

MENTAL HEALTH AND HEPATITIS C

Julie Nelligan, PhD, David W. Indest, PsyD, and Peter Hauser, MD

SECTION

I

MENTAL HEALTH AND NEUROCOGNITIVE ISSUES ASSOCIATED WITH HCV INFECTION

Introduction

As with many long-term illnesses, *chronic hepatitis C* infection frequently has associated mental health issues. Because mental health affects every part of life, it is important to understand the many ways mind and body work together in people with the *hepatitis C virus (HCV)*. We know that mental health conditions such as *depression* may occur along with physical symptoms and difficulties in daily functioning, ability to follow treatment directions, and quality of life. Furthermore, until recently, people with mental illness were discouraged from seeking treatment for HCV for fear of making their mental health problems worse.

This chapter will discuss the link between mental health and HCV, how mental health can affect coping with HCV, and eligibility for HCV treatment. Finally, we will discuss whether HCV can cause problems with thinking and memory.

Mental Health and HCV

Many people with HCV have mental health concerns. A study of Veterans Affairs Medical Centers (VAMCs) in the Northwest United States found that 78% of HCV-infected veterans had at least one psychiatric or substance use disorder.¹ In addition, 54% had a history of both a psychiatric disorder and a substance use disorder.¹ Research at the VAMC in Portland, Oregon found that 93% of HCV-infected veterans said they had a history of at least one psychiatric disorder, and 73% had two or more disorders. *Depression* (81%) was the most common disorder, followed by posttraumatic stress disorder (62%), substance use disorders (58%), bipolar disorder (20%), and other psychotic disorders (17%).² Another study at the VAMC in Minneapolis, Minnesota found that 81% of patients being seen in the chronic hepatitis C clinic has at least one positive screening test for psychiatric problems. Among those with a positive screening test, only 38% had an established mental health provider.³

Studies in other settings (not limited veterans) support these findings and suggest that it is not uncommon for people with HCV to have mental health problems.⁴⁻⁷ Furthermore, it is well established that persons with serious mental health problems and/or substance abuse may be up to 10-times more likely to be infected with HCV than the general population.⁸

Depression

Depression is the most common mental health concern for people with HCV. Stress, loss, loneliness, and certain chemical imbalances in the brain can cause depression. Depression is also a side effect of the medication used to treat HCV (see *Chapter 22.2, Mental Health Issues in the Setting of Interferon-Based Therapy*). One recent study showed that 28% of HCV patients were depressed,⁹ compared with 2% to 9% of the general public. Another study found that 35% of HCV patients reported emotional distress. The percentage of patients with depression was similar to patients who reported other long-term medical illnesses such as *HIV* infection and arthritis, and higher than in people without medical illness.¹⁰ Finally, a recent study from the Portland VAMC found that 34% of veterans with HCV admitted to moderate to severe depressive symptoms.¹¹

Anxiety

Anxiety is another issue that many patients with HCV experience. One study found that 24% of HCV patients had a current anxiety disorder. It also suggested that many patients do not know they have an anxiety disorder until after they learn they have HCV.⁹ Most research about anxiety shows that it is at least as common as depression.^{10, 12-14} Despite that, it is common for anxiety disorders to be overlooked by doctors and other medical providers.⁹

POST-TRAUMATIC STRESS DISORDER (PTSD)

Among veterans, PTSD is particularly common. Early studies showed that between 21% and 43% of veterans with HCV had a diagnosis of PTSD.¹⁴⁻¹⁵ Another study at the Portland VAMC found that among 293 veterans with HCV, 62% screened positive for PTSD suggesting that they had either a diagnosis of PTSD or recent symptoms of PTSD.² Studies outside the VA healthcare network have found that PTSD is not nearly as common. For example, a study from 2005 that assessed 90 HCV patients from a university teaching hospital found 22 (24%) patients with an anxiety disorder, 25 (28%) patients with depression, but no patients with PTSD.⁹ Community-based studies suggest that PTSD affects about 8% of the general population.¹⁶ Taken together, these studies show that PTSD is common in veterans with HCV, but less common in nonveterans with HCV.

Treatment of Anxiety and Depression

Although patients with HCV have depression and anxiety at higher rates than the general population, medications that are used to treat these disorders are thought to be safe.¹⁷ This is fortunate because providers are often reluctant to give *interferon-based therapy* to patients who have mental health problems.¹⁸ The concern is that *interferon* therapy may make mental health problems worse.

