Title
Acute Hepatitis C in an HIV-Infected patient: A Case Report and Review of Literature

Journal
Journal of General Internal Medicine, 28(5)

ISSN
0884-8734

Authors
Driver, Todd H
Terrault, Norah
Saxena, Varun

Publication Date
2013-05-01

DOI
10.1007/s11606-012-2258-3

Peer reviewed

Clinical Vignettes

Acute Hepatitis C in an HIV-Infected patient: A Case Report and Review of Literature

Todd H. Driver, BA[1], Norah Terrault, MD, MPH[2], and Varun Saxena, MD[2,3]

[1]School of Medicine, University of California, San Francisco, San Francisco, CA, USA; [2]Department of Gastroenterology, University of California, San Francisco, San Francisco, CA, USA; [3]University of California, San Francisco, San Francisco, CA, USA.

With the decrease in transmission via transfusions and injection drug use, acute symptomatic hepatitis C is infrequently seen in developed countries. We report a case of a human immunodeficiency virus (HIV)–infected adult who presented with abdominal pain. His alanine aminotransferase was greater than sixty times the upper limit of normal without any evidence on examination of fulminant hepatic failure. His workup revealed an elevated hepatitis C viral level with a negative hepatitis C antibody. He was discharged once his liver function tests improved. As an outpatient, he had a recurrent bout of symptoms with an elevation of his alanine aminotransferase and hepatitis C viral levels that promoted anti-hepatitis C virus treatment. This case illustrates the importance of considering acute hepatitis C as a cause of acute hepatitis in HIV-infected men who have sex with men. While patients with acute symptomatic hepatitis C generally have a higher rate of spontaneous viral clearance compared to those with an insidious acute infection, most still progress to chronic hepatitis C infection, and patients with HIV coinfection carry a higher risk of progression to chronic disease.

KEY WORDS: acute hepatitis C virus; human immunodeficiency virus; hepatitis C virus treatment.
J Gen Intern Med 28(5):734–8
DOI: 10.1007/s11606-012-2258-3

CASE PRESENTATION

A 46-year-old Hawaiian–Japanese man with HIV presented to the emergency department with acute onset of abdominal pain. He was in his normal state of health until approximately 5 days prior to presentation, when he noted an acute onset of abdominal pain with intermittent nausea. The pain was dull, primarily epigastric with occasional shifting to the right flank and mid-back. The nausea occurred without vomiting and was not related to food intake. Two days prior to presentation, he began to have dark urine and a friend noted that his eyes and skin appeared yellowed. His past medical history was significant for HIV that was diagnosed 20 years ago, and he was being treated with antiretroviral medications (last CD4 count was 464/mm^3 and last HIV RNA was undetectable), anal condyloma with dysplasia status post-treatment with multiple fulgurations, treated secondary syphilis, herpes simplex virus infection on suppressive therapy, depression and chronic constipation. Medications included bupropion, darunavir, etravirine, maraviroc, raltegravir, ritonavir, acyclovir and stool softeners. He did not usually drink alcohol, but reported ingesting three drinks 5 days prior to presentation. He had a remote history of intravenous drug abuse with last use over 3 years ago. He preferred male sexual partners, with his last sexual encounter including oral and unprotected receptive anal intercourse two months prior to admission. He denied any recent inhalation drug use, tattoos, or other percutaneous exposures.

On initial presentation, physical examination demonstrated a temperature of 98.7 F, blood pressure of 133/94 mmHg, pulse of 73/min, and respiratory rate of 20/min with a room air oxygen saturation of 97 %. His sclera were icteric and his skin was jaundiced. His abdomen was diffusely tender to palpation with increased tenderness in the epigastrium and right upper quadrant without peritoneal signs. A liver edge was palpable 1 cm below the costal margin. There was no asterixis. Pertinent laboratory findings included aspartate aminotransferase of 2,101 U/L [5–35] and alanine aminotransferase of 3,491 U/L [7–56]), total bilirubin of 8.5 mg/dL [0.1–1.2] with direct bilirubin of 5.9 mg/dL [0.1–0.5]), and alkaline phosphatase (163 U/L [40–125]) (see Table 1). His complete blood count, serum chemistries, total protein, albumin, lipase and coagulation times were unremarkable. Contrast-enhanced computerized tomography (CT) scan of the abdomen showed periportal edema in the right hepatic lobe, suggesting hepatitis but without any other abnormalities.

