Acknowledgements

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Purpose

The purpose of this course is to provide you with a comprehensive overview of hepatitis C virus (HCV), from the basics of the virus to current algorithms for treatment.

Increasing your knowledge about HCV will enable you to be an informed provider of care, utilizing evidence-based research.

Learning Objectives

At the end of this course, you will be able to:
1. Explain how hepatitis C virus (HCV) impacts public health.
2. List the modes of HCV transmission.
3. Describe how HCV’s molecular structure impacts the pathogenesis of disease.
4. State the current CDC recommended guidelines for HCV testing by risk stratification and age cohort.
5. Explore current and new medications currently under development for the treatment of HCV infection.
6. Select evidence-based algorithms for treatment and monitoring of patients with chronic HCV infection.
7. Utilize a holistic nursing approach to the care of the patient with HCV infection.

Introduction

Hepatitis C (also referred to as HCV), can be an overwhelming subject not just for patients, but for health care providers as well. HCV is one of the more complicated types of viral hepatitis because there is no vaccine; there is also no cure, only treatment.

The treatment of HCV is evolving and advancing each day. With early detection and treatment and your holistic approach to care, your patients will live healthier and longer with this disease.
Module I: The Basics of HCV

In the first section of this course, we will review:

- How hepatitis C virus (HCV) impacts public health.
- The modes of HCV transmission.
- How HCV’s molecular structure impacts the pathogenesis of disease.


The Facts from the CDC

The Centers for Disease Control (CDC) estimates that there are between 2.7-3.9 million people in the United States living with hepatitis C virus (HCV), as of 2014 (CDC, 2017).

Because of the nature of the virus and slow progression of disease, many of these people are not aware they are carrying HCV. If people are infected and not receiving treatment, they are at high risk for liver disease and hepatocellular carcinoma.

Transmission

Unlike other forms of hepatitis, **HCV has no vaccine**, treatments are long term and for many, the side effects are difficult to manage. This is why it is important to review how the virus is transmitted.

Hepatitis C is a blood-borne disease. It can only be transmitted by:

- IV drug use
- Intra-institutional infection (healthcare workers, e.g., needle stick injuries)
- Transfusions (primarily prior to testing for HCV)
- Hemodialysis
- Sexual contact
- Household contact (when living with infected persons)
- Passage from HCV-infected mother to newborn

<table>
<thead>
<tr>
<th>Transmission Route</th>
<th>Hepatitis A</th>
<th>Hepatitis B</th>
<th>Hepatitis C</th>
<th>Hepatitis D</th>
<th>Hepatitis E</th>
</tr>
</thead>
<tbody>
<tr>
<td>Food-Borne</td>
<td>X</td>
<td>N/A</td>
<td>N/A</td>
<td>N/A</td>
<td>X</td>
</tr>
<tr>
<td>Fecal-Oral</td>
<td>X</td>
<td>N/A</td>
<td>N/A</td>
<td>N/A</td>
<td>X</td>
</tr>
<tr>
<td>Water-Borne</td>
<td>X</td>
<td>N/A</td>
<td>N/A</td>
<td>N/A</td>
<td>X</td>
</tr>
<tr>
<td></td>
<td>X</td>
<td>X</td>
<td>X</td>
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</tr>
<tr>
<td>Intra-Institutional</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>IV Drug Use</td>
<td>Infrequent</td>
<td></td>
<td></td>
<td></td>
<td>N/A</td>
</tr>
<tr>
<td>Transfusion</td>
<td>Infrequent</td>
<td></td>
<td></td>
<td>Infrequent</td>
<td>Infrequent</td>
</tr>
<tr>
<td>Hemodialysis</td>
<td>N/A</td>
<td></td>
<td></td>
<td></td>
<td>N/A</td>
</tr>
<tr>
<td>Sexual</td>
<td>Infrequent</td>
<td>Infrequent</td>
<td></td>
<td></td>
<td>Infrequent</td>
</tr>
<tr>
<td>Household</td>
<td>X</td>
<td>Infrequent</td>
<td>Infrequent</td>
<td>Infrequent</td>
<td>X</td>
</tr>
<tr>
<td>Mother-Newborn</td>
<td>Infrequent</td>
<td></td>
<td>Infrequent</td>
<td></td>
<td>Infrequent</td>
</tr>
</tbody>
</table>

Modified from C. Everett Coop Institute, 2017a.

**Test Yourself**

Hepatitis C is a blood borne pathogen, transmissible by the fecal-oral route.

A. True

B. False

The correct answer is false. Hepatitis C is a blood-borne pathogen; however, the virus is transmitted by:

- IV drug use
- Intra-institutional infection (healthcare workers, e.g., needle stick injuries)
- Transfusions (primarily prior to testing for HCV)
- Hemodialysis
- Sexual contact
- Household contact (when living with infected persons)
- Passage from HCV-infected mother to newborn
The Public Health and Fiscal Impact

- Hepatitis C affects 3 1/2 times more individuals than hepatitis B in the U.S.
- Nearly 80% of HCV patients will develop chronic liver disease.
- 15-20% will develop cirrhosis within the first five years of infection.
- Approximately 1% will develop hepatocellular carcinoma within 20 years and the risk increases every year thereafter.
- HCV accounts for a third of all the liver transplants in the U.S. annually.
- Approximately 1,000 liver transplants take place per year at a cost of $280,000 each.
- Total costs annually for transplants in the U.S. due to HCV is upwards of $300,000 million.
- The average lifetime cost for chronic hepatitis C per person is $100,000.

