

## Routes of transmission of hepatitis C virus

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### ABSTRACT

Hepatitis C is one of the most common causes of chronic liver disease in Latin America. It is essential to understand the different mechanisms of transmission of the infection in order to design control measures. The pattern of transmission of the infection in our region suggests that the peak of the infection occurred 30 to 50 years ago. While most infections in Latin America seem to be the result of blood transfusion and unsafe therapeutic injection practices in the past, there is still a need to identify and notify infected blood donors. Intravenous drug use and sexually transmitted hepatitis C virus among human immunodeficiency virus-positive patients are current problems that need to be addressed.

**Key words.** Hepatitis C virus. HCV. Transmission, Epidemiology.

### INTRODUCTION

Hepatitis C virus (HCV) infection is one of the leading causes of chronic liver disease and hepatocellular carcinoma in Latin America.<sup>1</sup> This disease may spread by several routes, with blood transfusion and intravenous drug use being considered the most significant methods of transmission,<sup>2</sup> although the means of transmission vary between specific geographic areas. It is important, therefore, to consider epidemiological data from a particular region when planning recommendations regarding prevention of this disease.

### EPIDEMIOLOGICAL PATTERNS OF TRANSMISSION

There is considerable variation in incidence and prevalence of HCV infection, but age-specific prevalence is a good way of estimating the time of infection and hence the probable route of infection.

There are three well-recognized patterns of HCV transmission.<sup>3</sup> In the first pattern, typical in the

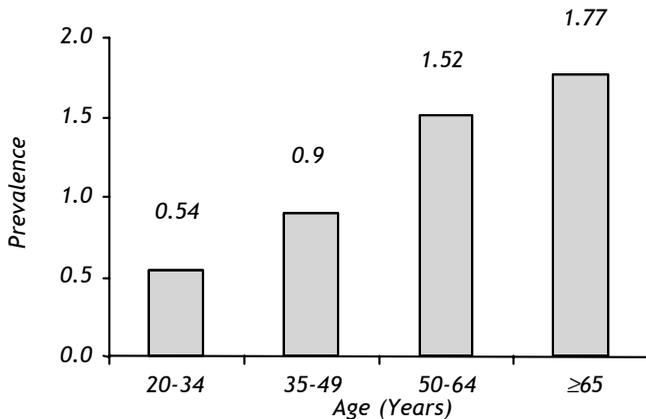
United States and in Australia, infected patients are predominantly 40 to 49 years old.<sup>4</sup> They acquired the infection as young adults, mainly through intravenous drug use, and to a lesser extent from blood transfusions. In the second pattern, found in countries like Japan and Italy, infected patients are older and acquired the infection in the distant past. Unsafe injection techniques and blood transfusions are the most important means of transmission in these regions. A third epidemiological pattern can be identified, where the prevalence of HCV infection is high in all age groups, with an ongoing risk of infection. This is best exemplified by Egypt.

The available epidemiological data in Latin America is consistent with the second pattern of transmission.<sup>5</sup> The evidence to support this statement comes from several observations:

- The described age-specific prevalence is consistent with an increasing prevalence at older age (Figure 1).<sup>6</sup>
- Blood transfusion is the most common risk factor among infected patients,<sup>7,8</sup> but a significant proportion of infected patients do not have a history of blood transfusion or intravenous drug use,<sup>9</sup> suggesting that unsafe therapeutic injection practices are an important route of transmission.
- The study of some specific towns in Argentina with high prevalence of HCV infection has shown that infection may be related to the use of inadequately sterilized glass syringes.<sup>10</sup> Based on

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**Figure 1.** Seroprevalence of HCV infection in a representative sample of the general population of Santiago older than 20 years. N = 1115. Adapted from.<sup>6</sup> This pattern of age-specific prevalence is suggestive of infection in the distant past, mainly by unsafe injection practices and blood transfusion.

molecular clock analysis, the peak of infection in one of these towns was estimated to occur 50 years ago.<sup>11</sup>

### BLOOD TRANSFUSION

Transfusion of blood products is a well-recognized method of transmission of HCV and resulted in up to a 10% risk of acquiring the infection before screening of blood donors was instituted.<sup>12</sup> Mandatory screening for HCV infection was gradually adopted in Latin America during the 1990s, leading to a currently very low risk of transmission. Improved antibody assays have reduced the risk of infection to a calculated frequency of 1:100 000 units. New technologies, such as nucleic acid testing (NAT) may yield a 10-fold reduction of the residual risk.<sup>13</sup> The high prevalence still seen in hemophiliacs and patients heavily exposed to blood products is explained by infection prior to the institution of universal screening. One of the pending issues in Latin America is follow-up of the infected; while in most countries, screening is mandatory, notification of positive blood donors is not.