The patient's symptoms and significant hepatitis coupled with the CT scan suggested acute hepatitis, and prompted admission to the hospital. The differential diagnosis included drug-related hepatotoxicity (unreported acetaminophen use, antiretroviral medications, particularly the ritonavir-boosted darunavir) or acute viral hepatitis (A, B, C, disseminated herpes simplex, Epstein–Barr or cytomeg-

Received May 31, 2011
Revised September 18, 2012
Accepted October 10, 2012
Published online November 14, 2012

Table 1. Trend of Relevant Liver Tests and Hepatitis C Virus (HCV) RNA Results

	Aspartate aminotransferase (U/L)	Alanine aminotransferase (U/L)	Total Bilirubin/Direct Bilirubin (mg/dL)	Hepatitis C RNA (IU/mL)
Reference range	5–35	7–56	0.1–1.2/0.1–0.5	< 43
3 months before admission	42	46	1.1/0.1	
2 weeks before admission	38	58	0.9/0.1	
Hospital Day 1	2,101	3,491	8.5/5.9	8,250,342
Hospital Day 2	1,728	3,051	10.3/6.6	
Hospital Day 3	1,574	2,469	9.5/6.4	
3 days after discharge	1,375	2,037	12.8/8.1	
5 days after discharge	846	1,424	11.1/6.8	
3 weeks after discharge	43	79	2.7/1.2	6,262
5 weeks after discharge	2,067	2,524	6.1/4.1	1,233,404
7 weeks after discharge	39	179	1.8/0.7	39,118
8 weeks after discharge	193	604	2.1/0.8	
14 weeks after discharge, start of anti-HCV therapy	36	105	1.3/0.3	34,738
2 weeks after anti-HCV therapy initiation	28	30	1.5/0.3	< 43
18 weeks after anti-HCV therapy initiation	23	19	0.8/0.1	< 43
24 weeks after anti-HCV therapy initiation/completion of therapy	25	21	0.9/0.2	< 43

alovirus), autoimmune hepatitis and Wilson's disease. The patient's medications were temporarily held. Serum tests for salicylate, acetaminophen, and ethanol were negative, as was the urine toxicology screen. Laboratory studies showed him to be hepatitis A immune, hepatitis B immune and hepatitis C antibody negative (see Table 2). Additional workup, including autoimmune and infectious etiologies, was unremarkable. A hepatitis C RNA viral load was ordered because a significant proportion of patients with acute hepatitis C are HCV antibody negative,[1,2] and HIV-infected men who have sex with men are at risk of contracting hepatitis C.[3–27] His hepatitis C RNA viral load was 8,250,342 international units/mL [< 43]), which informed a diagnosis of acute HCV infection. Serial liver function tests showed persistent hepatitis (see Table 1). After 3 days of supportive care, the patient was tolerating oral intake and was discharged with close outpatient follow-up.