Assuming 3.6 million people are infected, that’s a lifetime cost of $360,000 million times a 40-year lifespan = $9 billion US dollars!

(C. Everett Coop Institute, 2017b)
Test Yourself

Chronic HCV infection without liver transplant:

A. Affects half as many individuals as hepatitis B and costs $280,000 per person for lifetime treatment.
B. Affects the same number of persons as hepatitis B and costs $100,000 per person annually for treatment.
C. Affects two and a half times as many persons with hepatitis B and costs $360,000 per person for lifetime treatment.
D. Affects three and a half times more persons than those with hepatitis B and costs $100,000 per person for lifetime treatment.

The correct answer is D. Hepatitis C affects three and a half times more people than hepatitis B and costs an average of $100,000 for lifetime treatment of chronic HCV without liver transplant.

A Brief Background of the Virus

While there are many forms of viral hepatitis, we have seen that HCV poses the most severe health and financial impacts on the public. This is primarily because of the peculiarities of the HCV virus itself. Let’s look at the virus itself for a moment so you can see how it affects transmission, testing and ultimately, treatment.
The Complex Nature of HCV

HCV is a very small RNA virus – only 50nm in size. RNA is “unstable” as compared to DNA making it an ideal mechanism for reproduction of viral contents. RNA mutates easily and reproduces quickly, making it difficult for the host’s immune system to develop effective antibodies against the virus. Because of this, it was also difficult to detect in an effective laboratory test. For many years, people were unknowingly receiving blood transfusions and organ transplants from infected donors due to an inability to test for HCV.

It was only in 1988 when the technology became available for researchers to identify the elusive, small hepatitis C virus (which, since 1965, was previously referred to as “non-A”, “non-B”). The first test for HCV was then developed and licensed in 1992. Because there was no way to test for HCV prior to 1992, many people were infected with HCV and donated blood and organs not knowing that they were passing their disease on to others.

(C. Everett Coop Institute, 2017a; McCance et al., 2014)

No Vaccine Available

Why is it that there are vaccines for hepatitis A and B, but not for type C? On the surface, it would seem logical that a vaccine for HCV would be available soon. After all, the disease is devastating and costly and mass vaccination programs for the other forms of hepatitis are proving successful in worldwide campaigns. Hepatitis C, however, remains elusive.

The size of the virus and the mutagenic nature of an RNA virus versus a DNA virus make creating a vaccine more difficult. There are approximately 50-67 known subtypes of hepatitis C.

However, because approximately 15-45% of all acutely infected persons achieve spontaneous viral clearance without remission or progression to chronic HCV, it can be inferred that they have immunity to the disease. This is exactly how a vaccine works to prevent disease. Even those that relapse seem to handle secondary infection better with lower viremia, however, naturally occurring infection and the subsequent antibodies produced do not guarantee immunity from disease. In addition, research is difficult based on limited animal models and ethical concerns (Smith et al., 2014; Steckelberg, 2014).

Given this data, how effective would a vaccine be? Would an HCV vaccine eradicate the disease, slow the progression or just lessen the impact of liver disease and hepatocellular carcinoma? In theory, just lessening the impact on liver disease would be a step in the right direction and increase the quality of life for millions of people living with HCV.
Test Yourself

The nurse caring for the patient with chronic HCV understands that the virus is difficult to treat because:

A. DNA mutates easily and reproduces quickly making it difficult for the host’s immune system to develop effective antibodies against the virus.
B. RNA mutates easily and reproduces quickly making it difficult for the host’s immune system to develop effective antibodies against the virus.
C. Antigens mutate easily and reproduce quickly making it difficult for the host’s immune system to develop effective antibodies against the virus.

The correct answer is B. HCV is an RNA virus. RNA is “unstable” as compared to DNA making it an ideal mechanism for reproduction of viral contents. RNA mutates easily making development of antibodies difficult and sometimes ineffective.

If There Was a Vaccine for HCV

The question then becomes, what type of vaccine should be developed and who should be vaccinated? HCV is a blood-borne disease, so theoretically the best prevention is abstinence from the behaviors that place a person at risk for contracting the disease. This would mean that infants and children, for example, would not have to be immunized for HCV. Only high-risk populations would be recommended to receive a vaccine if it were available. The other option would be to develop a vaccine that prevents progression of acute HCV to chronic HCV, thereby preventing cirrhosis and hepatocellular carcinoma.

Feasibility of producing DNA vaccines and potential biological responses are a challenge. Currently, there are HCV vaccines in Stage II and III clinical trials. It remains to be seen if and how they will work and when they will be commercially available for use (Naderi et al., 2014).

HCV Types

Because HCV is constantly mutating, it is not a self-limiting disease like other viral forms of hepatitis.