Patients who are being considered for interferon-based therapy will often have a pretreatment psychiatric evaluation. If the evaluation suggests the patient has a mental health problem such as anxiety or depression, then a recommendation for treatment will likely be made that includes medication. Other treatment recommendations may include education about the treatment process (this includes treatment for HCV, as well as depression or anxiety) and regular follow-ups with adjustments as needed.¹⁷

Severe Mental Illness

Persons with a severe mental illness such as a psychotic disorder (schizophrenia) or bipolar disorder are infected with HCV at much higher rates than the general population. A multi-site study funded by the National Institute of Mental Health found that approximately 20% of adults who have a severe mental illness also have HCV.¹⁹ In contrast, only about 2% of the general population has HCV.

Unfortunately, most people with a severe mental illness do not know they have hepatitis C. Also, they commonly do not have access to or seek medical care as often as people without a severe mental illness. This means they are less likely to be tested for HCV.¹⁹ People with severe mental illness have higher rates of substance use disorders and other behaviors that put them at higher risk of getting HCV. The rate of substance use disorders in people with schizophrenia is almost 5 times higher than the rate in the general population.^{20, 21} In addition to injection drug use, crack cocaine is a common problem for this group. Smoking crack cocaine leads to other high-risk behaviors such as unsafe injection practices, unsafe sex, multiple sex partners, and trading sex for drugs. All of these behaviors have been linked with increased risk of HCV infection.²²

Substance Use Disorders

Many people who have HCV acquired the virus through activities related to injection drug use (IDU).²³ A recent population survey found that of people aged 20 to 59 years, a history of IDU at some point in their lives was the risk factor most strongly associated with HCV.²⁴ Sixty percent of all HCV infection within the United States is attributed to IDU. It is well-documented that injection drug users often have *clinical* depression.^{25, 26} One study recently found that

injection drug users who were depressed were more likely to share their “works”, increasing their risk of getting HCV.²⁷ Substance use disorders associated with HCV are not limited to IDU. *Alcohol*, cocaine, methamphetamine, marijuana, and other drugs are also risk factors even if not used intravenously. One study found that 58% of veterans with HCV said they had a history of substance abuse and 51% reported both a psychiatric and substance abuse history.² Not only does a history of substance abuse increase a person’s risk for acquiring HCV, but often individuals with substance use disorders also have mood or anxiety disorders.

Alcohol use in patients with hepatitis C is a dangerous combination. The more alcohol consumed, the greater the increased risk of cirrhosis.

Alcohol use in patients who have HCV is of particular concern. This is because the combination of heavy alcohol use along with the hepatitis C virus causes more damage to the liver than either alcohol or HCV alone causes.²⁸ One study found that drinking 75 grams of alcohol per day on average (a little more than a 6-pack of beer) increased the risk of liver *cirrhosis* in people with HCV 26-fold. The more alcohol consumed, the greater the risk of cirrhosis.²⁸ Heavy alcohol use is usually considered to be more than 4 standard drinks per day for men and more than 3 standard drinks per day for women. A standard drink is one 12-ounce beer, one 4-ounce glass of wine, or one 1.5-ounce shot of hard liquor.

Cognitive Problems

Another common issue that patients with HCV report is problems with thinking and memory, also called cognition. Research looking into the relationship between cognition and hepatitis C has only recently been conducted. There are several factors that may play a role in a link between HCV and cognitive problems. These factors include:

- direct effects of HCV on the brain
- indirect effects of HCV caused by severe liver damage and its consequences
- direct effects of substance use on the brain
- taking the medication that treats HCV (interferon-based therapy)

Direct Effects of HCV

Although HCV primarily affects the liver, it might also affect the brain. Patients with HCV often complain of depression, *fatigue*, and impairments in quality of life. In the hepatitis C community, these symptoms are sometimes called “brain fog.” These complaints are not associated with degree of liver disease.²⁹⁻³² Many patients also report cognitive changes. Sometimes these are from damage to the brain from substance abuse. But studies have found mild cognitive problems in patients with HCV that are not from substance use.^{30,33} However, one study found that greater liver damage was related to poorer performance on cognitive tests.³⁴ Overall, individuals with HCV appear to perform below expected levels on tests of attention, concentration, and other functions such as planning and controlling impulses.^{32,34} The reason why is not clear. It could be from liver disease, substance use, the hepatitis C virus, or some combination of these or other factors.