Table 2. Laboratory Findings During Inpatient Admission

	On admission	Reference range
Lactate dehydrogenase (U/L)	574	100 – 190
Haptoglobin (mg/dL)	63	20 – 190
Ferritin (mcg/L)	518	29 – 371
Transferrin (mg/dL)	236	181 – 335
Transferrin Sat (%)	15	16 – 60
Ceruloplasmin (mg/dL)	28	17 – 48
ANA (IU/mL)	< 7.5	< 7.5
ANA (calculated titer)	< 1:40	< 1:40
Anti-smooth muscle Ab(titer)	< 1:40	< 1:40
Herpes simplex I, IgM (index)	< 0.80	< 0.80
Herpes simplex I, IgG (index)	1.34	< 0.90
Herpes simplex II, IgM (index)	< 0.80	< 0.80
Herpes simplex II, IgG (index)	3.75	< 0.90
CMV Ab, IgM (index)	< 0.90	< 0.90
CMV Ab, IgG (index)	4.28	< 0.91
EBV VCA Abs, IgM (titer)	< 1:10	< 1:10
EBV VCA Abs, IgG (titer)	1:160	< 1:10
EBV nuclear antigen Abs, IgG (titer)	≥1:80	< 1:5
EBV early antigen Abs, IgG (titer)	1:10	< 1:10
Hepatitis A Ab, IgM	Negative	Negative
Hepatitis A Ab, Total	Positive	Negative
Hepatitis B surface Ab	Positive	Negative
Hepatitis B core Ab	Positive	Negative
Hepatitis C Ab	Negative	Negative
Hepatitis C RNA (IU/mL)	8,250,342	< 43

In follow-up, the patient's liver tests nearly normalized (Table 1) and his HCV RNA viral load dropped dramatically (Fig. 1), suggesting he may clear the hepatitis C virus spontaneously. Three weeks after discharge, he was restarted on his anti-HIV medications. However, 5 weeks after discharge, the patient had a recurrence of his symptoms, with a corresponding increase in aspartate aminotransferase (AST), alanine aminotransferase (ALT) and total bilirubin, along with an increase in his HCV RNA viral level. His HCV genotype was 1a and 14 weeks after discharge, he began anti-HCV therapy with ribavirin 400 mg orally twice a day and peginterferon alfa-2a 180mcg subcutaneously weekly. Inclusion of an anti-HCV protease inhibitor, telaprevir or boceprevir, was considered, but was not used due to significant drug–drug interactions with the patient's anti-HIV therapy. At week two of anti-HCV treatment, the patient's HCV RNA viral load decreased to undetectable levels (< 43 IU/mL), and this was maintained throughout his treatment course to 24 weeks. After completion of 24 weeks of anti-HCV therapy, the patient continued to have an undetectable HCV RNA viral load, representing achievement of sustained virologic response.

DISCUSSION

The initial challenge in this case was to deduce the etiology of the patient's severe hepatitis. The differential diagnosis

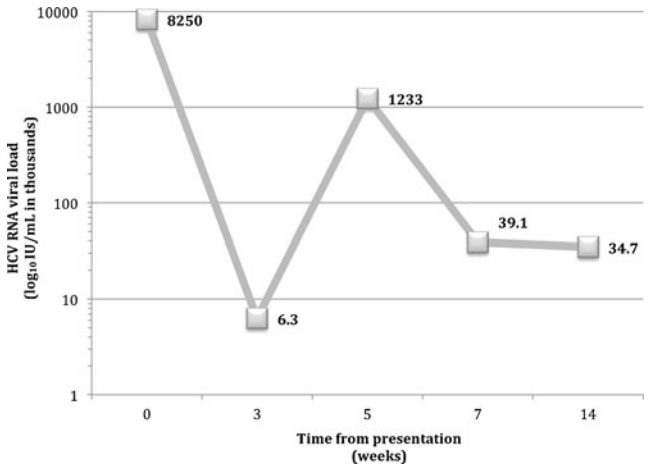

Figure 1. Hepatitis C RNA viral load from initial presentation before treatment.

for acute hepatitis is broad, and in HIV-infected individuals includes drug hepatotoxicity, viral and non-viral infections. Highly active antiretroviral therapy (HAART)–related hepatotoxicity, defined as greater than five times the upper limit of normal elevation in ALT, has been reported for almost every anti-HIV medication currently available.[28] The patient's darunavir and ritonavir were the most concerning, with rates of HAART-related hepatotoxicity of 5.6–6.9 % and 5.3–6.9 %, respectively.[28] Raltegravir, darunavir and ritonavir pose even a higher risk of HAART-related hepatotoxicity in HBV or HCV coinfected patients, which could explain the severe ALT elevation noted in this case on presentation and with reinstitution of anti-HIV therapy.[28]