HCV also has seven genotypes, 67 subtypes and numerous variations in the genotype, further complicating the ability to develop a vaccine or additional treatment options. Genotype seven of HCV has been reported in the past few years as a new strain, originating in Africa. It also creates a situation where infected individuals that have been treated may become re-infected with other strains as mutations occur.

Treatment of HCV is in part, based on genotype as well as patient clinical status and ability to tolerate treatment. Of the four, the most common genotypes found are:
• Type 1 represents approximately 75% of cases
• Type 2 and 3 represent approximately 20-25% of cases
• Types 4-7 are rare, and most frequently found in persons of Egyptian or African descent

Note! Genotype 1 and 4 are more difficult to eradicate which is a problem since 75% of cases are Type 1.

(Smith et al., 2014)

Barriers to Testing

It may seem like hepatitis C is alarming based on the information you’ve been provided thus far. However, the issue is that risk-based testing has historically been unsuccessful. As many as 17-87% of infected persons have not been tested. It is impossible to determine exactly how many are infected and how many go untested.

Barriers to Testing:
1. 72% of persons with a history of injection-drug use who are infected with HCV remain unaware of their infection status.
2. Many that are infected with HCV have inadequate health insurance coverage and/or limited access to regular healthcare.
3. Even those with access to healthcare remain untested.
4. Primary care providers’ knowledge of testing guidelines remains limited further compounding the problem.

(CDC, 2012)

Current CDC Recommendations for HCV Testing

<table>
<thead>
<tr>
<th>Persons who ever injected illegal drugs</th>
<th>HCV testing is recommended.</th>
</tr>
</thead>
</table>
| • Includes those who injected once or a few times many years ago and do not consider themselves “drug users”.
| Select medical conditions               | HCV testing is recommended for the following: |
| • Received clotting factor concentrates produced before 1987. |
| • Chronic hemodialysis. |
Persistently abnormal alanine adminotransferase levels.
HIV-infected patients should be tested routinely for evidence of chronic HCV infection.

| Prior recipients of blood transfusions or organ transplants | HCV testing is recommended for the following:
<table>
<thead>
<tr>
<th></th>
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</thead>
<tbody>
<tr>
<td></td>
<td>• Persons who were notified that they received blood from a donor who later tested positive for HCV infection.</td>
</tr>
<tr>
<td></td>
<td>• Persons who received a transfusion of blood or blood components before July 1992.</td>
</tr>
<tr>
<td></td>
<td>• Persons who received an organ transplant before July 1992.</td>
</tr>
</tbody>
</table>

| Persons with recognized exposures | HCV testing is recommended with the following:
<table>
<thead>
<tr>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>• Healthcare, emergency medical, and public safety workers after needle sticks, sharps, or mucosal exposures to HCV-positive blood.</td>
</tr>
<tr>
<td></td>
<td>• Children born to HCV-positive women.</td>
</tr>
</tbody>
</table>

| Generational considerations | Adults born during 1945-1965 should receive one-time testing for HCV without prior ascertainment of HCV risk. |

| Alcohol use | All persons with identified HCV infection should receive a brief alcohol screening and intervention as clinically indicated, followed by referral to appropriate care and treatment of services for HCV infection and related conditions. |

<table>
<thead>
<tr>
<th>Follow up testing</th>
<th>Initial testing for HCV should be performed using the most sensitive immunoassays licensed for detection of antibody to HCV (anti-HCV) in blood.</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>For persons who might have been exposed to HCV within the past 6 months, testing for HCV RNA or follow-up testing for HCV antibody is recommended</td>
</tr>
</tbody>
</table>

(CDC, 2015)

**Benefits of Testing the Birth Cohort**

After much research, in 2012, CDC added the 1945-1965 birth cohort to testing based on the fact that risk stratification testing for HCV infection (e.g., testing based on high risk behaviors, environments, or potentials for exposure) was inadequate. This means that all persons born between 1945 and 1965 should be tested for HCV regardless of risk factors, behaviors, or potential exposure.

The research revealed that there was a disproportionately high number of infected persons born between the years 1945 and 1965, which account for **nearly 75% of all persons infected with chronic HCV**. CDC added this group as a target for testing in addition to other high-risk groups so that early treatment and management can be initiated to halt the progression of chronic disease and the spread of infection to others.
CDC’s research also concluded that the benefits of testing far outweighed the risks (actual and perceived). Although waiting for blood tests or a liver biopsy may cause anxiety and even physical pain and bleeding, the studies have shown that detection and effective treatment enhance sustained virologic response (SVR) in persons with HCV infection. (CDC, 2012)

**Test Yourself**

Who should be screened for HCV?

A. 56 year-old man without any prior history of IV drug use.
B. 42 year-old woman with hemophilia that received many transfusions during her childhood.
C. 60 year-old woman that received a kidney transplant in 1998.

**D. All of the above**

The answer is D: All of the above are correct.

A. This man would have been born in 1957 placing him in the CDC’s recommended timeframe for testing for those born between 1945-1965 even though he has no high-risk behavior.
B. This woman would have received transfusions as a child before testing of blood products began in 1992 and may have been exposed to HCV.
C. This woman should be tested because of her age (she would have been born around 1953), not because of the year of the kidney transplant.

**Module II – Go to the Guidelines!**

This section explores the current and new medications under development for the treatment of HCV infection.

