimated 17,000 new HCV infections in the United States in 2007, and 3.2 million persons in the United States are chronically infected with the virus.[2] HCV is primarily transmitted through exposure to infected blood, with needle sharing during injection-drug use as the most common mode of transmission.[2] Other parenteral means of transmission include blood products (rare since 1990, when routine screening of donated blood for HCV infection was instituted) and organs; needlestick injuries; non-injection-drug use, such as shared cocaine straws; and intrapartum transmission from mother to newborn. Although HCV can be present in semen[3] and vaginal secretions,[4] the occurrence of sexual transmission of HCV infection has been controversial. In 2006, CDC's sexually transmitted diseases (STD) treatment guidelines stated that sexual transmission was "possible but inefficient."[5] The 2010 version of CDC's STD-treatment guidelines state, however, that sexual transmission might play a larger role in HCV infection than previously thought, particularly among persons infected with human immunodeficiency virus (HIV).[6] This article reviews recent data indicating that HCV infection is an emerging STD, after describing virologic and clinical features of HCV infection and laboratory diagnosis of HCV infection.

Virologic and clinical features

HCV is an enveloped, single-stranded RNA virus that primarily replicates in hepatocytes. According to the CDC, the majority (60% to 70%) of newly infected HCV-infected persons might be unaware of their infection because they are asymptomatic; those persons are at risk of developing chronic liver disease and transmitting HCV infection to others. Those who do develop symptomatic acute HCV infection (20% to 30% of newly infected persons) can experience fatigue, jaundice, loss of appetite, or abdominal pain in the four to12 weeks after exposure to the virus.[2] Although some infected individuals clear HCV from the body, chronic infection develops in 55% to 85% of acutely infected persons.[7] During the 20 to 30 years after exposure, 5% to 20% of infected persons develop cirrhosis, and 1% to 5% eventually die as a result of infection.[2] Combination therapy, including pegylated interferon and ribavirin, can result in sustained virologic response in 40% to 80% of infected persons, depending on the HCV genotype.[2] Even for HCV-infected persons who do not respond to or are ineligible for therapy, HCV diagnosis and counseling can delay progression of disease by modifying behaviors that accelerate HCV progression, such as alcohol consumption, and by providing an opportunity to ensure that HCV-infected persons have been vaccinated against infections with hepatitis A virus and hepatitis B virus.

Laboratory diagnosis

Detection of HCV infection is critical for case management, treatment, and prevention of transmission to others. HCV infection can be detected by HCV RNA tests two to three weeks after infection and by antibody-screening tests (enzyme immunoassay [EIA] or enhanced chemiluminescence immunoassay) four to 10 weeks after infection. Sensitivity of antibody testing at six months after infection is >97%.[2] Positive HCV-antibody results represent a history of infection, past or current, but current infection status cannot be determined by antibody testing alone. For patients who test antibody positive, CDC recommends confirmatory testing to assess current infection status and rule out false-positive screening results, particularly in populations known to have low HCV prevalence.[2] Confirmatory testing is performed with more specific serologic tests, such as recombinant immunoblot assay (RIBA) for HCV antibody or nucleic-acid amplification tests to detect HCV RNA. High signal-to-cut-off ratios of third-generation EIA test results (e.g., >3.8 for the two FDA-approved HCV EIAs, manufactured by Abbott and Ortho-Clinical Diagnostics, respectively) can be used to predict positive confirmatory test results, minimizing the need for confirmatory RIBA testing in those cases.[7] Persons with confirmed HCV infection should be evaluated for evidence of chronic liver disease and treatment options. Additionally, genotyping assays can be used to help predict the likelihood of response to therapy and to determine the duration of therapy required.[7]

Sexual transmission

For many years, sexual HCV transmission had been considered rare and inefficient. That conclusion rested on studies showing that sexual HCV transmission was rare from HCV-positive to HCV-negative partners among serodiscordant heterosexual couples.[8] More recent studies, however, have indicated that sexual transmission of HCV might be a more substantial contributor to disease spread, particularly among HIV-infected men who have sex with men (MSM), among whom HCV infection has increased in the United States, Europe, and Australia since 2000.[9-14] Those more recent studies have not identified established risk factors, including injection drug use, for HCV infection among MSM. Many (but not all[15]) studies have found, rather, associations between HCV infection and having had HCV-infected sexual partners and having engaged in sexual practices associated with mucosal damage or bleeding. Highlights of those studies include the following:

- HCV infection among HIV-infected MSM was as high as

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17.8% at an STD clinic in Amsterdam[13] and 25.9% at a community clinic in Boston.[17]

- Among six of nine HIV-infected men presenting with acute HCV infection in San Francisco during 2002 to 2004, having had sex with men was the only identifiable risk factor for HCV infection.[16]
- Studies that have examined sexual risk factors for HCV infection among HIV-infected MSM have demonstrated associations between HCV infection and having had multiple sex partners,[18] unprotected anal sex,[10,19-20] group sex,[10] and having engaged in sexual practices, such as fisting or use of dilative sex toys, that can cause trauma to mucous membranes.[10,11,13]
- Phylogenetic analyses have provided evidence of an emerging MSM-specific HCV transmission network.[10,13,21-23]

By contrast, there are limited data on HCV seroprevalence among HIV-uninfected MSM, and findings have been equivocal. Studies at STD clinics and community health centers have found that HCV seroprevalence is lower among HIV-uninfected MSM compared with HIV-infected MSM, although cases of suspected sexual acquisition of HCV infection have been reported.

Several factors might explain why risk of sexual HCV acquisition and transmission is elevated among HIV-infected MSM, including the following:

- Higher blood and seminal HCV viral loads[3] among HIV-infected MSM could increase the likelihood of sexual transmission, particularly in sexual networks with a high prevalence of HIV serosorting (i.e., when persons seek sex partners who share their same HIV status, often for unprotected sex).[24]
- HIV infection can compromise the gastrointestinal immune system,[25] leaving HIV-infected MSM more susceptible to HCV acquisition during sex.
- Higher rates of ulcerative syphilis infection might render HIV-infected MSM more susceptible to sexual HCV acquisition through lesions on the penis or anus.[20]

Additionally, at least to some extent, higher reported prevalence of HCV infection among HIV-infected MSM compared with HIV-uninfected MSM might result from ascertainment bias rather than a true difference in disease prevalence. HIV-infected MSM are more likely than HIV-uninfected MSM to be screened and tested for HCV infection and for liver-function-test abnormalities leading to HCV-infection diagnosis.

In conclusion, HCV infection is an increasingly important clinical and public-health problem in the United States. Although sexual transmission of HCV infection appears to be rare overall, there is mounting evidence of increasing sexual transmission among HIV-infected MSM. Several sexual practices associated with risk of HCV acquisition have been identified, but a better understanding of the risk factors associated with HCV infection would allow public-health agencies and clinicians to make specific recommendations to patients on how to prevent sexual transmission and acquisition of HCV infection. Furthermore, data on the incidence of sexual HCV transmission in areas with high HIV prevalence among MSM would help refine screening practices in those settings. □

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