Given the patient's HIV positive status and his sexual exposures, acute symptomatic hepatitis C must be on the differential. Among HIV-infected people, hepatitis C virus (HCV) is a common coinfection, ranging from 10 to 40 % in most cohorts.[29] Most patients with acute HCV infection are asymptomatic and are diagnosed either in persons presenting with risk history (i.e. needlestick injury), or in the work-up of nonspecific symptoms or lab abnormalities (i.e. elevated ALT). However, acute symptomatic HCV infection can present with a wide range of symptoms, from mild icterus to vague abdominal discomfort, to severe hepatitis needing an acute hospitalization.[2] Compared to HIV-negative individuals, HIV-positive patients are more likely to present with symptomatic acute HCV infection.[30] However, HIV-positive and HIV-negative individuals diagnosed with acute HCV infection had similar transaminase elevations.[27]

While percutaneous exposures to HCV-infected blood or blood contaminated materials (needles) are the primary methods of HCV transmission, sexual transmission of HCV can occur.[29,31] Longitudinal studies in HIV-uninfected heterosexual couples with one partner having HCV have shown minimal to no risk of sexual transmission during long-term monogamy.[32] Moreover, in prior studies of people infected with HIV, drug use rather than sex was viewed as the factor associated with HCV positivity; those with a history of abuse of injection drugs had an incidence of HCV of 7.4 cases per 100 person years versus 0.23 cases per 100 person years in those without a history of intravenous drug abuse.[4] However, more recent reports highlight the role of sexual transmission of hepatitis C among men who have sex with men who have minimal reported exposure to injection drugs.[3–27] Additionally, recent increases in HCV and HIV coinfection have been noted in many countries among populations of men who have sex with men.[33] Specific sexual practices strongly associated with incident infection with hepatitis C virus include unprotected receptive or insertive anal intercourse, fisting, group sex, club drugs and increased number of sexual partners.[8,9,17] In addition, recent studies have implicated HIV infection as a putative cofactor for increased sexual transmissibility of hepatitis C virus. In a cohort of 948 men who have sex with men, 1.5 cases of acute hepatitis C per 1,000 person years was documented in HIV negative patients, compared to a case rate of 12 per 1,000 person years in men who have sex with men infected with HIV.[6] Similarly, a case–control study in Italy documented an increase in prevalence of anti-HCV antibody from 5 % in men who have sex with men to 15 % in men who have sex with men infected with HIV.[26]

Sexual transmission of HCV in HIV-infected people may be facilitated by the higher quantitative titers of HCV in their plasma, seminal fluid, and salivary secretions.[34] Immunological studies of acute infection with hepatitis C virus in humans have focused on adaptive T-cell immunity, and have shown that clearance of the virus during the acute phase needs an effective CD4 and CD8 T-cell response.[35–37] In a study evaluating T-cell function specific to HCV in patients infected with HIV, interferon gamma responses were substantially reduced by coinfection with HIV,[38] a response that is magnified with lower CD4-T-cell counts.[35,39] This emerging literature highlights the importance of this patient's HIV status and sexual habits as risk factors for acute hepatitis C infection.

