

Diagnosis of Acute HCV Infection

This is a PDF version of the following document:

Section 1: [Screening and Diagnosis of Hepatitis C Infection](#)

Topic 5: [Diagnosis of Acute HCV Infection](#)

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Definition of Acute HCV

Definitions of Acute HCV Infection

Most commonly, acute hepatitis C virus (HCV) infection is defined as the 6-month time period following acquisition of hepatitis C virus.[1,2,3] The definition of acute hepatitis C is irrespective to whether the patient has clinical signs or symptoms of acute hepatitis.[2] The rationale for choosing 6 months as the time period to define acute infection is based on evidence that most individuals who spontaneously clear HCV will do so by 6 months.[4,5,6]

Terminology Related to Acute HCV Infection

Clinical reviews and research studies have used numerous terms to refer to acute hepatitis C infection, including acute infection, acute phase infection, very early infection, recent infection, and newly acquired infection. Overall, consensus does not exist regarding the terminology and criteria for defining acute HCV infection. Very early infection typically refers to patients with a positive HCV RNA and documented HCV antibody seroconversion and this scenario is the most definitive for diagnosing acute HCV infection. Some experts have suggested limiting the multiple possible terms to acute infection and recent infection with the following definitions:[2]

- **Acute Infection:** estimated duration of infection less than 6 months
- **Recent Infection:** estimated duration of infection longer than 6 months, but shorter than 2 years.

Clinical Features of Acute HCV

Clinical Manifestations

Among individuals with acute HCV infection, only 15 to 25% develop a clearly distinguishable symptomatic illness.[\[7,8,9\]](#) In addition, most chronically infected patients cannot recall a time when they were acutely symptomatic. When patients develop symptomatic acute HCV infection, the clinical manifestations typically resemble those that occur with other types of viral hepatitis—fatigue, myalgias, low-grade fever, jaundice, dark urine, nausea, vomiting, right upper quadrant pain.[\[8,10\]](#) Symptoms may consist of malaise only, without jaundice or gastrointestinal symptoms ([Figure 1](#)). If symptoms from acute infection develop, they usually do so within 4 to 12 weeks (mean 7 to 8 weeks) after infection has occurred and they typically persist for 2 to 12 weeks.[\[7,8,11\]](#) Fulminant hepatic failure due to acute HCV infection very rarely occurs, but preexisting chronic hepatitis B infection increases this risk.[\[12,13\]](#)

Relationship of Symptoms and Spontaneous Clearance

Overall, when combining data from multiple historical studies, approximately 25 to 35% of person with acute HCV infection have spontaneous clearance of HCV.[\[14,15,16,17\]](#) The rates of spontaneous clearance are significantly lower in persons who have HIV coinfection—in the range of 10 to 20%.[\[18,19\]](#) Several studies have shown that patients who present with symptomatic acute HCV infection and jaundice have rates of spontaneous clearance of HCV of approximately 35 to 50%.[\[8,15,20\]](#) The presence of jaundice is believed to reflect hepatic inflammation caused by a more robust initial immune response against HCV.[\[4,15\]](#)

Clinical Scenarios that Suggest Acute HCV Infection

Symptomatic Presentation

Symptomatic individuals could present with the new onset of jaundice, fatigue, nausea, abdominal pain, and malaise. Acutely infected persons may have more limited symptoms, such as slight malaise and fatigue without jaundice.

History of a Recent HCV Exposure but Without Symptoms

Since acute HCV is usually asymptomatic, clinicians need to test patients as soon as possible following a new incident in which infection could have taken place; since most cases of acute hepatitis C are asymptomatic, clinicians should not rely on patients to appear clinically ill in order to decide to test patients for acute HCV infection. Providers should suspect the disease in patients exposed to potentially infectious sources ([Figure 2](#)) and understand that prompt testing can be critical to making the diagnosis of a new infection and distinguishing acute from chronic infection. Recent injection drug use with shared needles or equipment would be the most common recent exposure to HCV. Although the risk of HCV transmission through sexual contact is controversial, recent sexual exposure should be considered as a possible risk. The risk of sexual transmission appears to be highest with male-male exposures, particularly if this involves persons with HIV who have engaged in physically traumatic or rough sex.

Laboratory Diagnosis of Acute HCV

Laboratory Studies for Evaluation of Initial Infection

The key laboratory studies utilized in the evaluation of possible acute hepatitis C are HCV RNA, anti-HCV, and alanine aminotransferase (ALT). Patients who become infected with hepatitis C virus typically develop abnormal laboratory findings in the following order: detectable HCV RNA, followed by elevation in ALT, and then HCV antibody ([Figure 3](#)).[\[8,21\]](#) Patients who develop a clinical illness with acute HCV infection usually have onset of symptoms well after the onset of viremia, but soon after or concomitant with increases in ALT levels.