In this section, the healthcare professional will learn to select evidence-based algorithms for treatment and monitoring of patients with chronic HCV infection.

**Current Medications**

Before you can learn about the treatment guidelines, you must first review the medications used to treat HCV infection.
More treatment options have been approved over the past few years. The current, U.S. Food and Drug Administration (FDA)-approved medications for the treatment of hepatitis C infection are:

- **CoPegus® (ribavirin):** A nucleoside inhibitor, this medication that is taken orally and is weight-based, stops viral RNA synthesis. Indicated for adults with chronic hepatitis C virus infection who have compensated liver disease and have not been previously treated with interferon alpha. Must be used in combination with peginterferon, never used alone.

- **Daklinza® (daclatasvir):** An NS5A replication complex inhibitor is indicated for use with sofosbuvir for the treatment of patients with chronic HCV genotype 3 infection. Taken orally in combination with sofosbuvir.

- **Epclusa® (sofosbuvir and velpatasvir):** A combination of sofosbuvir (HCV nucleotide analog NS5B polymerase inhibitor), and velpatasvir (HCV NS5A inhibitor). Indicated for the treatment of adult patients with chronic HCV genotypes 1-6 infection.

- **Harvoni® (ledipasvir and sofosbuvir):** A combination of ledipasvir (HCV NSSA inhibitor), and sofosbuvir (HCV nucleotide analog NS5B polymerase inhibitor). Indicated for the treatment of chronic hepatitis C (CHC) genotype 1 infection in adults.

- **Incivek® (telaprevir):** NS3/4A protease inhibitor. Indicated for the treatment of genotype 1 chronic HCV in adult patients with compensated liver disease, who are treatment-naive or who have been previously treated with interferon-based treatment. Must be used in combination with peginterferon alfa and ribavirin.

- **Infergen® (interferon alphacon-1):** Interferons are cytokines that literally “interfere” with a virus’ ability to replicate. Interferons also stimulate natural killer cells in the body as well as aid in promoting uninfected cells to resist new viral infection. Indicated for treatment of chronic hepatitis C in patients 18 years of age or older with compensated liver disease who have anti-HCV serum antibodies and/or HCV RNA.

- **Intron A® (interferon alpha-2b):** Interferon indicated for treatment of chronic hepatitis C in patients 18 years of age or older with compensated liver disease who have a history of blood or blood-product exposure and/or are HCV antibody positive.

- **Mavyret® (glecaprevir and pibrentasvir):** Indicated for the treatment of adult patients with chronic HCV genotype 1-6 infection without cirrhosis, with compensated cirrhosis (Child-Pugh A), and adult patients with HCV genotype 1 infection, who previously have been treated with a regimen containing an HCV NS5A inhibitor or an NS3/4A protease inhibitor (PI), but not both.

- **Olysio® (simeprevir):** NS3/4A protease inhibitor. Indicated for the treatment of chronic HCV genotype 1 infection as a component of a combination antiviral treatment regimen.

- **Pegasys® (pegylated interferon):** Long acting interferon-α, also called peginterferon. Indicated for treatment of adults with chronic hepatitis C virus infection who have compensated liver disease and have not been previously treated with interferon alphaPeginterferon is taken as a once weekly subcutaneous injection.

- **Pegintron® (pegylated interferon alpha-2b):** Indicated for treatment of chronic hepatitis C in patients three years of age and older with compensated liver disease. Also
used in combination with ribavirin for adults with chronic HCV and compensated liver disease previously untreated with interferon alpha and who are intolerant to ribavirin

- **Rebetol® (ribavirin):** Used in combination with Pegintron® for treatment of chronic hepatitis C in patients with compensated liver disease who have not been previously treated with interferon alpha and are at least 18 years of age
- **Roferon® (interferon alpha-2a):** Interferon indicated for treatment of chronic hepatitis C in patients 18 years of age or older
- **Sovaldi® (sofosbuvir):** Indicated for the treatment of chronic HCV infection as a component of a combination antiviral treatment regimen
- **Technivie® (ombitasvir, paritaprevir and ritonavir):** A combination containing ombitasvir (a HCV NS5A inhibitor), paritaprevir (NS3/4A protease inhibitor), and ritonavir (a CYP3A inhibitor). The product is indicated in combination with ribavirin for the treatment of patients with genotype 4 chronic HCV infection without cirrhosis.
- **Victrrelis® (boceprevir):** NS3/4A protease inhibitor. Indicated for treatment of chronic HCV genotype 1 infection, in combination with peginterferon alfa and ribavirin, in adult patients with compensated liver disease, who are previously untreated or who have failed previous interferon and ribavirin therapy
- **Viekira Pak® (ombitasvir, paritaprevir and ritonavir tablets co-packaged with dasabuvir tablets):** Indicated for use with or without ribavirin for the treatment of patients with genotype 1 chronic HCV infection including those with compensated cirrhosis
- **Vosevi® (sofosbuvir, velpatasvir, and voxilaprevir):** Combination medication. Indicated for treatment approved for patients who have been previously treated with the direct-acting antiviral drug sofosbuvir, or other drugs for HCV that inhibit a protein called NS5A
- **Zepatier® (elbasvir and grazoprevir):** A combination product containing elbasvir (NS5A inhibitor), and grazoprevir (NS3/4A protease inhibitor). Indicated with or without ribavirin for treatment of chronic HCV genotypes 1 or 4 infection in adults

(U.S. Food and Drug Administration, 2017)

**New Medications**

What are the newest drugs being tested?