### INTRAVENOUS AND INTRANASAL DRUG USE

The use of contaminated needles and paraphernalia is one of the most efficient ways of transmission of HCV. It has been shown that 65% of injecting drug users acquire HCV infection during the first year of use.<sup>14</sup> There is a trend of increasing intrave-

nous drug use in the region, but there is great variation in prevalence among countries in Latin America.<sup>15</sup> Intranasal drug use, specifically cocaine snorting, may be a risk factor for acquiring this infection,<sup>16</sup> and drug users who declare that they do not inject still have a higher risk of HCV infection, either because of underreporting or because they are infected by a different route, such as sexual or household transmission.<sup>17</sup>

### SEXUAL AND HOUSEHOLD TRANSMISSION

HCV infection is not transmitted efficiently by the sexual route.<sup>18</sup> In effect, the risk of transmission among monogamous stable sexual partners is negligible, so no special recommendation for condom use is given in this situation.<sup>15-19</sup> The risk increases more than two fold for partners of HCV-HIV coinfecting patients.<sup>20</sup> For intrafamilial or household transmission of HCV, the risk is relatively low.<sup>21</sup> Mucosal exposure or percutaneous exposure through personal hygiene items such as toothbrushes and razors is a possible mechanism of transmission, so precautions are recommended in this setting.

In the last five to 10 years, there have been several reports of outbreaks of acute HCV among HIV infected men who have sex with men.<sup>22</sup> Most of these patients are not intravenous drug users and they have stable and controlled HIV infection; most are being treated with highly active anti-retroviral therapy and have normal CD4 counts. These outbreaks seem to correspond to transmission through sexual networks that rapidly spread the infection and are not associated with specific strains of the virus.<sup>23</sup>

### PERINATAL TRANSMISSION

Vertical transmission of HCV infection takes place at the time of birth in approximately 5% of children born to an infected mother.<sup>24</sup> This risk doubles for babies born to HIV-HCV coinfecting mothers.<sup>25</sup> There is insufficient evidence for recommending a particular method of delivery, either vaginal or by cesarean section.<sup>26</sup>

### HEMODIALYSIS

Patients on hemodialysis have an increased risk of being infected with HCV compared with the general population. The prevalence of HCV infection among patients on dialysis varies greatly between

different centers and countries. Prevalence in Latin America has been reported from 6.7% in Mexico<sup>27</sup> to 71% in Venezuela.<sup>28</sup> Factors associated with infection in this setting include duration of dialysis, type of dialysis (hemodialysis carries a higher risk than peritoneodialysis), number of blood transfusions and the prevalence of HCV infection in the unit.<sup>29</sup> There is ample evidence suggesting that the risk of transmission in the setting of hemodialysis units is nowadays most related to breakdowns in universal precautions, hence current guidelines do not support isolation of HCV-infected patients or the use of a dedicated dialysis machine for this group.<sup>30,31</sup>

### HEALTHCARE WORKERS

HCV infection may be transmitted via needlestick or other percutaneous injuries and rarely by mucosal exposure in healthcare workers. Most accidents occur with disposable syringes, followed by suture needles and scalpels.<sup>32</sup> The risk of acquiring HCV infection after a needlestick accident is 1.8%.<sup>33</sup>

### ORGAN TRANSPLANTATION

Patients receiving organs from HCV-positive donors have a very high risk of becoming infected.<sup>34</sup> Thus, the rationale for screening potential donors and not accepting organs from infected patients seems justified.

