Hepatitis C virus: epidemiology and transmission risks

Hepatitis C infection is caused by an RNA virus that was first identified in 1989. Chronic hepatitis C infection is a major cause of chronic liver disease and death throughout the world. Approximately 3% of the world’s population is infected with hepatitis C virus (HCV). Six distinct but related genotypes and multiple subtypes have been identified. In western Europe genotypes 1a and 1b are most common, followed by genotypes 3 and 2.

Transmission

HCV is transmitted by blood and now occurs primarily through injecting drug use, and less frequently through sex with an infected partner, occupational exposure, and maternal-foetal transmission. In some cases no risk factors can be identified. Transfusion-related HCV infection is rare now since the introduction of routine screening of blood for HCV antibodies in the early 1990s.

Clinical information

In general, acute HCV infection is relatively mild, with only 20-30% of infected persons developing symptoms or clinically evident acute infection. In most persons who become infected with HCV, viraemia persists. Antibody to HCV (anti-HCV) is present in acute, chronic and resolved infection. HCV RNA/HCV Ag is an indication of HCV viraemia. Chronic HCV infection is marked by persistence of HCV RNA for at least 6 months after onset of infection. Spontaneous resolution after 6 or 12 months of infection is unusual. Between 55 and 85% of those infected develop chronic infection. Chronically infected people are at risk for progressive liver disease characterised by hepatocellular inflammation, hepatic fibrosis, cirrhosis and hepatocellular carcinoma (HCC). These complications develop only in a proportion of patients and only after many years or decades of infection. It has been estimated that up to 20% of chronically infected individuals will develop cirrhosis of the liver over a 20 to 25 year period, and that, of patients with cirrhosis, approximately 3% to 4% will develop HCC per year. Factors that have been shown to be associated with progression of liver fibrosis include older age at infection, male gender, genetic factors, metabolic factors (steatosis, diabetes and obesity), co-infection with human immunodeficiency virus (HIV) or hepatitis B, duration of infection, and alcohol intake.

Highly effective all-oral treatment with direct-acting antivirals is now available in Ireland. This eradicates the virus in over 90% of cases.

Prevalence of HCV infection in Ireland, Europe and the world

Ireland

A previous study has estimated that the prevalence of chronic HCV infection in Ireland is 0.5-1.2%. This study took undiagnosed cases into account. More recent estimates of levels of undiagnosed hepatitis C in Ireland indicate the overall prevalence of hepatitis C in Ireland is more likely to be between 0.5 and 0.7% (23,000 to 32,000). This is similar to other countries in northern Europe and in line with the WHO estimate of <1%. However, it is more prevalent in certain sub-groups of the population, in particular people who inject drugs (PWID) and prisoners. HCV may also be more prevalent in immigrants to Ireland from endemic countries.

Blood donors

Of 313,019 first time blood donors tested by the IBTS between 1997 and 2015, 48 (0.015%) were found to be HCV positive. (Personal communication, Dr Joan O’Riordan, IBTS, July 2016).

Asylum seekers

Screening of asylum seekers in the HSE eastern region 1999-2003 found a prevalence of anti-HCV of 1.5%. A reception centre in HSE East, reported that 1% of those tested under the voluntary health screening programme, between 2004 and 2012, were positive for chronic HCV infection.

Prisoners and people who inject drugs

Studies of PWID in prisons and PWID attending methadone clinics, specialist addiction treatment centres and GPs have estimated the HCV prevalence in this population to be between 62% and 81%.

A national cross sectional survey of Irish prisoners in 1998 showed a prevalence of anti-HCV of 37% of all prisoners, and of 81.3% in prisoners who were prisoners who inject drugs.