1. HCV NS3/4 protease Inhibitors
2. Nucleos(t)ide HCV NS5B polymerase inhibitors
3. Non-nucleos(t)ide HCV NS5B polymerase inhibitors
4. HCV NS5A inhibitors
5. Combination medications

All of the above drugs are direct acting antivirals or DAAs. Until clinical trials and testing are complete, patients will have to wait and see how the newest treatment regimens will be prescribed.
Testing for HCV

The first step in treating HCV is confirming presence of HCV infection. Further tests will determine if there is liver impairment or not and if there are other comorbidities such as HIV. Once the PCR test is run, the results may vary. Review the table below to see the four possible outcomes from the hepatitis screening highly sensitive PCR test.

<table>
<thead>
<tr>
<th>Anti HCV</th>
<th>HCV RNA</th>
<th>Interpretation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Positive</td>
<td>Positive</td>
<td>Acute or chronic HCV – depends on the patient/presenting clinical context and condition</td>
</tr>
<tr>
<td>Positive</td>
<td>Negative</td>
<td>Resolution of HCV; or acute HCV during period of low-level viremia</td>
</tr>
<tr>
<td>Negative</td>
<td>Positive</td>
<td>Early acute HCV infection; chronic HCV in setting of immunosuppressed state; or false positive HCV RNA test</td>
</tr>
<tr>
<td>Negative</td>
<td>Negative</td>
<td>Patient not infected with HCV</td>
</tr>
</tbody>
</table>

To Treat or Not to Treat?

Now that a patient has been tested for HCV, many questions may arise about being treated or not and what’s right for them. Patients may ask/state:

1. What do the results mean?
2. What’s the difference between acute and chronic? Which one am I?
3. But I’m asymptomatic. Is it worth it to put me through weekly injections and side effects?
4. Do I have a choice? Will I die if I don’t?
5. What are my chances of the hepatitis being cured?
6. Will the treatment work?
7. Will my family and spouse be hurt or exposed if I don’t treat myself now?
8. I know people who’ve had the treatment – it was bad and it didn’t work. Why should I do this?
9. I don’t care that I’m not symptomatic now; I want to be treated immediately. I don’t want to be sick and die.

Begin with the Test Results
The previous patient questions are valid and unfortunately, there are no easy answers. Each patient is different. Depending on the results of each individual’s lab work, testing and situation, treatment may be initiated immediately, or deferred.

For example, if a patient wishes to get pregnant in the next year, she cannot start peginterferon treatment now or for six months after giving birth. After discussing this with her hepatologist, her family and the healthcare team may then decide it is safe for her to defer treatment until after pregnancy and delivery.

However, if her liver condition is decompensated, her physician may decide that treatment now is advisable, as she may not be healthy enough to be pregnant later if she is advancing towards liver failure. This is why there are no clear-cut answers regarding when to treat HCV. It must be on an individualized basis.
(Dhawan, 2016; U.S. Department of Veterans Affairs [VA], 2017)

**Acute HCV vs. Chronic Infection**

Once HCV presence has been established, the patient’s history and physical in addition to other lab work and physical presentation will help determine if the infection is acute or chronic.

Acute infections last approximately 12 weeks and may resolve without treatment. However, if the HCV has not cleared after 12 weeks, monotherapy with peginterferon for 24 weeks is recommended and has a success rate of 80-100%. Remember that up to 85% of acute infections last longer than six months and become chronic.

In either case, whether acute or chronic, after the PCR test has confirmed the presence of HCV infection, he or she should also be tested for other forms of hepatitis co-infection such as hepatitis A and B.
(Dhawan, 2016)

Now let’s review two basic treatment algorithms and apply them to two patients.

**Multiple Pathways**

There are many complex, branching pathways to treat patients with chronic HCV. The algorithm may change based on the considerations/examples listed below:

- Genotype 1 or 4
- HIV status
- Child-Pugh score
- Decompensated cirrhosis
- Relapse/failure to respond to initial treatment
• Persistently normal ALT
• Current alcohol abuse
• Age >65 years
• Renal disease
• History of solid organ transplant

(Dhawan, 2016)

To simplify the process, you will be provided with only two of the more basic pathways and apply them to two case studies.

Two Patients, Two Pathways

Rachel:
Meet Rachel. She is 54 years old and works full time as a social worker in a free clinic. She was recently hospitalized when she went to the ER after a syncopal episode and fall at work.

Routine blood work at that time showed elevated AST and ALT. She was kept for observation and further tests when she informed the ER doctor she had hepatitis C in the past and was treated for two years with interferon injections with a good result about ten years ago. Her last visit to the hepatologist about three years ago showed no detectable virus in her blood work.