### CONCLUSION

HCV infection in Latin America was principally transmitted by blood transfusion and unsafe therapeutic practices in the distant past (30 to 50 years ago). This translates to an older population of infected patients, with more advanced liver disease and a greater risk of developing hepatocellular carcinoma. The biggest challenges today for our region are to secure a 100% HCV screening policy for blood products and mandatory notification of positive blood donors, and address the increasing risk of ongoing transmission of HCV among intravenous drug users and sexually transmitted HCV infection in HIV-HCV coinfecting partners.

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### REFERENCES

1. Liang TJ, Rehermann B, Seeff LB, Hoofnagle JH. Pathogenesis, natural history, treatment, and prevention of hepatitis C. *Ann Intern Med* 2000; 132: 296-305.
2. Murphy EL, Bryzman SM, Glynn SA, Ameti DI, Thomson RA, Williams AE, Nass CC, et al. Risk factors for hepatitis C virus infection in United States blood donors. NHLBI Retrovirus Epidemiology Donor Study (REDS). *Hepatology* 2000; 31: 756-62.
3. Wasley A, Alter MJ. Epidemiology of hepatitis C: geographic differences and temporal trends. *Semin Liver Dis* 2000; 20: 1-16.
4. Armstrong GL, Wasley A, Simard EP, McQuillan GM, Kuhner WL, Alter MJ. The prevalence of hepatitis C virus infection in the United States, 1999 through 2002. *Ann Intern Med* 2006; 144: 705-14.
5. Soza A, Lopez-Lastra M. [Hepatitis C in Chile: burden of the disease]. *Rev Med Chil* 2006; 134: 777-88.
6. Gonzalez R, Soza A, Hernandez V, Perez RM, Alvarez M, Morales A, Arellano M, et al. Incidence and prevalence of hepatitis C virus infection in Chile. *Ann Hepatol* 2005; 4: 127-30.
7. Davalos MM. Epidemiology of hepatitis C virus in Peru and Latin America. *Rev Gastroenterol Peru* 2009; 29: 347-54.
8. Chiquete E, Panduro A. Low prevalence of anti-hepatitis C virus antibodies in Mexico: A systematic review. *Intervirol* 2007; 50: 1-8.
9. Soza A, Arrese M, Gonzalez R, Alvarez M, Perez RM, Cortes P, Patillo A, et al. Clinical and epidemiological features of 147 Chilean patients with chronic hepatitis C. *Ann Hepatol* 2004; 3: 146-51.
10. Picchio GR, Bare PC, Descalzi VI, Bussy MV, Soria SM, Raffia MP, Mazzencio NE, et al. High prevalence of infection with a single hepatitis C virus genotype in a small rural community of Argentina. *Liver Int* 2006; 26: 660-5.
11. Golemba MD, Di Lello FA, Bessone F, Fay F, Benetti S, Jones LR, Campos RH. High prevalence of hepatitis C virus genotype 1b infection in a small town of Argentina. Phylogenetic and Bayesian coalescent analysis. *PLoS One*;5:e8751.
12. Alter HJ, Purcell RH, Shih JW, Melpolder JC, Houghton M, Choo QL, Kuo G. Detection of antibody to hepatitis C virus in prospectively followed transfusion recipients with acute and chronic non-A, non-B hepatitis. *N Engl J Med* 1989; 321: 1494-500.
13. Schuttler CG, Caspari G, Jursch CA, Willems WR, Gerlich WH, Schaefer S. Hepatitis C virus transmission by a blood donation negative in nucleic acid amplification tests for viral RNA. *Lancet* 2000; 355: 41-2.
14. Garfein RS, Vlahov D, Galai N, Doherty MC, Nelson KE. Viral infections in short-term injection drug users: the prevalence of the hepatitis C, hepatitis B, human immunodeficiency, and human T-lymphotropic viruses. *Am J Public Health* 1996; 86: 655-661.
15. Terrault NA. Sexual activity as a risk factor for hepatitis C. *Hepatology* 2002; 36: S99-S105.
16. Aaron S, McMahon JM, Milano D, Torres L, Clatts M, Tortu S, Mildvan D, et al. Intranasal transmission of hepatitis C virus: virological and clinical evidence. *Clin Infect Dis* 2008; 47: 931-4.
17. van den Berg CH, van de Laar TJ, Kok A, Zuure FR, Coutinho RA, Prins M. Never injected, but hepatitis C virus-infected: a study among self-declared never-injecting drug users from the Amsterdam Cohort Studies. *J Viral Hepat* 2009; 16: 568-77.
18. Dienstag JL. Sexual and perinatal transmission of hepatitis C. *Hepatology* 1997; 26: 665-70S.