HCV RNA (HCV Nucleic Acid Testing)

In most patients, HCV RNA can be detected in blood within 1 to 2 weeks after infection.[\[22\]](#) Testing for HCV RNA is often referred to as HCV nucleic acid testing (NAT). This period from infection until HCV RNA is detectable in plasma by a commercially available assay is referred to as the previremic phase or eclipse phase ([Figure 4](#)).[\[22,23\]](#) During the eclipse phase, HCV has likely established infection in susceptible hepatocytes, and, in some patients, use of qualitative HCV RNA assays with very high sensitivity will reveal blips of HCV RNA (at levels less than 10 copies/mL) in blood.[\[22\]](#) The eclipse phase is followed by an 8 to 10 day “ramp-up” phase in which HCV replication increases exponentially and readily becomes detectable in plasma; the HCV RNA levels typically peak 6 to 10 weeks after infection (“plateau phase”) and remain near these peak levels for about 40 to 60 days ([Figure 5](#)).[\[22\]](#) Detection of HCV RNA during acute infection is not entirely reliable as HCV RNA levels may fluctuate significantly during this period—in some instances HCV RNA levels fall below detectable levels.[\[7,22,24\]](#) At the onset of symptoms, however, detectable HCV RNA levels are uniformly present. Among individuals who spontaneously clear HCV, most (73 to 86%) clear the infection within the first 6 months after HCV acquisition.[\[2,9\]](#)

Antibodies to HCV

Antibodies to HCV typically become detectable at about 50 to 60 days after infection (range 20 to 150 days); the detection of HCV-specific antibodies significantly lags behind detectable HCV RNA levels.[\[7,8,22\]](#) After 12 weeks, more than 90% of patients will have a positive HCV antibody test. The time period from initial infection until seroconversion is often referred to as the “serologic window period” ([Figure 6](#)).[\[25,26\]](#) The use of only an HCV antibody test to diagnose acute HCV is not reliable, since only approximately 50 to 70% of patients have detectable HCV antibodies at the onset of symptoms. Further, a positive HCV antibody test does not differentiate acute from chronic HCV infection.

Hepatitis C Core Antigen

Several studies have shown testing for HCV core antigen can enhance the diagnostic yield of persons with acute HCV when compared with HCV antibody testing alone.[\[26,27,28\]](#) The HCV antigen assays that have been developed for diagnostic purposes include HCV core antigen assays and a combination HCV antibody-HCV core antigen assay.[\[29,30,31\]](#) Although some experts have proposed use of HCV core antigen testing as a less expensive option than HCV RNA testing for detecting acute HCV with similar sensitivity, there are no HCV antigen assays (or HCV antigen-antibody combination assays) that are FDA approved for use in the United States.[\[32,33\]](#)

Alanine Aminotransferase (ALT)

Within 4 to 12 weeks after HCV infection, most patients will have some degree of liver cell injury, as manifested by an elevation in serum ALT levels. Typically the increases in ALT follow the presence of detectable HCV RNA levels by about 1 to 2 weeks, but generally precede the development of HCV antibodies. The mean ALT after acute infection reaches 800 IU/L range. The Centers for Disease

Control and Prevention uses an increase in ALT to a peak level greater than 200 IU/L during the period of acute illness as part of the diagnostic criteria.

Diagnosis of Acute HCV

In the United States, the gold standard for the laboratory diagnosis of acute HCV is an HCV antibody seroconversion (negative HCV antibody test before a suspected exposure and a positive antibody test following potential exposure), combined with a positive HCV RNA test and elevated ALT. In clinical practice, many patients do not present early enough after a potential exposure and so it is not always possible to demonstrate an initial negative antibody followed by a positive antibody. Thus, a probable diagnosis of acute HCV is made when an individual has a positive HCV RNA and evidence of a negative HCV antibody in the prior 6 months. It can be challenging to differentiate an acute infection from chronic infection in patients who have not previously undergone HCV antibody testing.

Potential Missed Diagnosis of Acute HCV with HCV Reflex Testing Protocol

In many laboratories in the United States, HCV testing protocols are in place whereby a positive HCV antibody test triggers automatic (reflex) testing of the sample for HCV RNA whereas a negative initial HCV antibody test does not trigger further testing. This protocol is ideal for detecting persons with chronic HCV infection and determining whether these individuals have resolved or chronic (active) infection. But, this reflex testing protocol can be problematic in the setting of acute HCV, since HCV antibody seroconversion may not yet have taken place and the HCV RNA test will not be run, thereby resulting in a false-negative HCV test. If a patient has suspected acute HCV infections, clinicians should inquire whether the laboratory performing the HCV testing uses a reflex testing protocol; if a HCV reflex testing protocol is in place, the clinician should intentionally place separate orders for the HCV antibody and the HCV RNA so that both tests will be run, regardless of the HCV antibody result. This approach, in the setting of suspected acute HCV infection, will allow for detection of HCV if the individual has not been infected with HCV long enough to have generated HCV antibodies.