Rachel’s Additional Labs and Evaluation:
• HCV viral load: 650,000
• Serum HBsAg, Anti-HBc, anti-HBs, anti-HAV: All negative
• Albumin: 3.0
• Bilirubin: 2.8
• INR: 2.2
• Creatinine: 1.0
• Platelets: 145
• H&H: 12.2/35.4
• HCV Genotype: 1
• HIV: Negative
• Splenomegaly: Negative
• Encephalopathy: Negative
• Ascites: Negative
• Liver biopsy: Reveals minimal fibrosis and early stage 1 cirrhosis
• EKG: Normal sinus rhythm, no ectopy rate 72
• BP: 144/78

Rachel’s continued history and physical show that she was treated ten years ago with interferon-α (monotherapy) and at the time had a sustained viral response (SVR). It is believed she may have been exposed to HCV after a blood transfusion in 1989 due to a traumatic birth and C-section with her youngest son that resulted in a total hysterectomy.
She admits to drinking alcohol more often for the past two years since her divorce and stressful
days at work. She consumes 3-4 alcoholic beverages per night and is a non-smoker. She takes
no daily medications and reports no illicit drug use present or past. She lives at home with her
youngest son. Her older son is married and lives close by. Rachel’s hepatologist is called and he
determines that her hepatitis C has now relapsed and she has mild stage 1 cirrhosis.

Two Patients, Two Pathways

Kevin:

Meet Kevin. He is 40 years old, teaches high school Environmental Science and is a father of
three children. He is also the music teacher at the school and plays in a band on the weekends.

Kevin’s wife was bothering him about going to the doctor for a “check-up” since he turned 40.
After his exam, his provider called to tell him his liver enzymes were slightly “elevated” and he
wanted him to come in for additional blood work and follow up.

Kevin returned two days later and had a frank discussion with his physician and agreed to be
screened for hepatitis based on his history on risk factors in the past.

Kevin’s Additional Labs and Evaluation:

- Anti-HCV: Positive
- HCV-RNA: Positive
- Viral load: 500,000
- Serum HBsAg, anti-HBc, anti-HBs, anti-HAV: All negative
- Albumin: 5.1
- Bilirubin: 1.6
- INR: 1.3
- Creatinine: 0.9
- Platelets: 353
- H&H: 15.5/43.1
- HCV Genotype: 1
- HIV: Negative
- Splenomegaly: Negative
- Encephalopathy: Negative
- Ascites: Negative
- EKG: Normal sinus rhythm, no ectopy rate 81
- BP: 136/72
- Liver biopsy: Deferred, no clinical indication of cirrhosis
Kevin’s history and physical revealed that while he was a teenager, he experimented with IV drugs; although, he never considered himself an “addict” and was more of a “recreational user” while touring with his band after high school. His IV drug use stopped at age 19 when he enrolled in college and began his education to become a teacher.

Kevin does not drink alcohol and does not smoke. He takes ibuprofen occasionally for headaches and has no pertinent medical or surgical history. His primary care provider refers him to a hepatologist for HCV infection and evaluation for treatment.

**Side-by-Side Comparison**

Both Rachel and Kevin have chronic hepatitis C, however, they have very different presentations. Let’s look at them side by side and compare. Ask yourself what are the similarities or differences between these two patients? Do you think their treatments will be the same?

<table>
<thead>
<tr>
<th></th>
<th>Rachel</th>
<th>Kevin</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Anti-HCV</strong></td>
<td>Positive</td>
<td>Positive</td>
</tr>
<tr>
<td><strong>HCV-RNA</strong></td>
<td>Positive</td>
<td>Positive</td>
</tr>
<tr>
<td><strong>Viral Load</strong></td>
<td>650,000</td>
<td>500,000</td>
</tr>
<tr>
<td><strong>Serum HBsAg, Anti-HBc, Anti-HAV</strong></td>
<td>All negative</td>
<td>All negative</td>
</tr>
<tr>
<td><strong>Albumin</strong></td>
<td>3.0</td>
<td>5.1</td>
</tr>
<tr>
<td><strong>Bilirubin</strong></td>
<td>2.8</td>
<td>1.6</td>
</tr>
<tr>
<td><strong>INR</strong></td>
<td>2.2</td>
<td>1.3</td>
</tr>
<tr>
<td><strong>Creatinine</strong></td>
<td>1.0</td>
<td>0.9</td>
</tr>
<tr>
<td><strong>Platelets</strong></td>
<td>145</td>
<td>353</td>
</tr>
<tr>
<td><strong>H&amp;H</strong></td>
<td>12.2/35.4</td>
<td>15.5/43.1</td>
</tr>
<tr>
<td><strong>HCV Genotype</strong></td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td><strong>HIV</strong></td>
<td>Negative</td>
<td>Negative</td>
</tr>
<tr>
<td><strong>Splenomegaly</strong></td>
<td>Negative</td>
<td>Negative</td>
</tr>
<tr>
<td><strong>Encephalopathy</strong></td>
<td>Negative</td>
<td>Negative</td>
</tr>
<tr>
<td><strong>Ascites</strong></td>
<td>Negative</td>
<td>Negative</td>
</tr>
<tr>
<td><strong>Liver Biopsy</strong></td>
<td>Reveals minimal fibrosis and early stage 1 cirrhosis</td>
<td>Deferred, no clinical indication of cirrhosis</td>
</tr>
<tr>
<td><strong>EKG</strong></td>
<td>Normal sinus rhythm, no ectopy rate 72</td>
<td>Normal sinus rhythm, no ectopy rate 81</td>
</tr>
<tr>
<td><strong>BP</strong></td>
<td>144/78</td>
<td>136/72</td>
</tr>
</tbody>
</table>
Child-Turcott Pugh Score Chart

There is one more value you must determine before proceeding with treatment. The Child-Pugh Score as it is more commonly known, is used to help determine prognosis of chronic liver disease and if a patient is a candidate for HCV treatment. The higher the score, the sicker the patient is and the less likely it will be that the patient can be treated at this time.