Indirect Effects of HCV

People with HCV are at increased risk of developing cirrhosis of the liver. About 20% of patients will develop cirrhosis within 20 years of being infected.³⁵ The liver damage caused by HCV may also cause cognitive problems. In advanced stages of liver disease, the liver cannot function properly. As a result, people often experience a condition called *hepatic encephalopathy* that affects their thinking and memory. Hepatic encephalopathy is thought to occur because substances that are toxic to brain cells (neurotoxins), such as *ammonia* and manganese, get into the brain. That makes brain cells not work as well as they normally do.

Symptoms of hepatic encephalopathy depend on the how much damage has been done to the liver. Initially patients have trouble with attention, concentration, coordination, changes in mood (depression or irritability), and mental slowness. As hepatic encephalopathy gets worse, the patient will experience *lethargy*, inappropriate behavior, slurred speech, and drowsiness. In the later more severe stages, patients become disoriented and confused. They may develop amnesia, become incoherent, and fall into a coma.

Direct Effects of Substance Use

It can be hard to tell whether substance abuse or HCV have led to cognitive problems. Many people that have HCV also have a history of substance abuse. That's because substance abuse is the most common way people get HCV. We know that substance abuse can cause permanent cognitive problems. Several studies have documented the negative effects of marijuana, cocaine, opiates, amphetamine, and alcohol use on cognitive function and the brain.³⁶ In HCV patients with a history of substance abuse, this makes it hard to tell whether substance abuse or the HCV infection caused their cognitive problems. It is likely that both adversely affect cognition and the brain.

Interferon-Based Therapy

Finally, the medication used to treat HCV, interferon, has many side effects. Depression is one of the most common side effects. People with depression often have cognitive problems. The cause of interferon-induced depression may be related to activation of the *immune system*, much like what happens when you have the flu. Common symptoms are irritability, fatigue, slowed movements, and changes in sleep and eating habits.³⁷ Another possible side effect from taking interferon is cognitive problems. One study³² found that 1/3 of study participants complained of concentration and memory problems during interferon treatment. As mentioned above, problems with concentration and memory can occur because of depression. However, this study found that cognitive complaints were not related to depression prior to or during interferon treatment.³⁸ Research into the typical cognitive problems people experience while on interferon is currently being conducted by several researchers. For now, little is known about the potential short- and long-term cognitive effects of interferon.

Coping with HCV

As might be expected, being diagnosed with HCV can seriously affect a person's mental health and quality of life. It is common to have trouble adjusting to a diagnosis of a long-term medical condition. But adjustment is more difficult for some patients than others. How would you know if you were having a hard time adjusting to life with HCV? How would you know if you were becoming depressed or anxious?

Common reactions to being diagnosed with a chronic infectious disease such as hepatitis C include:

- feeling emotionally numb and in shock
- becoming irritable or angry
- crying more than usual
- not spending time with friends and family
- worrying about infecting others
- feeling dirty
- feeling uncertain about your future
- feeling like no one understands
- feeling like life is not worth living

These feelings and reactions are normal, but if they are extreme or continue for more than 3 or 4 weeks, you may be experiencing the first signs of depression. It is important to be aware of changes in any of the following, which may signal depression:

- energy level
- sleeping more or less than normal
- eating more or less than normal
- not spending time with friends and family
- crying for no apparent reason
- feeling hopeless or worthless
- thinking about suicide
- no longer feeling like doing things you normally like doing
- feeling sad or down

A diagnosis of HCV can also cause people to worry more than normal. If you find yourself unable to control how much you are worrying, this may be a sign of an anxiety disorder. If this is the case, it is important to be aware of changes in any of the following, which may signal an anxiety problem:

- feeling restless or on edge
- becoming tired more quickly than normal
- having problems concentrating
- feeling more irritable than normal
- having headaches, cramps, stiffness, and muscle tension
- problems falling or staying asleep

Both of these issues (depression and anxiety) may become serious if they continue for more than a couple of weeks. They can also interfere with your ability to carry out normal activities of living. If this is the case, it is important to talk to someone who can help, such as your healthcare provider.

Summary

Many studies show that patients with chronic HCV infections also have mental health concerns. Concerns such as depression, anxiety, and problems with thinking and memory are common. However, it is unclear how much they are related to the presence of HCV or whether they are related to other factors.

