Expanding HCV Care Beyond The Specialty Setting: A Series for Primary Care Clinicians



The Risk of Unidentified HCV

An estimated 3.5 million people in the United States (US) are living with chronic hepatitis C virus (HCV) infection. Notably, chronic HCV is disproportionately prevalent among individuals born between 1945 and 1965; indeed, approximately two-thirds of those living with HCV are members of this birth cohort (also known as the "baby boomer" generation). Among these individuals, the presence of HCV is independently associated with increased mortality and resource utilization. Studies have repeatedly shown that 43% to 85% of this population are unaware of their HCV infection status and that 35% have advanced fibrosis at the time of diagnosis. Furthermore, despite the availability of therapies that can cure HCV and conceivably lead to the elimination of the virus, the incidence of HCV infection is increasing in the US. New infections are nearly entirely related to the opioid crises; indeed, between 2004 and 2014, there was a 133% increase in acute HCV infections and a 93% increase in admissions for substance use disorder related to the use of injection opioids.

Far too often, HCV infections are not identified until after notable disease progression has occurred. In fact, the suboptimal HCV diagnosis rate is an unrecognized risk in health systems across the US. A review of more than 2 million patient records from 4 health systems found that only approximately onefifth (16,662 of an estimated 80,000 cases) of HCVinfected persons who died of their disease had a documented diagnosis of HCV. HCV-related mortality has steadily increased in the US; by 2007, deaths due to HCV outnumbered those due to human immunodeficiency virus (HIV), and in 2011, the HCV mortality rate surpassed that of 60 other reportable infectious diseases combined. Beyond an increased mortality, unrecognized HCV confers substantial other risks for healthcare systems and the health of the patients they serve. Failure to

identify HCV infection early in the course of the disease allows for the potential development of numerous downstream sequelae related to advanced liver disease, including liver failure requiring transplant and the development of hepatocellular carcinoma. Indeed, HCV is the dominant risk factor for hepatocellular cancer in the US. The realistic case described below illustrates one such scenario.

Case Description

Sam, a 58-year-old male veteran, presented to his new primary care physician (PCP) with several complaints: fever, nasal congestion, coughing, muscle and joint pains, abdominal tenderness, weakness, nausea, and loss of appetite. The physician was new to the practice, taking over for the patient's previous family doctor, Dr. White, when he retired.

The PCP reviewed the patient's medical records and conducted a physical examination. He found that palpating Sam's abdomen over the area of his liver caused him to wince.

The medical record showed that Dr. White had been prescribing oxycodone to treat complaints of chronic back pain, secondary to injuries sustained while serving overseas during 2 consecutive deployments. However, the now-retired family physician had weaned the patient off opioids over the past year, after Sam complained that his pain levels were not improving, although the painkillers had been titrated to a relatively high level. Instead, the doctor had referred the veteran for physical therapy and behavioral therapy to address symptoms of posttraumatic stress disorder. Dr. White had also prescribed lidocaine patches and combination acetaminophen-ibuprofen pills to use as needed for pain.

When the PCP asked Sam how often he used alcohol or drugs, he said he drank "as much as the next guy" but denied using recreational drugs. However, the results of an immunoassay urine test conducted in the office were positive for opioid use. Sam again denied using street drugs but admitted he had taken a couple of "leftover" prescription opioid pills earlier that day because his back pain was severe. A check of the Prescription Drug Monitoring Program (PDMP) showed that the patient had not filled any controlled substance prescriptions since Dr. White had weaned him off oxycodone several months before.

The PCP diagnosed Sam with the flu, told him to get some rest, and advised him to call the office if he didn't feel better in a week. Before leaving, the patient asked the PCP for an oxycodone prescription, saying his back still hurt unbearably and he wanted to give the drug another try. The PCP declined, saying oxycodone has been shown to be ineffective for such pain and carried serious risks, especially because the patient admitted to drinking alcohol on a somewhat regular basis.

The patient didn't return to the PCP, but nearly 1 year later, his wife found him in an unresponsive state. Responding paramedics revived him with naloxone and rushed him to the emergency department (ED). The ED physician, noting his yellowish eyes and skin, determined that the patient must have been experiencing tiredness, nausea, vomiting, and stomachache "for a long time." An HCV antibody test confirmed HCV infection. Subsequent tests showed he had decompensated cirrhosis due to HCV infection.

Eventually, Sam admitted that he had turned to heroin after his previous doctor weaned him off opioids. The patient and his wife, who was later diagnosed with HCV she likely contracted from her husband, sued the practice for failing to diagnose his infection at a stage when it could have been effectively treated and before his wife was infected.