The score is obtained by adding the number for each parameter. A class or grade is determined by the total score. Generally, class A patients are immediately treatable, class B patients are treated on a case-by-case basis and class C are not candidates for HCV treatment and must be referred out for management of cirrhosis before the HCV infection can be addressed.

- Class A = 5-6 points
- Class B = 7-9 points
- Class C = 10-15 points

<table>
<thead>
<tr>
<th>Points*</th>
<th>1</th>
<th>2</th>
<th>3</th>
</tr>
</thead>
<tbody>
<tr>
<td>Encephalopathy</td>
<td>None</td>
<td>Grade 1-2 (or precipitant-induced)</td>
<td>Grade 3-4 (or chronic)</td>
</tr>
<tr>
<td>Ascites</td>
<td>None</td>
<td>Mild/moderate (diuretic-responsive)</td>
<td>Severe (diuretic-refractory)</td>
</tr>
<tr>
<td>Bilirubin (mg/dL)</td>
<td>&lt;2</td>
<td>2-3</td>
<td>&gt;3</td>
</tr>
<tr>
<td>Albumin (g/dL)</td>
<td>&gt;3.5</td>
<td>2.8-3.5</td>
<td>&lt;2.8</td>
</tr>
<tr>
<td>PT (sec prolonged) or INR</td>
<td>&lt;4</td>
<td>4-6</td>
<td>&gt;6</td>
</tr>
<tr>
<td></td>
<td>&lt;1.7</td>
<td>1.7-2.3</td>
<td>&gt;2.3</td>
</tr>
</tbody>
</table>

(VA, 2016)

Calculate the Child Pugh Score

Refer back to Rachel and Kevin’s labs and physical assessment in order to calculate the Child Pugh scores for both.

<table>
<thead>
<tr>
<th>Points*</th>
<th>1</th>
<th>2</th>
<th>3</th>
<th>Rachel</th>
<th>Kevin</th>
</tr>
</thead>
<tbody>
<tr>
<td>Encephalopathy</td>
<td>None</td>
<td>Grade 1-2 (or precipitant-induced)</td>
<td>Grade 3-4 (or chronic)</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Ascites</td>
<td>None</td>
<td>Mild/moderate (diuretic-responsive)</td>
<td>Severe (diuretic-refractory)</td>
<td>0</td>
<td>0</td>
</tr>
</tbody>
</table>
You have determined that Rachel’s score is 6 and Kevin’s score is 3. Remember these numbers in the next exercise when you are working through the treatment algorithms.

Now you are ready to begin. As you work through each algorithm, make decisions about where to go next as you read each step in the process based on what you know about each patient.

**Algorithm for Rachel**

(Dhawan, 2016; VA, 2017)
At first glance, Rachel is obviously “sicker” than Kevin, however the treatment is essentially the same but with another option (Zepatier®, Mavyret®, Harvoni®, Epclusa®, or Vosevi®). They both have genotype 1 which qualifies each of them for various therapies. The key difference in Rachel’s treatment is that initially she received monotherapy or dual therapy only in which she was a responder. If she was a null responder during her first treatment with triple therapy before, she would not be able to be treated again. A null responder is a patient that was treated but whose viral load remained elevated during therapy. Not all patients respond to treatment.
In Kevin’s case, however, Zepatier®, Mavyret®, Harvoni®, or Epclusa® are recommended for a treatment naïve patient with genotype 1. If either patient had a different genotype, only duel therapy would be initiated.

**Treat Now?**

- Early treatment means higher SVR rates
- Current triple therapy rates of SVR are excellent
- Patients with decompensated cirrhosis may advance to stage IV or HCC
- New drugs in the pipeline may not be available in time to be used by patients waiting for the FDA to approve them

(Dhawan, 2016; VA, 2017)
Defer Treatment?

- Current treatments are complex and pose a burden on many patients – adherence is an issue
- New/future treatments may have a better risk/benefit profile
- New/future treatments may have lesser adverse events profile
- Patients that have contraindications to interferon have the potential for an interferon-free regimen in the future

(Dhawan, 2016; VA, 2017)

Module III: Nursing Implications

- Utilize a holistic nursing approach to the care of the patient with HCV infection.

Treat the Whole Person

Patients undergoing treatment for HCV will need support in all aspects of their lives. As a nurse, your approach to care should always be holistic – treat the whole person, not just the disease. Here are some strategies to help you provide holistic care to the patient being treated for chronic HCV.