Laboratory Testing Following Known Exposure

In situations where patients have encountered high-risk exposures, follow-up with serial laboratory testing is the key to promptly establishing the diagnosis of acute HCV infection. The following outlines the recommended laboratory testing following a known exposure to hepatitis C virus:

- **At Initial Presentation:** HCV antibody, HCV RNA, and ALT
- **At 4 Weeks from Time of Suspected Exposure:** HCV antibody, HCV RNA, and ALT
- **At 12 Weeks from Time of Suspected Exposure:** HCV antibody, HCV RNA, and ALT

2016 CDC Case Definition for Acute HCV

The Centers for Disease Control and Prevention (CDC) has established criteria for the 2016 case definition of acute Hepatitis C.[\[34\]](#) This definition utilizes clinical criteria, laboratory criteria for diagnosis, criteria to distinguish a new case from an existing case, and a case classification (probable or confirmed). The following summarizes the 2016 CDC Case Definition for Acute HCV.[\[34\]](#)

Clinical Criteria

An illness with discrete onset of any sign or symptom consistent with acute viral hepatitis (e.g., fever, headache, malaise, anorexia, nausea, vomiting, diarrhea, and abdominal pain),

AND

(a) jaundice,

or

(b) a peak elevated serum alanine aminotransferase (ALT) level greater than 200 IU/L during the period of acute illness.

Laboratory Criteria for Diagnosis

- A positive test for antibodies to hepatitis C virus (anti-HCV)
- Hepatitis C virus detection test:
 - Nucleic acid test (NAT) for HCV RNA positive (including qualitative, quantitative or genotype testing)
 - A positive test indicating presence of hepatitis C viral antigen(s) (HCV antigen)*.

*When and if a test for HCV antigen(s) is approved by FDA and available.

Criteria to Distinguish a New Case from an Existing Case

A new acute case is an incident acute hepatitis C case that meets the case criteria for acute hepatitis C and has not previously been reported. A new probable acute case may be re-classified as confirmed acute case if a positive NAT for HCV RNA or a positive HCV antigen(s) test is reported within the same year. A confirmed acute case may be classified as a confirmed chronic case if a positive NAT for HCV RNA or a positive HCV antigen is reported one year or longer after acute case onset. A confirmed acute case may not be reported as a probable chronic case (i.e., HCV antibody positive, but with an unknown HCV RNA NAT or antigen status). States and territories may choose to track resolved hepatitis C cases in which spontaneous clearance of infection or sustained viral response to treatment are suspected to have occurred before national notification or are known to have occurred after national notification as a confirmed or probable case to CDC.

Case Classification

Probable

- A case that meets clinical criteria and has a positive anti-HCV antibody test, but has no reports of a positive HCV NAT or positive HCV antigen tests,

AND

- Does not have test conversion within 12 months or has no report of test conversion.

Confirmed

- A case that meets clinical criteria and has a positive hepatitis C virus detection test (HCV NAT

or HCV antigen),

OR

- A documented negative HCV antibody, HCV antigen or NAT laboratory test result followed within 12 months by a positive result of any of these tests (test conversion).

Summary Points

- Acute HCV infection is usually defined as an estimated duration of infection less than 6 months.
- Most patients with acute HCV infection do not have a symptomatic illness or have very mild non-specific symptoms that may include malaise, anorexia, and abdominal pain.
- In the less common situation when patients do develop symptomatic acute HCV infection, they most often present with jaundice, dark urine, nausea, abdominal pain, and malaise.
- The key laboratory studies utilized in the evaluation of possible acute hepatitis C are HCV RNA, HCV antibody, and ALT; the HCV antibody and the HCV RNA tests should be ordered simultaneously and as a separate order, not as an HCV antibody/HCV RNA reflex test.
- With acute HCV, patients usually first have detectable HCV RNA, followed by elevation in ALT, and followed last by development of HCV antibody.
- The gold standard for diagnosis is HCV antibody seroconversion combined with a positive HCV RNA test and elevated ALT.
- Acute HCV infection can rarely cause a life-threatening illness.
- The CDC 2016 case definition for acute hepatitis C includes clinical criteria, laboratory criteria, case classification as probable or confirmed, and criteria to distinguish a new case from an existing case.

Citations

1. Thomas DL, Seeff LB. Natural history of hepatitis C. Clin Liver Dis. 2005;9:383-98.
[\[PubMed Abstract\]](#) -
2. Hajarizadeh B, Grebely J, Dore GJ. Case definitions for acute hepatitis C virus infection: A systematic review. J Hepatol. 2012;57:1349-60.
[\[PubMed Abstract\]](#) -
3. Blackard JT, Shata MT, Shire NJ, Sherman KE. Acute hepatitis C virus infection: a chronic problem. Hepatology. 2008;47:321-31.
[\[PubMed Abstract\]](#) -
4. Kamal SM. Acute hepatitis C: a systematic review. Am J Gastroenterol. 2008;103:1283-97.
[\[PubMed Abstract\]](#) -
5. Grebely J, Page K, Sacks-Davis R, et al. The effects of female sex, viral genotype, and IL28B genotype on spontaneous clearance of acute hepatitis C virus infection. Hepatology. 2014;59:109-20.
[\[PubMed Abstract\]](#) -
6. Hofer H, Watkins-Riedel T, Janata O, et al. Spontaneous viral clearance in patients with acute hepatitis C can be predicted by repeated measurements of serum viral load. Hepatology. 2003;37:60-4.
[\[PubMed Abstract\]](#) -
7. Busch MP, Shafer KA. Acute-phase hepatitis C virus infection: implications for research, diagnosis, and treatment. Clin Infect Dis. 2005;40:959-61.
[\[PubMed Abstract\]](#) -
8. Maheshwari A, Ray S, Thuluvath PJ. Acute hepatitis C. Lancet. 2008;372(9635):321-32.
[\[PubMed Abstract\]](#) -
9. Grebely J, Matthews GV, Dore GJ. Treatment of acute HCV infection. Nat Rev Gastroenterol Hepatol. 2011;8:265-74.
[\[PubMed Abstract\]](#) -
10. Orland JR, Wright TL, Cooper S. Acute hepatitis C. Hepatology. 2001;33:321-7.
[\[PubMed Abstract\]](#) -
11. Marcellin P. Hepatitis C: the clinical spectrum of the disease. J Hepatol. 1999;31 Suppl 1:9-16.
[\[PubMed Abstract\]](#) -
12. Chu CM, Yeh CT, Liaw YF. Fulminant hepatic failure in acute hepatitis C: increased risk in chronic carriers of hepatitis B virus. Gut. 1999;45:613-7.
[\[PubMed Abstract\]](#) -
13. Hoofnagle JH, Carithers RL Jr, Shapiro C, Ascher N. Fulminant hepatic failure: summary of a workshop. Hepatology. 1995;21:240-52.
[\[PubMed Abstract\]](#) -
14. 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.
[\[PubMed Abstract\]](#) -