More recently, a 2011 prison study found that 54% of prisoners with a history of injecting heroin were anti-HCV positive and 41.5% of prisoners with a history of injecting any drugs were anti-HCV positive.
**Trends in HCV in Ireland**

Hepatitis C became a notifiable disease in Ireland in 2004. Between 2004 and 2015, 13,478 cases were notified. The highest annual number of notifications was in 2007 (n=1539). There has been a significant decrease in recent years and 678 cases were notified in 2015. Two thirds of cases were male and most were young to middle aged adults (median age: 34 years, mean age: 36.1 years). Where risk factor information was available, over 80% of cases between 2007 and 2015, were among people who inject drugs.9

**HCV in Europe**

In Europe, HCV infection shows a significant increasing trend in reported numbers. Every year there are 27,000 to 29,000 newly diagnosed cases in the EU/EEA.16

A recent systematic literature review of HCV prevalence in Europe, based on information from 14 countries, reported a prevalence range of 0.4-3.5%.16 The prevalence is higher in the southern part of Europe. Countries with high prevalence (more than 2%) include Italy, Romania and Spain. Medium prevalence was observed in Bulgaria, France, Greece, and Poland. Countries with low prevalence (less than 1%) include Belgium, Germany, the Netherlands, Sweden, and the United Kingdom.15

The most severely affected population groups are people who inject drugs, haemodialysis patients, persons living with HIV, inmates, and immigrants from high-endemic regions. Reported numbers are likely to reflect the current testing and screening practices in countries rather than the real incidence of infection. The reported number is an underestimate of the real occurrence of HCV due to the asymptomatic nature of the infection.15

Maps of HCV prevalence in different population groups by country in Europe are available in the ECDC Technical Report.16

**Global HCV distribution**

The estimated global prevalence of HCV is 2-3%.17,18 Countries with the highest reported prevalence rates are located in Africa and Asia. China has a reported seroprevalence of 3.2%. One community-based survey in India reported an overall rate of 0.9%. Indonesia’s rate is 2.1% in serosurveys of voluntary blood donors. The seroprevalence in Pakistan is reported to range from 2.4% to 6.5%. Egypt has the highest reported seroprevalence rate, 22%.17 Areas of lower prevalence include North America, northern and western Europe, and Australia.

The predominant source of new HCV infections in developed countries over the past few decades is injecting drug use. In developing countries, unsafe therapeutic injections and transfusions are likely to be the major modes of transmission.17 Anti-HCV prevalence in PWID globally varies greatly, from 9.8% to 97.4%.19 (See map, appendix 24).

**Transmission risks**

**Needlestick injuries**

There is a wide range of reported estimates for the risk of transmission of HCV after a needlestick or sharps injury from a source patient – between 0 and 10%.20-22 The estimated risk from a needlestick injury from a source with detectable HCV RNA is 6.1%.23 The risk of developing HCV is greater after an injury with a hollow-bore needle21, or deep injuries24, compared with other injuries. Also, one study showed an 11-fold increase in transmission of HCV from source patients with viral load >6 log10 copies/ml, compared with source patients with viral load ≤4 log10 copies/ml following percutaneous exposure.24 The risk of transmission is also influenced by whether the source is co-infected with HIV (see section below).

In cold temperatures, HCV can survive in syringes for many days in laboratory studies.25 The clinical implications of this are unknown, but the risk of becoming infected with HCV from an abandoned syringe depends on the prevalence of HCV in the local community. There are case reports of HCV transmission from needlestick injuries in the community26, but as the exact incidence of injuries in the community is not known, the risk of transmission from such injuries cannot be accurately quantified.

**Other percutaneous exposures**

The risk of acquiring HCV during an operation performed by an infected surgeon is reported to be between 0 and 3.7%.27,28,29 In general the risk of contracting HCV following an injury from an unknown source is negligible.30

Sharps in the workplace, other than in the healthcare setting, such as razors and meat slicers have also been implicated in the transmission of HCV.31,32

There is an increased incidence of HCV in those who have a tattoo, with a pooled odds ratio of 2.73 (95% CI 2.38-3.15). Large tattoos, and those received in non-professional locations are associated with the greatest risk.33

**Splashes/mucocutaneous exposures**

Several case reports have been published describing the transmission of HCV following a splash of blood into the eye of the recipient.34,35 Also, transmission of HCV has occurred following splashes of infected blood onto broken skin.36 The exact risk associated with these exposures is unknown.
**Exposure to saliva (including injuries caused by human bites)**

HCV RNA has been demonstrated in saliva.\textsuperscript{37, 38} Case reports describe transmission of HCV following human bites, but precise details of the nature of the bites, and whether blood was present in the mouth of the biter, or whether skin was broken at the time of the bite, are not known.\textsuperscript{39} Inoculation with saliva has caused transmission of the virus in experimental studies.\textsuperscript{40, 41}