First, use your nursing process to assess your patient...
**Possible Side Effects of Treatment**

<table>
<thead>
<tr>
<th>Side Effect</th>
<th>Holistic Interventions/Suggestions</th>
</tr>
</thead>
<tbody>
<tr>
<td>Flu-like symptoms (muscle aches, joint pain, nausea)</td>
<td>Regular exercise (low impact), massage therapy, ginger tea, peppermint oil, take injection at night before sleep</td>
</tr>
<tr>
<td>Anorexia</td>
<td>Small frequent meals, protein shakes</td>
</tr>
<tr>
<td>Insomnia</td>
<td>Warm drink at bedtime, no caffeine, light stretching before bed, warm bath or shower, no alcoholic beverages</td>
</tr>
<tr>
<td>Depression/irritability</td>
<td>Engage in hobbies and activities daily, exercise daily, join a hep C support group, start a meditation practice, no alcoholic beverages</td>
</tr>
<tr>
<td>Diarrhea</td>
<td>Avoid milk and dairy products, increase fluid intake</td>
</tr>
<tr>
<td>Fatigue</td>
<td>Assess patient’s rest/wake patterns, encourage good nutrition with proper periods of rest with exercise (as tolerated)</td>
</tr>
</tbody>
</table>

(Crusse & Kent, 2015; Dhawan, 2016)
Balance Your Care

After having your patient implement your suggested interventions, remember to continue to monitor for effect and evaluate his or her response(s).

Keep in mind that if side effects become severe, treatment may need to be adjusted (e.g., titrating dosages of medications, etc.). Patients have also required hospitalization secondary to side effects such as electrolyte imbalances due to diarrhea and subsequent dehydration.

For example, if diarrhea became severe and continuous, the patient must be monitored for dehydration. Teach the patient the signs and symptoms of dehydration and how to manage fluid replacement with electrolyte-infused drinks and adequate nutrition. Know when to tell the patient to come in to the office to be assessed or to go to the emergency department to be further evaluated.
(Crusse & Kent, 2015; Dhawan, 2016)

Resources for Living

If you have a patient that is recently diagnosed with HCV, there are many resources that he or she can access for information and support. Providing resource and recommended support groups for patients are important strategies to assist with their ability to cope with the disease.

The CDC’s website is packed with the most up to date information on all forms of viral hepatitis. There are videos, downloadable brochures and fact sheets, articles and research papers filled with easy to read information in different languages that you can refer your patient(s) to: [https://www.cdc.gov/hepatitis/hcv/cfaq.htm](https://www.cdc.gov/hepatitis/hcv/cfaq.htm)

For those patients wondering about their current risk for exposure to HCV, the CDC has an online tool that assesses a person’s risk for contracting HCV and when to be screened for the virus: [http://www.cdc.gov/hepatitis/RiskAssessment/](http://www.cdc.gov/hepatitis/RiskAssessment/)

Other Helpful Sites

Additional online resources that you may direct your patients to are:

- Chronic Liver Disease Foundation: [http://www.chronicliverdisease.org/](http://www.chronicliverdisease.org/)
If you have a patient that is a candidate for a clinical trial or is interested in participating in a clinical trial or following studies currently under way, clinicaltrials.gov is an excellent resource categorized by disease. The link for hepatitis C is: [http://www.clinicaltrials.gov/ct2/results?cond=%22Hepatitis+C%22](http://www.clinicaltrials.gov/ct2/results?cond=%22Hepatitis+C%22)

Please note, these are high quality sites with medical-grade information intended for support and information only. Please tell your patients to be careful of general internet searches of random websites concerning his or her medical condition. Your patients should be aware that they should never change their treatments or medications based on information “found online”, and they should always check in with his or her medical provider with questions about care!

**Test Yourself**

Kristin started triple therapy four weeks ago. She is feeling very exhausted and short-tempered at home. At her visit today, she explains that she’s been fighting with her fiancé a lot and she’s not sleeping. What would you suggest at this point?

- A. Recommend she stop treatment. She is obviously not tolerating the side effects of the medications.
- B. Recommend to the hepatologist that the dosage be reduced to minimize her obvious side effects.
- C. Recommend to her fiancé to be more tolerant. She’s the sick one, not him.
- **D. Recommend she start a sleep journal and have her fiancé and herself start going for walks in the evening to wind down from the day and talk before going to bed.**

The correct answer is D. Kristin is having a rough time, but if she starts monitoring her sleep and starts walking as an exercise program, it may help. Also engaging her finance in the activity will give her support and time for them to talk about how they’re feeling. Stopping or changing treatment would not be advisable and may hinder her progress and prevent SVR.

**Conclusion**

You are now ready to face hepatitis C with the latest evidence-based research and knowledge available. Throughout this course, you have learned:

- How hepatitis C virus (HCV) impacts public health.
- The modes of HCV transmission.
- How HCV’s molecular structure impacts the pathogenesis of disease.
• What the current CDC recommended guidelines are for HCV testing by risk stratification and age cohort.
• Current and new medications currently under development for the treatment of HCV infection.
• Evidence-based algorithms for treatment and monitoring of patients with chronic HCV infection.
• How to utilize a holistic nursing approach to the care of the patient with HCV infection.

References


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