Healthcare providers may not always notice when patients are depressed or anxious, so it may be up to you to tell your healthcare providers if you have any of the symptoms of these disorders (see lists above).

Substance abuse is a significant issue that should be discussed with your healthcare provider. Use of some substances (such as IV drugs) increases a person's risk of acquiring and transmitting HCV. Use of alcohol damages the liver and if a person has HCV, damage to the liver may be increased by continuing to drink alcohol.

Fortunately, patients with depression and anxiety and HCV benefit from treatment for these disorders.³⁹ Treatment can stabilize mental health conditions, support *abstinence* from drugs and alcohol, and allow for treatment of HCV.

References

1. Loftis JM and Hauser P. Hepatitis C in patients with psychiatric disease and substance abuse: Screening strategies and comanagement models of care. *Current Hepatitis Reports*. 2003;2:93-100.
2. Fireman M, Indest DW, Blackwell A, et al. Addressing tri-morbidity (Hepatitis C Psychiatric and Substance Use Disorders): the importance of routine mental health screening as a component of a co-management model of care. *Clinical Infectious Diseases*. 2005;40(Suppl 5):S286-91.
3. Knott A, Dieperink E, Willenbring ML, et al. Integrated psychiatric/medical care in a chronic hepatitis C clinic: effect on antiviral treatment evaluation and outcomes. *Am J Gastroenterol*. 2006;101(10):2254-62.
4. Carta MG, Hardoy MC, Garofalo A, et al. Association of chronic hepatitis C with major depressive disorders: irrespective of interferon-alpha therapy. *Clin Pract Epidemiol Ment Health*. 2007;3:22.
5. Golden J, O'Dwyer AM, Conroy RM. Depression and anxiety in patients with hepatitis C: prevalence, detection rates and risk factors. *Gen Hosp Psychiatry*. 2005;27(6):431-438.
6. Cruz Neves A, Dickens C, Xavier M. [Comorbidity between hepatitis C and depression. Epidemiological and etiopathogenic aspects. Article in Portuguese.] *Acta Med Port*. 2006;19(1):21-28.
7. Butt AA, Evans R, Skanderson M, Shakil AO. Comorbid medical and psychiatric conditions and substance abuse in HCV infected persons on dialysis. *J Hepatol*. 2006;44(5):864-886.
8. Osher FC, Goldberg RW, McNary SW, et al. Substance Abuse and the Transmission of Hepatitis C Among Persons With Severe Mental Illness. *Psychiatric Services*. 2003;54:842-847.
9. Golden J, O'Dwyer AM, and Conroy RM. Depression and anxiety in patients with hepatitis C: prevalence, detection rates and risk factors. *Gen Hosp Psychiatry*. 2005;27(6):431-8.
10. Fontana RJ, Hussain KB, Schwartz SM, et al. Emotional distress in chronic hepatitis C patients not receiving antiviral therapy. *J Hepatol*. 2002;36(3):401-7.
11. Nelligan J, Loftis JM, Matthews AM, et al. Depression co-morbidity and antidepressant use in veterans with chronic hepatitis C. Submitted.
12. Loftis JM, Matthews AM, and Hauser P. Psychiatric and substance use disorders in individuals with hepatitis C: epidemiology and management. *Drugs*. 2006;66(2):155-74.
13. Yovtcheva SP, Rifai MA, Moles JK, et al. Psychiatric comorbidity among hepatitis C-positive patients. *Psychosomatics*. 2001;42(5):411-5.
14. El-Serag HB, Kunik M, Richardson P, et al. Psychiatric disorders among veterans with hepatitis C infection. *Gastroenterology*. 2002;123(2):476-82.
15. Lehman CL and Cheung RC. Depression, anxiety, post-traumatic stress, and alcohol-related problems among veterans with chronic hepatitis C. *Am J Gastroenterol*. 2002;97(10):2640-6.
16. American Psychiatric Association. Diagnostic and statistical manual of mental disorders. Fourth Edition, Text Revision ed. 2000, Washington, DC: American Psychiatric Association.
17. Rifai MA, Indest D, Loftis J, et al. Psychiatric management of the hepatitis C patient. *Curr Treat Options Gastroenterol*. 2006;9(6):508-19.
18. National Institutes of Health. National Institutes of Health Consensus Development Conference Statement: Management of Hepatitis C. *Hepatology*. 2002. November: p. S3-S20.
19. Rosenberg SD, Goodman LA, Osher FC, et al. Prevalence of HIV, hepatitis B, and hepatitis C in people with severe mental illness. *Am J Public Health*. 2001;91(1):31-7.
20. Mueser K, Bennett M, and Kushner M. Epidemiology of substance use disorders among persons with chronic mental illnesses. In *Double Jeopardy: Chronic Mental Illness and Substance Use Disorder*. A Lehman and L Dixon, Editors. Chur, Switzerland: Harwood Academic; 1995.
21. Regier DA, Farmer ME, Rae DS, et al. Comorbidity of mental disorders with alcohol and other drug abuse. Results from the Epidemiologic Catchment Area (ECA) Study. *JAMA*. 1990;264(19):2511-8.
22. Osher FC, Goldberg RW, McNary SW, et al. Substance abuse and the transmission of hepatitis C among persons with severe mental illness. *Psychiatr Serv*. 2003;54(6):842-7.
23. Alter MJ. Epidemiology of hepatitis C. *Hepatology*. 1997;26(3 Suppl 1):62S-65S.
24. Armstrong GL, Wasley A, Simard EP, et al. The prevalence of hepatitis C virus infection in the United States, 1999 through 2002. *Ann Intern Med*. 2006;144(10):705-14.
25. Golub ET, Latka M, Hagan H, et al. Screening for depressive symptoms among HCV-infected injection drug users: examination of the utility of the CES-D and the Beck Depression Inventory. *J Urban Health*. 2004;81(2):278-90.
26. Sulkowski, M.S. and Thomas, D.L., Epidemiology and natural history of hepatitis C virus infection in injection drug users: implications for treatment. *Clin Infect Dis*. 2005;40 Suppl 5:S263-9.
27. Wild TC, el-Guebaly N, Fischer B, et al. Comorbid depression among untreated illicit opiate users: results from a multisite Canadian study. *Can J Psychiatry*. 2005;50(9):512-8.
28. Corrao G and Arico S. Independent and combined action of hepatitis C virus infection and alcohol consumption on the risk of symptomatic liver cirrhosis. *Hepatology*. 1998;27(4):914-9.
29. Dwight MM, Kowdley KV, Russo JE, et al. Depression, fatigue, and functional disability in patients with chronic hepatitis C. *J Psychosom Res*, 2000;49(5):311-7.
30. Forton DM, Taylor-Robinson SD, and Thomas HC. Cerebral dysfunction in chronic hepatitis C infection. *J Viral Hepat*. 2003;10(2):81-6.
31. Kramer L, Hofer H, Bauer E, et al. Relative impact of fatigue and subclinical cognitive brain dysfunction on health-related quality of life in chronic hepatitis C infection. *AIDS*. 2005;19 Suppl 3:S85-92.
32. Weissenborn K, Krause J, Bokemeyer M, et al. Hepatitis C virus infection affects the brain-evidence from psychometric studies and magnetic resonance spectroscopy. *J Hepatol*. 2004;41(5):845-51.
33. Forton DM, Thomas HC, Murphy CA, et al. Hepatitis C and cognitive impairment in a cohort of patients with mild liver disease. *Hepatology*. 2002;35(2):433-9.

