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Caring for patients with chronic hepatitis C infection

BY AMANDA CHANEY, DNP, APRN, FNP-BC, FAANP

Abstract: Hepatitis C virus (HCV) infection is the most common chronic bloodborne infection in the US. This article discusses the pathophysiology of HCV infection, new treatment options, and nursing care and patient teaching for patients with chronic HCV infection.

Keywords: acute hepatitis, chronic hepatitis, cirrhosis, direct-acting antivirals, hepatitis, hepatitis C infection, liver disease, liver fibrosis, METAVIR scale

AFFECTING OVER 170 MILLION people worldwide, chronic hepatitis C virus (HCV) infection is a leading cause of end-stage liver disease. HCV can cause both acute and chronic hepatitis. The acute process is self-limited, rarely causes hepatic failure, and usually leads to chronic infection. Chronic HCV infection often follows a progressive course over many years and can ultimately result in cirrhosis, hepatocellular carcinoma, and the need for liver transplantation.[1]

HCV is the most common chronic bloodborne infection in the US. The CDC estimates that 41,200 cases of acute HCV occurred in 2016 and that about 2.4 million people in the US are living with HCV infection.[2]

Historically, treatments for HCV have been associated with severe adverse reactions, including pancytopenia and renal failure, and were often unsuccessful, with only half of patients achieving virologic cure or sustained virologic response. In 2011, the development of direct-acting antivirals (DAAs) dramatically improved treatment options for patients with HCV infection. Besides causing minimal adverse reactions, these newer medications have been shown to reduce hepatic fibrosis and are associated with a reduction in the risk of hepatocellular carcinoma.[3]

This article discusses the pathophysiology of HCV infection, new treatment options, and nursing care and patient teaching for patients with chronic HCV infection.

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About HCV

Discovered in 1989, HCV is a small, enveloped, single-stranded RNA virus belonging to the Flaviviridae family. Because it is genetically unstable, it has multiple genotypes and

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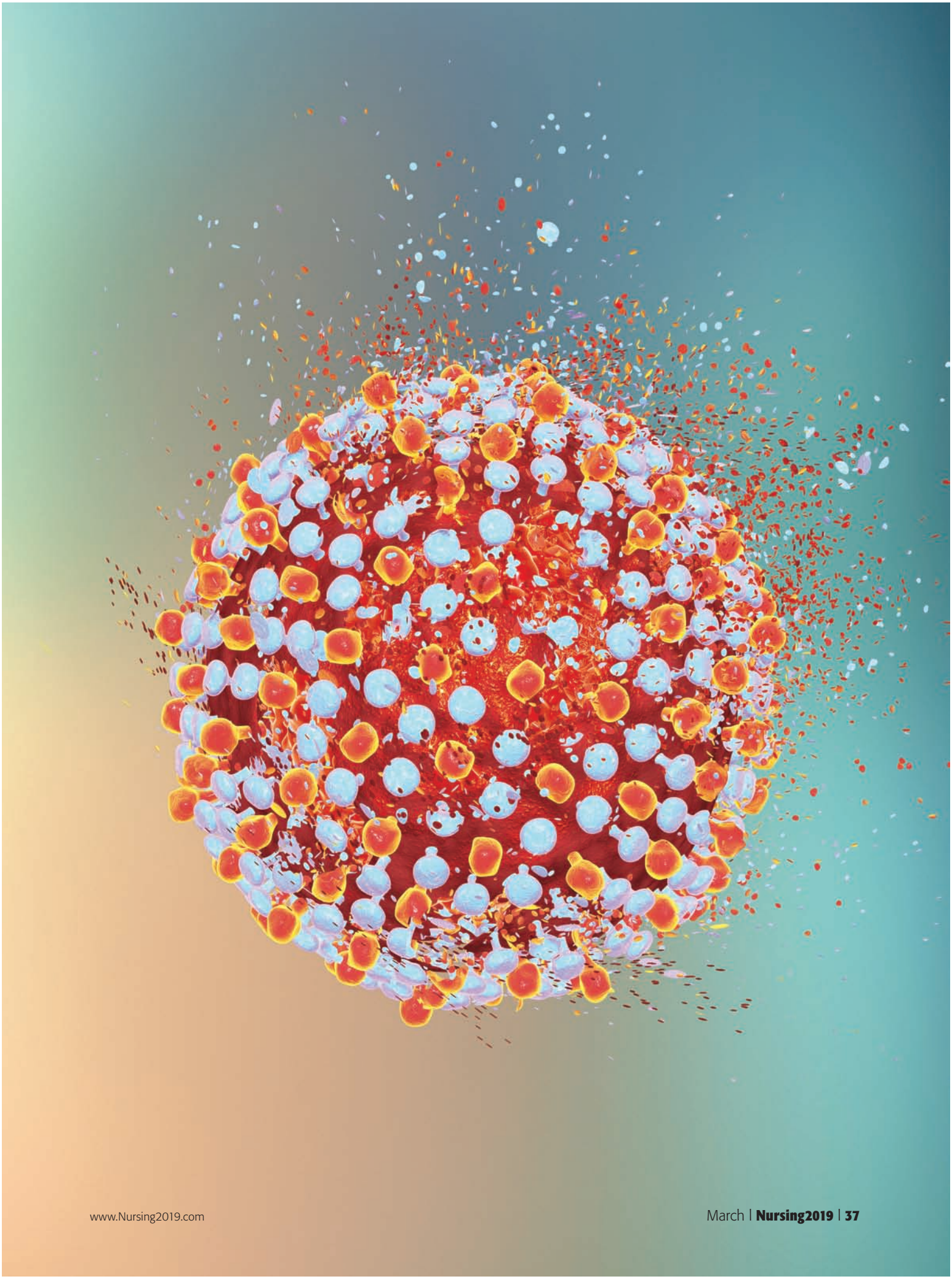
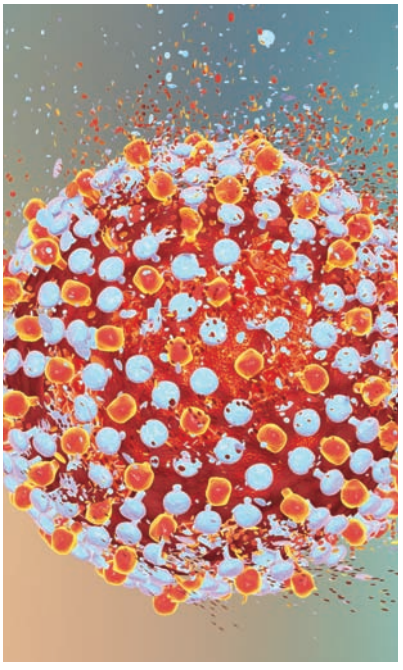