15. Chung RT. Acute hepatitis C virus infection. Clin Infect Dis. 2005;41 Suppl 1:S14-7.
[\[PubMed Abstract\]](#) -
16. Barrera JM, Bruguera M, Ercilla MG, et al. Persistent hepatitis C viremia after acute self-limiting posttransfusion hepatitis C. Hepatology. 1995;21:639-44.
[\[PubMed Abstract\]](#) -
17. Smith DJ, Jordan AE, Frank M, Hagan H. Spontaneous viral clearance of hepatitis C virus (HCV) infection among people who inject drugs (PWID) and HIV-positive men who have sex with men (HIV+ MSM): a systematic review and meta-analysis. BMC Infect Dis. 2016;16:471.
[\[PubMed Abstract\]](#) -
18. Newsum AM, Schinkel J, van de Laar TJW, van der Meer JTM, Prins M. Spontaneous Clearance of Hepatitis C Virus Infection Among Human Immunodeficiency Virus-Infected Men Who Have Sex With Men. Open Forum Infect Dis. 2017;4:ofx090.
[\[PubMed Abstract\]](#) -
19. Ragonnet R, Deuffic-Burban S, Boesecke C, et al. Estimating the Time to Diagnosis and the Chance of Spontaneous Clearance During Acute Hepatitis C in Human Immunodeficiency Virus-Infected Individuals. Open Forum Infect Dis. 2017;4:ofw235.
[\[PubMed Abstract\]](#) -
20. 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.
[\[PubMed Abstract\]](#) -
21. Cox AL, Netski DM, Mosbrugger T, et al. Prospective evaluation of community-acquired acute-phase hepatitis C virus infection. Clin Infect Dis. 2005;40:951-8.
[\[PubMed Abstract\]](#) -
22. Glynn SA, Wright DJ, Kleinman SH, et al. Dynamics of viremia in early hepatitis C virus infection. Transfusion. 2005;45:994-1002.
[\[PubMed Abstract\]](#) -
23. Busch MP, Murthy KK, Kleinman SH, et al. Infectivity in chimpanzees (Pan troglodytes) of plasma collected before HCV RNA detectability by FDA-licensed assays: implications for transfusion safety and HCV infection outcomes. Blood. 2012;119:6326-34.
[\[PubMed Abstract\]](#) -
24. Nübling CM, Unger G, Chudy M, Raia S, Löwer J. Sensitivity of HCV core antigen and HCV RNA detection in the early infection phase. Transfusion. 2002;42:1037-45.
[\[PubMed Abstract\]](#) -
25. Stramer SL, Glynn SA, Kleinman SH, et al. Detection of HIV-1 and HCV infections among antibody-negative blood donors by nucleic acid-amplification testing. N Engl J Med. 2004;351:760-8.
[\[PubMed Abstract\]](#) -
26. Laperche S, Nübling CM, Stramer SL, et al. Sensitivity of hepatitis C virus core antigen and antibody combination assays in a global panel of window period samples. Transfusion. 2015;55:2489-98.
[\[PubMed Abstract\]](#) -
27. Tuke PW, Grant PR, Waite J, Kitchen AD, Eglin RP, Tedder RS. Hepatitis C virus window-phase infections: closing the window on hepatitis C virus. Transfusion. 2008;48:594-600.