19. Vandelli C, Renzo F, Romano L, Tisminetzky S, De Palma M, Stroffolini T, Ventura E, et al. Lack of evidence of sexual transmission of hepatitis C among monogamous couples: results of a 10-year prospective follow-up study. *Am J Gastroenterol* 2004; 99: 855-9.
20. Lissen E, Alter HJ, Abad MA, Torres Y, Perez-Romero M, Leal M, Pineda JA, et al. Hepatitis C virus infection among sexually promiscuous groups and the heterosexual partners of hepatitis C virus infected index cases. *Eur J Clin Microbiol Infect Dis* 1993; 12: 827-31.
21. Velasco M, Poniachik J, Alegria S, Brahm J. [Familial transmission of hepatitis C virus infection in Chilean subjects]. *Rev Med Chil* 2003; 131: 1123-7.
22. Gotz HM, van Doornum G, Niesters HG, den Hollander JG, Thio HB, de Zwart O. A cluster of acute hepatitis C virus infection among men who have sex with men—results from contact tracing and public health implications. *AIDS* 2005; 19: 969-74.
23. van de Laar T, Pybus O, Bruisten S, Brown D, Nelson M, Bhagani S, Vogel M, et al. Evidence of a large, international network of HCV transmission in HIV-positive men who have sex with men. *Gastroenterology* 2009; 136: 1609-17.
24. Ohto H, Terazawa S, Sasaki N, Hino K, Ishiwata C, Kako M, Ujiiie N, et al. Transmission of hepatitis C virus from mothers to infants. The Vertical Transmission of Hepatitis C Virus Collaborative Study Group. *N Engl J Med* 1994; 330: 744-50.
25. Zanetti AR, Tanzi E, Paccagnini S, Principi N, Pizzocolo G, Caccamo ML, D'Amico E, et al. Mother-to-infant transmission of hepatitis C virus. Lombardy Study Group on Vertical HCV Transmission. *Lancet* 1995; 345: 289-91.
26. McIntyre PG, Tosh K, McGuire W. Caesarean section versus vaginal delivery for preventing mother to infant hepatitis C virus transmission. *Cochrane Database Syst Rev* 2006: CD005546.
27. Mendez-Sanchez N, Motola-Kuba D, Chavez-Tapia NC, Bahena J, Correa-Rotter R, Uribe M. Prevalence of hepatitis C virus infection among hemodialysis patients at a tertiary-care hospital in Mexico City, Mexico. *J Clin Microbiol* 2004; 42: 4321-2.
28. Pujol FH, Ponce JG, Lema MG, Capriles F, Devesa M, Sirit F, Salazar M, et al. High incidence of hepatitis C virus infection in hemodialysis patients in units with high prevalence. *J Clin Microbiol* 1996; 34: 1633-6.
29. Natov SN, Pereira BJ. Hepatitis C in dialysis patients. *Adv Ren Replace Ther* 1996; 3: 275-83.
30. Recommendations for preventing transmission of infections among chronic hemodialysis patients. *MMWR Recomm Rep* 2001; 50: 1-43.
31. KDIGO clinical practice guidelines for the prevention, diagnosis, evaluation, and treatment of hepatitis C in chronic kidney disease. *Kidney Int* 2008; (Suppl.): S1-99.
32. House A. Alleged link between hepatitis B vaccine and chronic fatigue syndrome. *CMAJ* 1992; 146: 1145.
33. Updated U.S. Public Health Service Guidelines for the Management of Occupational Exposures to HBV, HCV, and HIV and Recommendations for Postexposure Prophylaxis. *MMWR Recomm Rep* 2001; 50: 1-52.
34. Pereira BJ, Milford EL, Kirkman RL, Levey AS. Transmission of hepatitis C virus by organ transplantation. *N Engl J Med* 1991; 325: 454-60.