subtypes: Six major genotypes of HCV have been defined, with more than 50 subtypes. The wide diversity of genotypes helps HCV resist the body's immune system and antiviral medications, explaining why creating an effective preventive vaccine is difficult.[4,5]

In the US, the most common HCV genotype is genotype 1, which infects over 80% of patients with HCV in the US and 46% worldwide.[6] However, patients can be infected with more than one genotype, and even after treatment, can become reinfected with a different genotype. To treat HCV, establishing the genotype is essential, because medications are effective only for specific genotypes.[7]

Who is at risk?

Exposure to HCV-infected blood is the primary mode of HCV transmission. In the US, injection drug use is blamed for approximately 60% of acute HCV infections. Sexual transmission is possible but considered inefficient except between men who have unprotected sex with men. HCV is not transmitted by kissing or hugging, breast milk, food, or water.[2,7,8] People at risk for HCV infection include healthcare workers; children born to HCV-positive mothers; people who have used recreational injection or intranasal drugs; patients who have had hemodialysis or who received a blood transfusion or organ or tissue transplant before 1992; and people who have been incarcerated.[7,8]



In the US, genotype 1, which infects over 80% of patients with HCV, is the most common HCV genotype.

Extrahepatic complications of HCV infection[35]

Chronic HCV infection has been associated with development of immune-related and inflammatory-related extrahepatic manifestations. Examples of extrahepatic manifestations include:

- arthralgia/myalgia
- autoantibody production
- cardiovascular disorders, such as ischemic heart disease
- cognitive impairment
- cryoglobulinemic vasculitis
- depression
- fatigue
- glomerulonephritis
- immune thrombocytopenia
- polyarthritis/fibromyalgia
- renal insufficiency
- type 2 diabetes/insulin resistance.