Case Discussion and Lessons for the Future

HCV is the most common chronic viral infection among Americans today. Of an estimated 4 million people exposed to the virus, chronic HCV infection develops in 60% to 85% of those infected; if left untreated, these individuals can potentially infect others. Roughly 10% to 20% of individuals with HCV develop cirrhosis of the liver, with a 1% to 5% annual risk of liver cancer. In more than one-half of cases associated with illicit drug use, infection occurs within 6 to 12 months of the initial injection.

Chronic HCV infection has been dubbed the "silent killer" due to it being largely asymptomatic until progression results in noticeable, often irreversible health effects. Fortunately, the risk of hepatocellular carcinoma, need for liver transplant, and premature death due to HCV are now preventable scenarios with the advent of direct-acting antiviral therapies, which offer nearly all patients the opportunity for a cure. To cure patients, reduce transmission, and prevent the downstream morbidity and mortality associated with HCV, however, clinicians must appropriately screen, diagnose, and treat infected persons. Primary care clinicians in particular are well-poised to reverse the tide of rising infections and the downstream complications by identifying individuals with risk factors, including those in the highest-risk birth cohort (born between 1945 and 1965).

Physicians whose patients complain of fever, muscle and joint pains, abdominal tenderness, weakness, nausea, loss of appetite, or some combination of these symptoms should include HCV in the list of possible causes and begin or facilitate treatment for patients with confirmed infection. Studies show that antiviral treatment has a very high cure rate, including among those who use injection drugs. In addition, patients with confirmed HCV should be advised not to drink alcohol and counseled on the appropriate use of acetaminophen (no more than 3 g per day).

Suggested Readings

- Smith BD, Morgan RL, Beckett GA, et al; Centers for Disease Control and Prevention. Recommendations for the identification of chronic hepatitis C virus infection among persons born during 1945-1965. *MMWR Recomm Rep.* 2012;61(RR-4):1-32.
- Sayiner M, Wymer M, Golabi P, Ford J, Srishord I, Younossi ZM. Presence of hepatitis C (HCV) infection in baby boomers with Medicare is independently associated with mortality and resource utilisation. *Aliment Pharmacol Ther*. 2016;43(10):1060-1068.
- Denniston MM, Jiles RB, Drobeniuc J, et al. Chronic hepatitis C virus infection in the United States, National Health and Nutrition Examination Survey 2003 to 2010. Ann Intern Med. 2014;160(5):293-300.
- Spradling PR, Rupp L, Moorman AC, et al; Chronic Hepatitis Cohort Study Investigators. Hepatitis B and C virus infection among 1.2 million persons with access to care: factors associated with testing and infection prevalence. *Clin Infect Dis*. 2012;55(8):1047-1055.
- Younossi ZM, Stepanova M, Afendy M, Lam BP, Mishra A. Knowledge about infection is the only predictor of treatment in patients with chronic hepatitis C. J Viral Hepat. 2013;20(8):550-555.
- Galbraith JW, Franco RA, Donnelly JP, et al. Unrecognized chronic hepatitis C virus infection among baby boomers in the emergency department. *Hepatology*. 2015;61(3):776-782.
- McGarry LJ, Pawar VS, Panchmatia HR, et al. Economic model of a birth cohort screening program for hepatitis C virus. *Hepatology*. 2012;55(5):1344-1355.
- 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(2):175-181.

- 9. Mahajan R, Xing J, Liu SJ, et al; Chronic Hepatitis Cohort Study (CHeCS) Investigators. Mortality among persons in care with hepatitis C virus infection: the Chronic Hepatitis Cohort Study (CHeCS), 2006-2010. *Clin Infect Dis*. 2014;58(8):1055-1061.
- Ly KN, Hughes EM, Jiles RB, Holmberg SD. Rising mortality associated with hepatitis C virus in the United States, 2003-2013. *Clin Infect Dis*. 2016;62(10):1287-1288.
- Ly KN, Xing J, Klevens RM, Jiles RB, Ward JW, Holmberg SD. The increasing burden of mortality from viral hepatitis in the United States between 1999 and 2007. *Ann Intern Med*. 2012;156(4):271-278.
- 12. Hellard M, Sacks-Davis R, Gold J. Hepatitis C treatment for injection drug users: a review of the available evidence. *Clin Infect Dis.* 2009;49(4):561-573.

Developed in Collaboration