[\[PubMed Abstract\]](#) -

28. Hulleger SJ, GeurtsvanKessel CH, van der Eijk AA, Ramakers C, Rijnders BJA. HCV antigen instead of RNA testing to diagnose acute HCV in patients treated in the Dutch Acute HCV in HIV Study. *J Int AIDS Soc.* 2017;20:21621.
[\[PubMed Abstract\]](#) -
29. Ottiger C, Gygli N, Huber AR. Detection limit of architect hepatitis C core antigen assay in correlation with HCV RNA, and renewed confirmation algorithm for reactive anti-HCV samples. *J Clin Virol.* 2013;58:535-40.
[\[PubMed Abstract\]](#) -
30. Ross RS, Viazov S, Salloum S, Hilgard P, Gerken G, Roggendorf M. Analytical performance characteristics and clinical utility of a novel assay for total hepatitis C virus core antigen quantification. *J Clin Microbiol.* 2010;48:1161-8.
[\[PubMed Abstract\]](#) -
31. Laperche S, Le Marrec N, Girault A, et al. Simultaneous detection of hepatitis C virus (HCV) core antigen and anti-HCV antibodies improves the early detection of HCV infection. *J Clin Microbiol.* 2005;43:3877-83.
[\[PubMed Abstract\]](#) -
32. Freiman JM, Tran TM, Schumacher SG, et al. Hepatitis C Core Antigen Testing for Diagnosis of Hepatitis C Virus Infection: A Systematic Review and Meta-analysis. *Ann Intern Med.* 2016;165:345-55.
[\[PubMed Abstract\]](#) -
33. Khan H, Hill A, Main J, Brown A, Cooke G. Can Hepatitis C Virus Antigen Testing Replace Ribonucleic Acid Polymearse Chain Reaction Analysis for Detecting Hepatitis C Virus? A Systematic Review. *Open Forum Infect Dis.* 2017;4:ofw252.
[\[PubMed Abstract\]](#) -
34. Centers for Disease Control and Prevention (CDC). National Notifiable Diseases Surveillance System (NNDSS). Hepatitis C, Acute: 2016 Case Definition.
[\[CDC and NNDSS\]](#) -

References

- Aisyah DN, Shallcross L, Hully AJ, O'Brien A, Hayward A. Assessing hepatitis C spontaneous clearance and understanding associated factors-A systematic review and meta-analysis. *J Viral Hepat.* 2018;25:680-698.
[\[PubMed Abstract\]](#) -
- Araujo AC, Astrakhantseva IV, Fields HA, Kamili S. Distinguishing acute from chronic hepatitis C virus (HCV) infection based on antibody reactivities to specific HCV structural and nonstructural proteins. *J Clin Microbiol.* 2011;49:54-7.
[\[PubMed Abstract\]](#) -
- Bulteel N, Partha Sarathy P, Forrest E, et al. Factors associated with spontaneous clearance of chronic hepatitis C virus infection. *J Hepatol.* 2016;65:266-72.
[\[PubMed Abstract\]](#) -
- Deterding K, Wiegand J, Grüner N, et al. The German Hep-Net acute hepatitis C cohort: impact of viral and host factors on the initial presentation of acute hepatitis C virus infection. *Z Gastroenterol.* 2009;47:531-40.

[\[PubMed Abstract\]](#) -

- Dustin LB, Rice CM. Flying under the radar: the immunobiology of hepatitis C. *Annu Rev Immunol.* 2007;25:71-99.
[\[PubMed Abstract\]](#) -
- Dustin LB. Too low to measure, infectious nonetheless. *Blood.* 2012;119:6181-2.
[\[PubMed Abstract\]](#) -
- Hullege SJ, Arends JE, Rijnders BJ, et al. Current knowledge and future perspectives on acute hepatitis C infection. *Clin Microbiol Infect.* 2015;21:797.e9-797.e17.
[\[PubMed Abstract\]](#) -
- Lamoury FMJ, Soker A, Martinez D, et al. Hepatitis C virus core antigen: A simplified treatment monitoring tool, including for post-treatment relapse. *J Clin Virol.* 2017;92:32-38.
[\[PubMed Abstract\]](#) -
- Maheshwari A, Ray S, Thuluvath PJ. Acute hepatitis C. *Lancet.* 2008;372(9635):321-32.
[\[PubMed Abstract\]](#) -
- McGovern BH, Birch CE, Bowen MJ, Reyor LL, Nagami EH, Chung RT, Kim AY. Improving the diagnosis of acute hepatitis C virus infection with expanded viral load criteria. *Clin Infect Dis.* 2009;49:1051-60.
[\[PubMed Abstract\]](#) -
- Mondelli MU, Cerino A, Cividini A. Acute hepatitis C: diagnosis and management. *J Hepatol.* 2005;42 Suppl(1):S108-14.
[\[PubMed Abstract\]](#) -
- Recommendations for prevention and control of hepatitis C virus (HCV) infection and HCV-related chronic disease. Centers for Disease Control and Prevention. *MMWR Recomm Rep.* 1998;47(RR-19):1-39.
[\[CDC and MMWR\]](#) -
- 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.
[\[PubMed Abstract\]](#) -
- Wawrzynowicz-Syczewska M, Kubicka J, Lewandowski Z, Boroń-Kaczmarek A, Radkowski M. Natural history of acute symptomatic hepatitis type C. *Infection.* 2004;32:138-43.
[\[PubMed Abstract\]](#) -
- Wietzke-Braun P, Manhardt LB, Rosenberger A, Uy A, Ramadori G, Mihm S. Spontaneous elimination of hepatitis C virus infection: a retrospective study on demographic, clinical, and serological correlates. *World J Gastroenterol.* 2007;13:4224-9.
[\[PubMed Abstract\]](#) -
- Zibbell JE, Asher AK, Patel RC, et al. Increases in Acute Hepatitis C Virus Infection Related to a Growing Opioid Epidemic and Associated Injection Drug Use, United States, 2004 to 2014. *Am J Public Health.* 2018;108:175-181.
[\[PubMed Abstract\]](#) -
- Zibbell JE, Iqbal K, Patel RC, et al. Increases in hepatitis C virus infection related to injection drug use among persons aged ≤30 years - Kentucky, Tennessee, Virginia, and West Virginia,

2006-2012. MMWR Morb Mortal Wkly Rep. 2015;64:453-8.
[\[PubMed Abstract\]](#) -

Figures

Figure 1 Symptoms with Acute Hepatitis C Infection

This graph shows the clinical features among 51 patients with symptomatic acute hepatitis C infection.