In the US, people born between 1945 and 1965 in the US (baby boomers) account for most cases of HCV. Because of this, the CDC and the United States Preventive Services Task Force now recommend a one-time screening test for HCV (antibody HCV) for all patients who were born between 1945 and 1965. Those who meet high-risk criteria should receive additional screening.[2,9]

How HCV infection progresses

When HCV attacks the liver, it targets hepatocytes and, possibly, B lymphocytes.[10] In most infected people, infection leads to variable degrees of hepatic inflammation and fibrosis. HCV infection induces immunoregulatory and proinflammatory pathways that may contribute to liver fibrosis.[11]

The incubation period for HCV ranges from 2 weeks to 6 months.[12] Most patients with HCV infection are asymptomatic and it is rare for a patient to be diagnosed with HCV in the acute phase.[13] However, 20% to 30% of those newly infected with HCV experience fatigue, abdominal pain, anorexia, or jaundice.[2]

In many patients, extrahepatic manifestations of HCV involving the joints, muscle, and skin are among the earliest signs and symptoms (see *Extrahepatic complications of HCV infection*). Signs and symptoms of advanced or decompensated liver disease, which are related to hepatic dysfunction and portal hypertension, include pruritus, jaundice, hepatic encephalopathy, edema, ascites, and hematemesis or melena.[7,10]

Testing for HCV

Diagnostic tests for HCV can be divided into two broad categories: serologic assays that detect antibodies to hepatitis C, and molecular assays that detect HCV RNA. HCV antibodies can be detected in the

blood 2 to 3 weeks after exposure.[14] An estimated 15% to 45% of patients with HCV infection clear the virus without treatment after 6 months.[12]

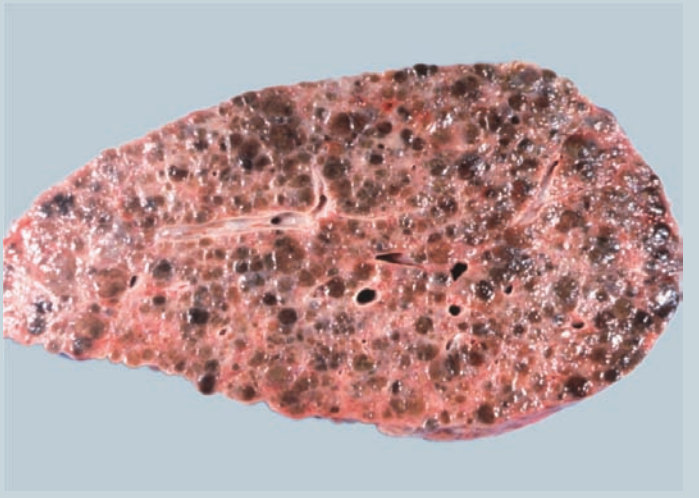
If an antibody test is negative, HCV infection is unlikely in most patients and further testing may not be indicated. However, HCV antibodies may not be detectable in some patients with HCV infection; for example, those who are severely immunocompromised and those on hemodialysis. For these patients, HCV RNA testing is indicated to rule out infection.[14]

After HCV infection has been confirmed, providers should proceed with further testing to determine the extent of liver damage because the degree of liver damage guides treatment.[7,15] For example, certain medications are not recommended for advanced disease, such as decompensated cirrhosis.[7]

Additional testing may include a metabolic panel, international normalized ratio (INR), liver function tests, complete blood cell count, liver biopsy, HCV genotype, viral resistance testing, HIV antibody and antigen, and HBV surface antigen. Patients may be at risk for HBV or HIV coinfection due to high-risk behaviors.[7,16]

Common lab abnormalities indicating cirrhosis include elevated serum bilirubin, abnormal aminotransferases, elevated alkaline phosphatase, a prolonged prothrombin time/elevated INR, hypoalbuminemia, and thrombocytopenia. However, many patients with chronic HCV have normal liver function test results because the liver has compensated over the course of a long-term infection.[7,16]

A closer look at cirrhosis



Note the nodular pattern in this gross liver section. The liver is divided into nodules by a web of fibrous (scar) tissue. Dark discoloration of some nodules is caused by the accumulation of bile pigment in lobules.

Source: McConnell TH. *The Nature of Disease: Pathology for the Health Professions*. 2nd ed. Baltimore, MD: Wolters Kluwer Health; 2013.

Stages of fibrosis

Liver biopsy is the gold standard for determining the severity of liver disease, but it carries the risk of complications, such as infection and bleeding.[14,15] Fibrosis stage can be assessed indirectly through history, physical examination, lab tests, and other noninvasive studies, such as ultrasound-based transient elastography.[17]

This noninvasive imaging study is used to measure liver stiffness in units measured as kilopascals (kPa). Normal is 5.0 kPa. Higher degrees of liver stiffness are associated with higher degrees of fibrosis.[17,18]

Several scoring systems are available to stage chronic liver disease. The five-point METAVIR scale grades fibrosis as follows:

- F0: no fibrosis
- F1: portal fibrosis without septa (fibrous scar tissue)
- F2: few septa
- F3: numerous septa without cirrhosis
- F4: cirrhosis.[19,20]