Most acute infections with HCV will become chronic in the absence of antiviral therapy, with an average spontaneous viral clearance rate of only 25 % (95 % confidence interval 22-29 %, range 0–80 %) at least 6 months after diagnosis.[40] Risk factors for progression to chronic HCV infection include asymptomatic acute infection, male sex, African-American ethnicity, coinfection with HIV, and lower HCV viral loads.[40–43] There are few prospective analyses of the natural history of acute hepatitis C during infection with HIV. The literature suggests, however, that people infected with HIV seem less likely to eradicate the infection spontaneously, compared to HIV negative individuals with reported clearance rates varying widely from 4–26 %.[3,42,44–50] Because acute symptomatic hepatitis C

infection is correlated to higher spontaneous viral clearance rates, this patient was closely observed for spontaneous viral clearance before treatment was considered. However, with a recurrent flare of his serum aminotransferase levels and HCV viral load 5 weeks after discharge, it was felt that his chance of achieving spontaneous viral clearance was low. Studies have shown a doubled risk of cirrhosis, a six-fold increased risk of end stage liver disease,[51] and increased risk of death[52] in patients with coinfections with HIV and chronic HCV compared with HCV mono-infected patients.[51] As a result, anti-HCV therapy was initiated 14 weeks after discharged.

It is important to identify acute HCV among people infected with HIV because, in the absence of spontaneous clearance, early anti-HCV treatment is associated with higher response than treatment of chronic HCV.[53,54] Treatment outcomes for acute hepatitis C are largely derived from prospective cohort trials of mono-infected patients that include various regimens with differing treatment duration. These studies report sustained virologic response (SVR) rates ranging from 57 to 94 %.[53,54] While it remains unclear when it is appropriate to begin treatment in patients with acute HCV infection, most trials allow 12 weeks for spontaneous viral clearance, in order to minimize unnecessary exposure to peginterferon and ribavirin.[41,55] However, it is clear that waiting for prolonged periods is detrimental, as several trials have shown that promptly starting treatment (after 8–12 weeks) is associated with a higher SVR rate.[41,55] The European AIDS Treatment Network recently reported the treatment of acute HCV infection in HIV-positive patients with peginterferon and ribavirin with an SVR rate of 91 %.[56] The treatment strategy used in this study was what this patient received. Triple therapy (the use the new anti-HCV protease-inhibitors, telaprevir or boceprevir, in combination with peginterferon and ribavirin) has not been studied in acute HCV infection. It is likely that triple therapy will be of little added benefit in treatment of acute HCV infection, given the increased drug toxicity profile of telaprevir or boceprevir and the already high rates of SVR with peginterferon and ribavirin alone. Additionally, telaprevir and boceprevir are substrates and inhibitors of CYP3A, giving them significant drug–drug interactions with anti-HIV therapy.[57]

CONCLUSION

In summary, this is a case of acute symptomatic hepatitis C in an HIV-infected patient that did not spontaneously clear after greater than 12 weeks of follow-up, but was subsequently eradicated with a 24-week course of peginterferon and ribavirin.

This case reviews the differential diagnosis for severe hepatitis and the importance of considering acute hepatitis C virus infection in the differential for HIV-infected men who have sex with men. While symptomatic acute hepatitis C virus is correlated with higher rates of spontaneous viral clearance, patients frequently progress to chronic HCV infection in the absence of antiviral therapy. Early HCV antiviral treatment is associated with a high rate of sustained virologic response, in both HIV-infected and uninfected patients.

Key Points:

1. Acute hepatitis C virus should be on the differential diagnosis of acute ALT/AST elevation in HIV-infected men who have sex with men without a history of injection drug use.
2. Most acute infections with hepatitis C virus will become chronic.
3. Patients with HIV and hepatitis C virus coinfection are at higher risk of cirrhosis, end-stage-liver disease and death than hepatitis C virus mono-infected patients.
4. Early anti-hepatitis C virus therapy with peginterferon and ribavirin is effective in achieving sustained virologic response.