Source: 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.

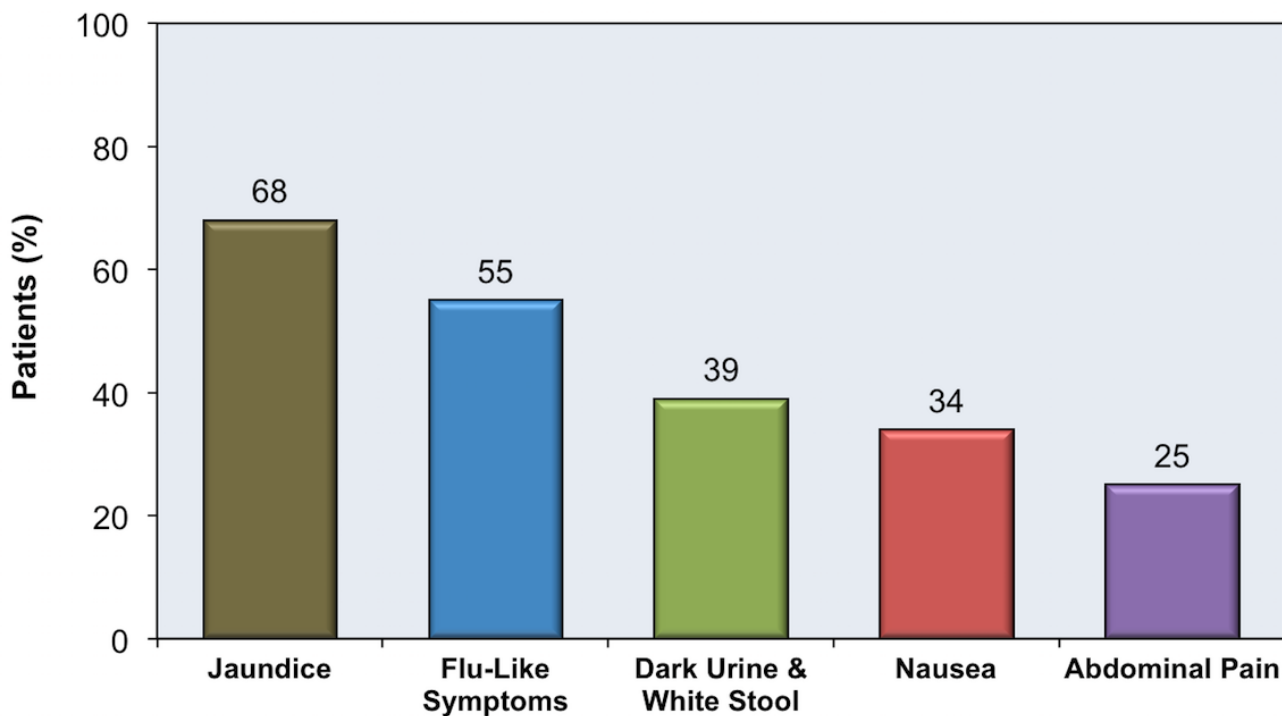


Figure 2 Potential Hepatitis C Exposures

Potential Sources of Exposure to Hepatitis C Virus
Recent injection drug use
Needle stick injury
Procedures involving potentially reused needles: tattooing, body-piercing, acupuncture
Exposure to re-used sharp objects or reused vials of injectable materials
Nosocomial exposure to contaminated equipment, or potential direct exposure to blood
Sexual practices that may induce bleeding: fisting and use of sharp objects during sex
Sexual contact with a known partner with HCV infection
Sexual contact with partner who has HIV infection
Sexual contact where either partner has an active sexually transmitted infection
Blood transfusion or unsafe therapeutic procedures during travel in a developing country

Figure 3 Laboratory Markers with Acute Hepatitis C Infection

Note the temporal appearance of laboratory markers typically observed with acute hepatitis C infection: HCV RNA levels first become detectable, followed by increases in ALT levels, and then detectable HCV antibody.

Source: Centers for Disease Control and Prevention (CDC).