On transient elastography, more than 7 kPa is considered significant fibrosis (stages F2 to F4), and more than 11 kPa indicates cirrhosis (stage F4).[17]

Transient elastography is becoming more common in clinical settings and insurance companies may ask for the kPa measurement when the provider submits prior authorization paperwork for HCV treatment.[15,18] Due to the high cost of the newer DAA medications, many insurance companies require a degree of liver stiffness and fibrosis grade before approving these medications for HCV treatment. The study has limitations for patients with ascites or obesity, and the high cost limits availability in some rural settings.[7,15]

Treatment options

According to guidelines issued by the American Association for the Study of Liver Disease (AASLD) and

Bonus content

Visit www.nursing2019.com to see an animation illustrating normal liver anatomy and function, as well as the pathophysiology of cirrhosis.

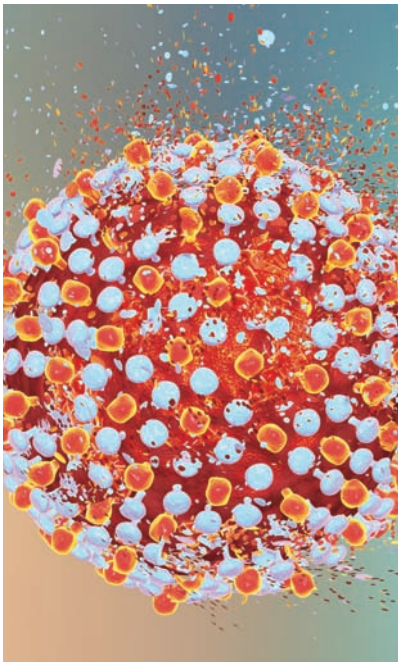
the Infectious Diseases Society of America (IDSA), patients with HCV infection who are at considerable risk for morbidity and mortality if untreated should be given the highest priority.[7] This population includes patients with substantial fibrosis, HIV coinfection, coexisting liver disease, or severe extrahepatic manifestations of HCV infection, including diabetes. Patients with detectable HCV viral levels over a 6-month period should be considered for treatment.[1,7]

Historically, HCV was treated with interferon-based therapy. Once the only treatment option, it provided only a 50% to 60% cure rate if combined with ribavirin, and the treatment regimen caused many serious adverse reactions, including hematologic toxicity and neuropsychiatric symptoms.[21,22]

In 2011, the protease inhibitors (PIs) boceprevir and telaprevir were introduced, resulting in improved treatment rates (sustained virologic response rates as high as 75%), but some treatment regimens still required ribavirin and interferon.[23] The first-generation PIs, telaprevir and boceprevir, were the first DAAs available for the treatment of chronic HCV infection.[24]

Late in 2013, the second-generation DAAs, simeprevir and sofosbuvir, became available.[21] Taken once daily, simeprevir is indicated to treat chronic HCV infection in combination with pegylated interferon and ribavirin in patients with HCV genotype 1 with compensated liver disease, including cirrhosis.[25] In October 2014, ledipasvir and sofosbuvir were approved for HCV genotypes 1 and 4, providing a 94% to 99% cure rate without an interferon/ribavirin regimen, greatly reducing adverse reactions.[21]

Newer DAA medications, called pangenotypic drugs, have been developed to treat all 6 HCV genotypes and provide a 90% to 98% cure rate.[21]



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In 2017, glecaprevir/pibrentasvir (Mavyret) and sofosbuvir/velpatasvir/voxilaprevir (Vosevi), two of the newest pangenotypic HCV medications, were approved by the FDA.[7] The downside of these promising medications is their high cost, often more than $100,000 for a course of therapy.[21] Insurance companies often require prior authorization, detailed information on the patient's health history, documentation of other attempted therapies, and degree of fibrosis or advanced liver disease. For the latest treatment regimens recommended by infectious disease and hepatology experts, the AASLD/IDSA website is an excellent resource (see *HCV resources*).

Most patients take medication for 8 to 16 weeks, based on the prescribed treatment regimen.[26] To assess response to treatment, lab specimens should be obtained at regular intervals: at initiation of therapy (4 weeks), at the end of treatment (8, 12, or 16 weeks), and post treatment (14 to 20 weeks). Sustained virologic response has been achieved if the patient's viral load remains undetectable.