Acknowledgements: *We thank all the members of the multidisciplinary teams involved in the care of the patient presented here. We particularly thank Dr. Michael Shlipak and Dr. Nancy Ann Oberheim Bush, who were part of the primary team caring for the patient during his inpatient stay.*

Conflict of Interest/Funding: *The authors declare that they do not have any conflicts of interest.*

Corresponding Author: *Varun Saxena, MD; University of California, San Francisco, Box 0538, 513 Parnassus Avenue, Med Sci 357, San Francisco, CA 94143-0538, USA (e-mail: Varun.Saxena @ucsf.edu).*

REFERENCES

1. **Maheshwari A, Ray S, Thuluvath PJ.** Acute hepatitis C. Lancet. 2008;372:321–32.
2. **Orland JR, Wright TL, Cooper S.** Acute hepatitis C. Hepatology. 2001;33:321–7.
3. **Serpaggi J, Chaix ML, Batisse D, et al.** Sexually transmitted acute infection with a clustered genotype 4 hepatitis C virus in HIV-1-infected men and inefficacy of early antiviral therapy. AIDS. 2006;20:233–40.
4. **Rauch A, Rickenbach M, Weber R, et al.** Unsafe sex and increased incidence of hepatitis C virus infection among HIV-infected men who have sex with men: the Swiss HIV Cohort Study. Clin Infect Dis. 2005;41:395–402.
5. **Fox J, Nastouli E, Thomson E, et al.** Increasing incidence of acute hepatitis C in individuals diagnosed with primary HIV in the United Kingdom. AIDS. 2008;22:666–8.
6. **Richardson D, Fisher M, Sabin CA.** Sexual transmission of hepatitis C in MSM may not be confined to those with HIV infection. J Infect Dis. 2008;197:1213–4. author reply 4–5.