Studies in dentists indicate a low incidence of nosocomial transmission of HCV.\textsuperscript{42} It is also thought, however, that HCV can be transmitted via sharing a toothbrush with an index case.\textsuperscript{38, 43}

**Sexual exposures**

In general, transmission of HCV via sexual contact is inefficient in stable monogamous heterosexual couples.\textsuperscript{44} There is evidence, however, of a low rate of transmission of HCV between discordant heterosexual couples and a prevalence of 2-6% of anti-HCV in the non-index partner.\textsuperscript{44-46} Higher prevalence of anti-HCV has been observed in those with multiple sexual partners, in the absence of other risks, such as PWID or recipients of blood products, as further evidence of the plausibility of sexual transmission. If a risk is present, it is likely to be very low, and a rate of transmission per heterosexual exposure has not been calculated.

Recent outbreaks of acute HCV among HIV-positive MSM who deny PWID suggest that the epidemiology of HCV transmission is changing in this population. In several European countries as well as in the United States and Australia, HCV has unexpectedly emerged as an STI among HIV-positive MSM. Longitudinal cohort studies have confirmed a marked increase in HCV incidence among HIV-positive MSM, but not HIV-negative MSM, after the year 2000.\textsuperscript{49} Studies in Australia, UK, Switzerland and the Netherlands have reported an incidence of HCV infection ranging from 0.6 to 0.9/100 person years in HIV positive MSM who were not PWID.\textsuperscript{50}

**Exposure to other body fluids**

HCV RNA has been identified in blood, saliva\textsuperscript{37}, bile\textsuperscript{51}, sweat\textsuperscript{52}, semen\textsuperscript{53}, and cervicovaginal secretions.\textsuperscript{54} The infective potential of cervicovaginal secretions is questioned\textsuperscript{55}, but may increase during menstruation.\textsuperscript{54}

**Transmission of infection following exposure to a source with HIV and HCV**

The risk of developing HCV infection after simultaneous exposure to HIV and HCV is estimated at 2.8% (in this study, no one developed HIV after simultaneous exposure). 100% of patients who received an injection drawn from a vial contaminated with HIV and HCV developed acute HCV infection, but no one developed HIV.\textsuperscript{57}

HIV and HCV transmission from a patient to a healthcare worker occurred after contact with the patient’s emesis, faeces and urine, to non-intact skin on the healthcare worker’s hands.\textsuperscript{58}

A case report describes the transmission of HCV, but not HIV, via a human bite to the hand from a source co-infected with HIV and HCV.\textsuperscript{59} Although the recipient had a wound on his hand prior to the bite, it is not known whether there was blood in the mouth of the source at the time of the incident. Studies have not shown an increased incidence of HCV RNA in saliva of co-infected patients compared to those infected with only HCV.\textsuperscript{60}

The odds ratio of sexual transmission of HCV increased in women co-infected with HIV or another sexually transmitted infection (adjusted odds ratio 3.3-3.9) or homosexual men co-infected with HIV (adjusted odds ratio 4.1-5.7).\textsuperscript{61}

There is an increased incidence of HCV-antibodies in patients who had acquired HIV via heterosexual transmission, than in those who had developed HIV from a different exposure.\textsuperscript{62}

HIV status does not seem to influence the presence of HCV in semen in men co-infected with HCV and HIV.\textsuperscript{63} HCV RNA is detected more frequently in cervicovaginal fluid from women co-infected with HIV, than in those not infected with HIV, especially if HCV viremia is present, or if HIV RNA is also found in the cervicovaginal secretions.
## Hepatitis C transmission risk by exposure type