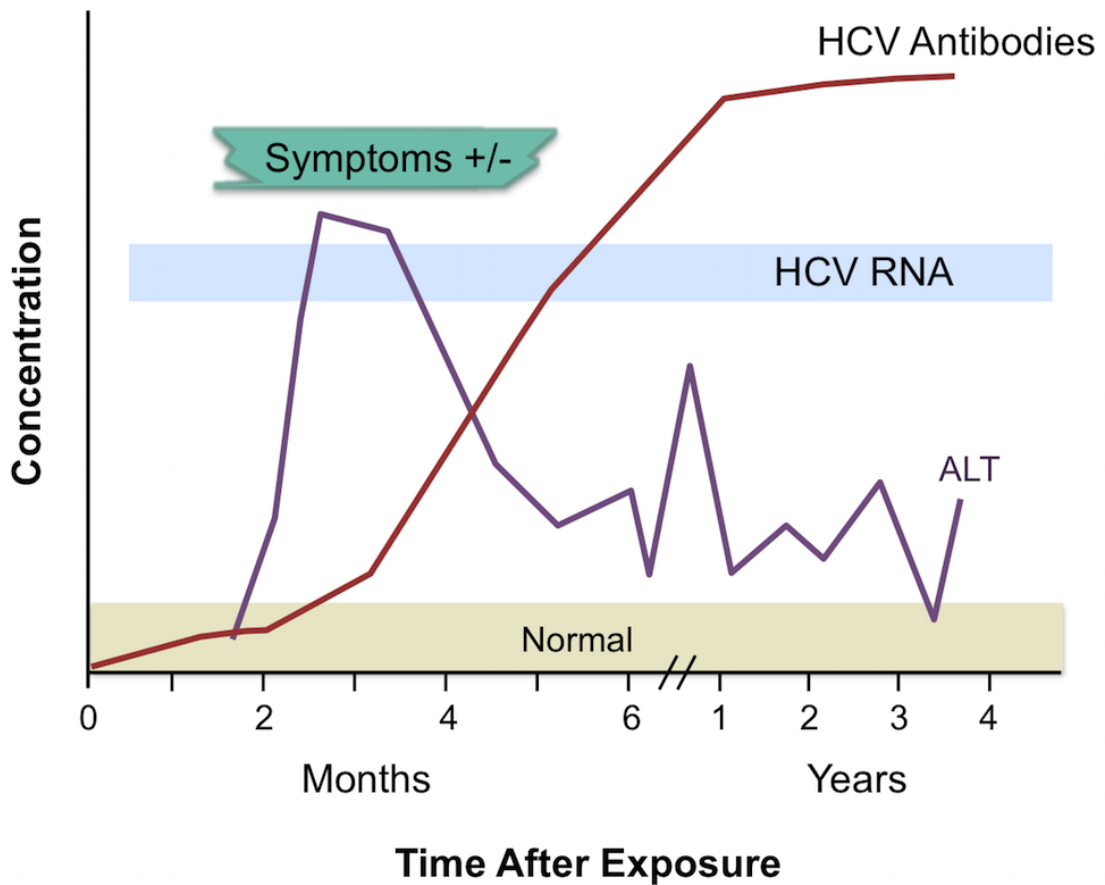


Figure 4 Acute Hepatitis C Infection: Eclipse Phase

The eclipse phase is the time between HCV infection and the appearance of detectable HCV RNA.

Source: Glynn SA, Wright DJ, Kleinman SH, et al. Dynamics of viremia in early hepatitis C virus infection. *Transfusion*. 2005;45:994-1002.