7. **Buffington J, Murray PJ, Schlanger K, et al.** Low prevalence of hepatitis C virus antibody in men who have sex with men who do not inject drugs. Public Health Rep. 2007;122(Suppl 2):63–7.
8. **Danta M, Brown D, Bhagani S, et al.** Recent epidemic of acute hepatitis C virus in HIV-positive men who have sex with men linked to high-risk sexual behaviours. AIDS. 2007;21:983–91.
9. **Dougan S, Evans BG, Elford J.** Sexually transmitted infections in Western Europe among HIV-positive men who have sex with men. Sex Transm Dis. 2007;34:783–90.
10. **Matthews GV, Hellard M, Kaldor J, Lloyd A, Dore GJ.** Further evidence of HCV sexual transmission among HIV-positive men who have sex with men: response to Danta et al. AIDS. 2007;21:2112–3.
11. **van de Laar TJ, van der Bij AK, Prins M, et al.** Increase in HCV incidence among men who have sex with men in Amsterdam most likely caused by sexual transmission. J Infect Dis. 2007;196:230–8.
12. **Wang CC, Krantz E, Klarquist J, et al.** Acute hepatitis C in a contemporary US cohort: modes of acquisition and factors influencing viral clearance. J Infect Dis. 2007;196:1474–82.
13. **Santantonio T, Medda E, Ferrari C, et al.** Risk factors and outcome among a large patient cohort with community-acquired acute hepatitis C in Italy. Clin Infect Dis. 2006;43:1154–9.
14. **Turner JM, Rider AT, Imrie J, et al.** Behavioural predictors of subsequent hepatitis C diagnosis in a UK clinic sample of HIV positive men who have sex with men. Sex Transm Infect. 2006;82:298–300.
15. **Alary M, Joly JR, Vincelette J, Lavoie R, Turmel B, Remis RS.** Lack of evidence of sexual transmission of hepatitis C virus in a prospective cohort study of men who have sex with men. Am J Public Health. 2005;95:502–5.
16. **Gambotti L, Batisse D, Colin-de-Verdiere N, et al.** Acute hepatitis C infection in HIV positive men who have sex with men in Paris, France, 2001–2004. Euro Surveill. 2005;10:115–7.
17. **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.
18. **Amin J, Kaye M, Skidmore S, Pillay D, Cooper DA, Dore GJ.** HIV and hepatitis C coinfection within the CAESAR study. HIV Med. 2004;5:174–9.
19. **Browne R, Asboe D, Gilleece Y, et al.** Increased numbers of acute hepatitis C infections in HIV positive homosexual men; is sexual transmission feeding the increase? Sex Transm Infect. 2004;80:326–7.
20. **Ghosn J, Pierre-Francois S, Thibault V, et al.** Acute hepatitis C in HIV-infected men who have sex with men. HIV Med. 2004;5:303–6.
21. **Diamond C, Thiede H, Perdue T, et al.** Viral hepatitis among young men who have sex with men: prevalence of infection, risk behaviors, and vaccination. Sex Transm Dis. 2003;30:425–32.
22. **Fletcher S.** Sexual transmission of hepatitis C and early intervention. J Assoc Nurses AIDS Care. 2003;14:87S–94S.
23. **Hammer GP, Kellogg TA, McFarland WC, et al.** Low incidence and prevalence of hepatitis C virus infection among sexually active non-intravenous drug-using adults, San Francisco, 1997–2000. Sex Transm Dis. 2003;30:919–24.
24. **Marx MA, Murugavel KG, Tarwater PM, et al.** Association of hepatitis C virus infection with sexual exposure in southern India. Clin Infect Dis. 2003;37:514–20.
25. **Saxton PJ, Hughes AJ, Robinson EM.** Sexually transmitted diseases and hepatitis in a national sample of men who have sex with men in New Zealand. N Z Med J. 2002;115:U106.
26. **Filippini P, Coppola N, Scolastico C, et al.** Does HIV infection favor the sexual transmission of hepatitis C? Sex Transm Dis. 2001;28:725–9.
27. **Matthews GV, Hellard M, Haber P, et al.** Characteristics and treatment outcomes among HIV-infected individuals in the Australian Trial in Acute Hepatitis C. Clin Infect Dis. 2009;48:650–8.
28. **Nunez M.** Clinical syndromes and consequences of antiretroviral-related hepatotoxicity. Hepatology. 2010;52:1143–55.
29. **Anderson KB, Guest JL, Rimland D.** Hepatitis C virus coinfection increases mortality in HIV-infected patients in the highly active antiretroviral therapy era: data from the HIV Atlanta VA Cohort Study. Clin Infect Dis. 2004;39:1507–13.
30. **Vogel M, Deterding K, Wiegand J, et al.** Initial presentation of acute hepatitis C virus (HCV) infection among HIV-negative and HIV-positive individuals-experience from 2 large German networks on the study of acute HCV infection. Clin Infect Dis. 2009;49:317–9. author reply 9.
31. **Romanowski B, Preiksaitis J, Campbell P, Fenton J.** Hepatitis C seroprevalence and risk behaviors in patients attending sexually transmitted disease clinics. Sex Transm Dis. 2003;30:33–8.