Consultation with a specialist in gastroenterology, hepatology, and/or infectious diseases should be considered for patients starting HCV treatment and for patients with fibrosis or cirrhosis.[9,20] Annual follow-up with a specialist is recommended for patients with advanced liver disease. Patients with cirrhosis should have screenings at least annually for esophageal varices and semiannual screenings for hepatocellular carcinoma.[7,26]

Complications of cirrhosis include ascites, hepatorenal syndrome, hepatopulmonary syndrome, spontaneous bacterial peritonitis, portal hypertension with esophageal or gastric varices, and hepatocellular carcinoma. Development of one or more of these complications changes the patient's status from compensated to decompensated and increases the mortality risk to approximately 50% within a year.[27] At this point, the patient should be referred for liver transplant evaluation at a transplant center.

Best practices for patients with HCV

The American Gastroenterology Association Institute created the "Hepatitis C Virus Infection Care Pathway" to provide best practices on appropriate care for HCV patients.[26] Screening for patients born between 1945 and 1965 and those who meet high-risk criteria is a quality reporting core measure from the Centers for Medicare and Medicaid Services in the US.[28] Treatment success largely depends on coordination with a multidisciplinary team, including a mental health and substance abuse

HCV resources

American Association for the Study of Liver Diseases/Infectious Diseases Society of America: HCV guidelines
www.hcvguidelines.org

Centers for Disease Control and Prevention: Hepatitis C questions and answers for health professionals
www.cdc.gov/hepatitis/hcv/hcvfaq.htm#a1

University of Liverpool: HEP drug interactions
www.hep-druginteractions.org/mission

World Health Organization: Hepatitis C
www.who.int/news-room/fact-sheets/detail/hepatitis-c

provider, care coordinator, clinical pharmacist, and HCV specialist.[26]

Patients and family members should be educated about risk factors for HCV and routes of transmission. If family or friends have also participated in high-risk behaviors or have been exposed to the patient's blood or body fluids, HCV screening is recommended.[7,16]

All patients with HCV should be vaccinated against hepatitis A and B to prevent additional viral hepatitis infection and injury to the liver. Patients also should be advised not to consume alcohol or take hepatotoxic medication, such as acetaminophen.[7,16] Assisting the patient with options for drug or alcohol abuse rehabilitation is essential to preventing further liver damage.

Teach patients starting drug therapy about the importance of adhering to the treatment regimen as prescribed. Review adverse reactions and drug-drug interactions, especially if the patient is taking other medications as is common in patients with comorbidities or coinfections.[19] Some medications may need to be stopped or a different DAA treatment regimen chosen based on patient response. The University of Liverpool provides a useful drug-drug interaction resource.[29]

Nursing-care guidelines have been established to improve HCV patient outcomes. In a study, Namba and colleagues found that nursing support increases the efficacy of HCV treatment. Patients enrolled in this study received weekly nurse visits based on a questionnaire tailoring to the patient's needs. Results included improved adherence to therapy and improved virologic response rates.[30]

Some clinics have started nurse-driven chronic HCV intervention pathways to manage patients with HCV. In a quality improvement project, Redulla and colleagues created a standardized approach that provided a resource for the nurse and incorporated the nurse's input for prompt symptom management in this select group of patients. Patient outcomes and adherence to therapy were improved.[31]

Another study revealed that patients with HCV have multiple treatment needs.[32] The authors stated that nurses need to provide not only the basic education surrounding adherence to therapy and HCV information, but also to consider the psycho-emotional effects and social concerns that the patient may be dealing with due to this new diagnosis. Other factors to consider include the willingness to learn about the HCV diagnosis and the presence of societal barriers, such as fear of sharing the diagnosis with others and social stigma. A nursing-led structured support program may assist with these challenges.[32]

Removing treatment barriers

To date, treatment of HCV has largely been provided by specialists in infectious disease, gastroenterology, or hepatology. With the advent of simpler treatment regimens, some argue that many patients with newly diagnosed HCV can be safely and effectively treated by primary care providers, including physicians, NPs, and physician assistants.[33] Removing barriers to allow primary care providers to treat HCV is a goal of the National Academies of Sciences, Engineering, and Medicine to eliminate HCV by 2030.[34] Referral to a specialist should be reserved for patients with cirrhosis and those whose previous DAA treatment regimens failed.[33] With this expansion of who can treat HCV, the goal of eradicating HCV is a possibility.

Promising future

With the development of new DAA medications, HCV infection can now be cured and many patients live long, healthy lives after treatment. Nurses play a key role in patient education and guiding optimal care for patients with HCV infection during all phases of treatment. The future holds new possibilities for successful treatment for even the most complicated infection. ■

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The author and planners have disclosed no potential conflicts of interest, financial or otherwise.

DOI-10.1097/01.NURSE.0000553271.39804.a4

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