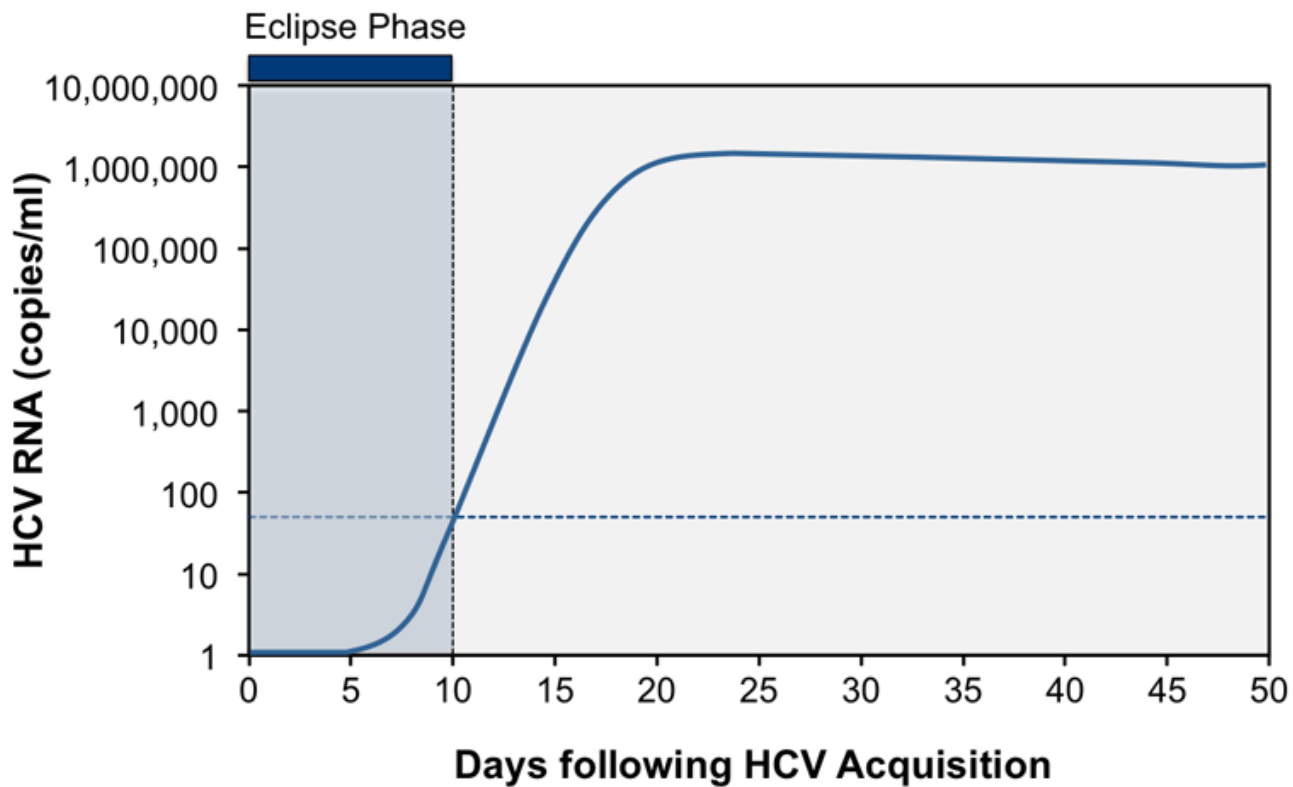


Figure 5 Acute Hepatitis C Infection: Viral Dynamics

This graph illustrates early phases of viral dynamics observed following acquisition of HCV: eclipse, ramp up, and plateau.

Source: Glynn SA, Wright DJ, Kleinman SH, et al. Dynamics of viremia in early hepatitis C virus infection. *Transfusion*. 2005;45:994-1002.

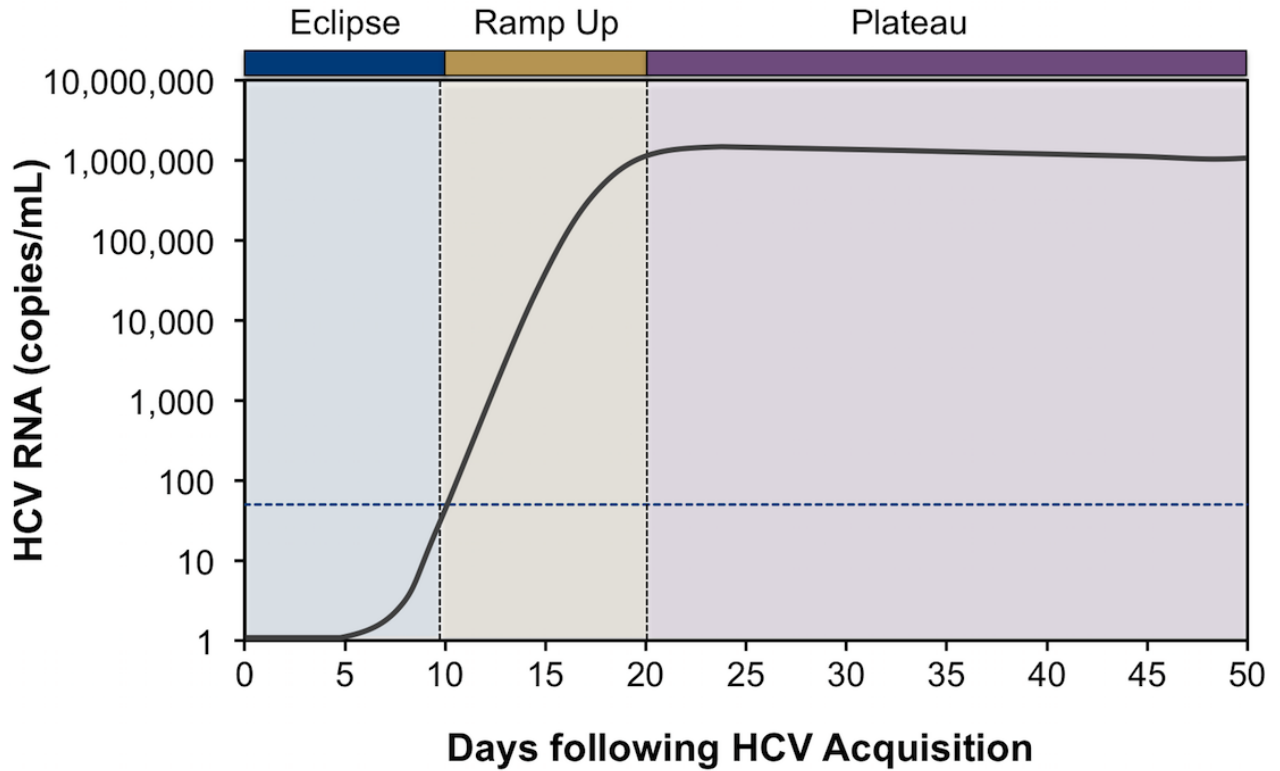


Figure 6 Acute Hepatitis C Infection: Serologic Window Period

The serologic window period is the time between HCV infection and clinically detectable HCV antibodies. The window period with HCV infection is typically 50 to 60 days.