<table>
<thead>
<tr>
<th>Exposure</th>
<th>Risk per exposure (unless otherwise stated)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Needlestick</strong></td>
<td></td>
</tr>
<tr>
<td>Healthcare setting, source patient (serology) known</td>
<td>0-10%.20-22 Average 1.8%65</td>
</tr>
<tr>
<td>Increased risk if hollow needle21, deep injuries 24, co-infection with HIV56, high viral load.24</td>
<td></td>
</tr>
<tr>
<td>Healthcare setting, source patient unknown, or unable to test source patient (serology unknown)</td>
<td>Unknown source – negligible risk.30</td>
</tr>
<tr>
<td>Risk assessment required</td>
<td></td>
</tr>
<tr>
<td>Community setting</td>
<td>Risk not accurately determined.26 Risk assessment required. If local PWID population has a seroprevalence of 50-90%, the estimated risk of HCV transmission in a community needlestick injury is 1.62%.66</td>
</tr>
<tr>
<td>Exposure prone procedure by infected healthcare worker</td>
<td>0-3.7%.27, 28, 29 Risk may increase to 6% for certain procedures, e.g. open heart surgery.28 Risk assessment required.</td>
</tr>
<tr>
<td>Non healthcare related occupational sharp injuries</td>
<td>Risk not accurately determined, but transmission possible.31, 32 Risk assessment required.</td>
</tr>
<tr>
<td>Tattoos</td>
<td>Risk not accurately determined. Pooled odds ratio 2.73 (95% CI 2.38-3.15)33</td>
</tr>
<tr>
<td>Risk assessment required. Increased risk if larger tattoos or tattoos in non-professional locations</td>
<td></td>
</tr>
<tr>
<td>Mucous membrane exposure to blood</td>
<td>Very low risk. Case reports only.34, 35 Risk assessment required</td>
</tr>
<tr>
<td>Intact skin exposed to blood</td>
<td>No recognised risk</td>
</tr>
<tr>
<td>Non-intact skin, body fluid exposure</td>
<td>Very low risk. Case report describes transmission of HIV and HCV from co-infected source.58 Risk assessment required.</td>
</tr>
<tr>
<td>Human bite injuries</td>
<td>Very low risk.39 Case reports only. Risk assessment required. Possible higher risk of transmission of HCV than HIV if the source patient is co-infected with HCV and HIV.50</td>
</tr>
<tr>
<td>Sexual exposures</td>
<td></td>
</tr>
<tr>
<td>Heterosexual exposures in general</td>
<td>Inefficient transmission61, but transmission possible as seen in stable heterosexual relationships44-46, and in those with history of multiple sexual partners.47, 48 Possible increased risk of transmission if source co-infected with HIV61</td>
</tr>
<tr>
<td>MSM</td>
<td>Inefficient transmission.62, 68 Co-infection with HIV increases the risk of transmission61, 69-71</td>
</tr>
</tbody>
</table>

Note: In England, between 1997 and 2007, there were only 14 reported cases of HCV transmission from a patient to a healthcare worker, with a transmission rate calculated as 1.6%.72

### Risk assessment
- Type/details of injury – as above
- Source status – increased risk with high viral load
- Recipient status – increased risk if immunocompromised
- For unknown source, consider where injury occurred – community setting versus hospital setting
  - If in hospital – consider high-risk ward/patients
  - If in community – consider prevalence of HCV and of PWID locally
- Consider where the needle was found and the temperature of environment – longer virus survival in cold temperatures thus potential increased risk of transmission.26
Hepatitis C transmission risk by exposure type

Exposure Risk per exposure (unless otherwise stated)

- 0-10%. 
- 20-22 Average 1.8% 
- increased risk if hollow needle, deep injuries, co-infection with HIV, high viral load.

Healthcare setting, source patient unknown, or unable to test source patient (serology unknown).

Risk assessment required.

Estimated risk of HCV transmission in a community needlestick injury is 1.62%.

Exposure prone procedure by infected healthcare worker 0-3.7%. Risk may increase to 6% for certain procedures, e.g. open heart surgery. Risk assessment required.

Intact skin exposed to blood: No recognised risk.

Non-intact skin, body fluid exposure: Very low risk. Case report describes transmission of HIV and HCV from co-infected source. Risk assessment required.

Human bite injuries: Very low risk. Case reports only. Risk assessment required. Possible higher risk of transmission of HCV than HIV if the source patient is co-infected with HCV and HIV.

Sexual exposures: Heterosexual exposures in general inefficient transmission, but transmission possible as seen in stable heterosexual relationships and in those with history of multiple sexual partners. Possible increased risk of transmission if source co-infected with HIV.

MSM: Inefficient transmission. Co-infection with HIV increases the risk of transmission.

Risk assessment:

- if in hospital – consider high-risk ward/patients
- if in community – consider prevalence of HCV and of PWiD locally

References