32. **Vandelli C, Renzo F, Romano L, 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.
33. **Boesecke C, Vogel M.** HIV and hepatitis C co-infection: acute HCV therapy. Curr Opin HIV AIDS. 2011;6:459–64.
34. **Matthews-Greer JM, Caldito GC, Adley SD, et al.** Comparison of hepatitis C viral loads in patients with or without human immunodeficiency virus. Clin Diagn Lab Immunol. 2001;8:690–4.
35. **Bowen DG, Walker CM.** Adaptive immune responses in acute and chronic hepatitis C virus infection. Nature. 2005;436:946–52.
36. **Dustin LB, Rice CM.** Flying under the radar: the immunobiology of hepatitis C. Annu Rev Immunol. 2007;25:71–99.
37. **Gruner NH, Gerlach TJ, Jung MC, et al.** Association of hepatitis C virus-specific CD8+ T cells with viral clearance in acute hepatitis C. J Infect Dis. 2000;181:1528–36.
38. **Danta M, Semmo N, Fabris P, et al.** Impact of HIV on host-virus interactions during early hepatitis C virus infection. J Infect Dis. 2008;197:1558–66.
39. **Kim AY, Schulze zur Wiesch J, Kuntzen T, et al.** Impaired hepatitis C virus-specific T cell responses and recurrent hepatitis C virus in HIV coinfection. PLoS Med. 2006;3:e492.
40. **Micallef JM, Kaldor JM, Dore GJ.** Spontaneous viral clearance following acute hepatitis C infection: a systematic review of longitudinal studies. J Viral Hepat. 2006;13:34–41.
41. **Gerlach JT, Diepolder HM, Zachoval R, et al.** Acute hepatitis C: high rate of both spontaneous and treatment-induced viral clearance. Gastroenterology. 2003;125:80–8.
42. **Thomas DL, Astemborski J, Rai RM, et al.** The natural history of hepatitis C virus infection: host, viral, and environmental factors. JAMA. 2000;284:450–6.
43. **Villano SA, Vlahov D, Nelson KE, Cohn S, Thomas DL.** Persistence of viremia and the importance of long-term follow-up after acute hepatitis C infection. Hepatology. 1999;29:908–14.
44. **Luetkemeyer A, Hare CB, Stansell J, et al.** Clinical presentation and course of acute hepatitis C infection in HIV-infected patients. J Acquir Immune Defic Syndr. 2006;41:31–6.
45. **Dominguez S, Ghosn J, Valantin MA, et al.** Efficacy of early treatment of acute hepatitis C infection with pegylated interferon and ribavirin in HIV-infected patients. AIDS. 2006;20:1157–61.
46. **Gilleece YC, Browne RE, Asboe D, et al.** Transmission of hepatitis C virus among HIV-positive homosexual men and response to a 24-week course of pegylated interferon and ribavirin. J Acquir Immune Defic Syndr. 2005;40:41–6.
47. **Vogel M, Bieniek B, Jessen H, et al.** Treatment of acute hepatitis C infection in HIV-infected patients: a retrospective analysis of eleven cases. J Viral Hepat. 2005;12:207–11.
48. **Vogel M, Nattermann J, Baumgarten A, et al.** Pegylated interferon-alpha for the treatment of sexually transmitted acute hepatitis C in HIV-infected individuals. Antivir Ther. 2006;11:1097–101.
49. **Vogel M, Rockstroh J.** The Treatment of Chronic Hepatitis C Virus Infection in HIV Co-infection. Eur J Med Res. 2009;14:507–15.
50. **Vogel M, Dominguez S, Bhagani S, et al.** Treatment of acute HCV infection in HIV-positive patients: experience from a multicentre European cohort. Antivir Ther. 2010;15:267–79.
51. **Graham CS, Baden LR, Yu E, et al.** Influence of human immunodeficiency virus infection on the course of hepatitis C virus infection: a meta-analysis. Clin Infect Dis. 2001;33:562–9.
52. **Weber R, Sabin CA, Friis-Moller N, et al.** Liver-related deaths in persons infected with the human immunodeficiency virus: the D:A:D study. Arch Intern Med. 2006;166:1632–41.
53. **Broers B, Helbling B, Francois A, et al.** Barriers to interferon-alpha therapy are higher in intravenous drug users than in other patients with acute hepatitis C. J Hepatol. 2005;42:323–8.
54. **Santantonio T, Fasano M, Sinisi E, et al.** Efficacy of a 24-week course of PEG-interferon alpha-2b monotherapy in patients with acute hepatitis C after failure of spontaneous clearance. J Hepatol. 2005;42:329–33.
55. **Nomura H, Sou S, Tanimoto H, et al.** Short-term interferon-alfa therapy for acute hepatitis C: a randomized controlled trial. Hepatology. 2004;39:1213–9.
56. **Dorward J, Garrett N, Scott D, Buckland M, Orkin C, Baily G.** Successful treatment of acute hepatitis C virus in HIV positive patients using the European AIDS Treatment Network guidelines for treatment duration. J Clin Virol. 2011;52:367–9.
57. **Kiser JJ, Burton JR, Anderson PL, Everson GT.** Review and management of drug interactions with boceprevir and telaprevir. Hepatology. 2012;55:1620–8.