34. Hilsabeck RC, Hassanein TI, Ziegler EA, et al. Effect of interferon-alpha on cognitive functioning in patients with chronic hepatitis C. *J Int Neuropsychol Soc.* 2005;11(1):16-22.
35. Van der Poel CL, Cuypers HT, and Reesink HW. Hepatitis C virus six years on. *Lancet.* 1994;344(8935):1475-9.
36. Verdejo-Garcia A, Rivas-Perez C, Lopez-Torrecillas F, et al. Differential impact of severity of drug use on frontal behavioral symptoms. *Addict Behav.* 2006;31(8):1373-82.
37. Raison CL, Demetrashvili M, Capuron L, et al. Neuropsychiatric adverse effects of interferon-alpha: recognition and management. *CNS Drugs.* 2005;19(2):105-23.
38. Reichenberg A, Gorman JM, and Dieterich DT. Interferon-induced depression and cognitive impairment in hepatitis C virus patients: a 72 week prospective study. *AIDS.* 2005;19 Suppl 3:S174-8.
39. Lang JP, Meyer N, and Doffoel M. [Benefits of a preventive psychiatric accompaniment in patients Hepatitis C Virus seropositive (HCV): prospective study concerning 39 patients]. *Encephale.* 2003;29(4 Pt 1):362-5.

