

# **HCSP TRAINING MANUAL**

## *SECTION III: AN INTRODUCTION TO THE HEPATITIS A, B, D, E AND G ALPHABET*

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**T**he information in this guide is designed to help you understand and manage HCV and is not intended as medical advice. All persons with HCV should consult a medical practitioner for diagnosis and treatment of HCV.

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# THE HEPATITIS ALPHABET

## **Objectives:**

- *Be able to list the different types of viral hepatitis*
- *Be able to discuss transmission, prevention, symptoms, and treatment of hepatitis A and hepatitis B*
- *Be able to discuss the HAV and HBV vaccines*

## **Viral Hepatitis**

Hepatitis is a general term for inflammation of the liver. It can be caused by various factors, including viruses. The viral hepatitis alphabet includes hepatitis A, B, C, D, E and G each of which is caused by a different virus. The most common types of viral hepatitis in the United States are hepatitis A virus (HAV), hepatitis B virus (HBV), and hepatitis C virus (HCV). Other less common types of viral hepatitis include hepatitis D, hepatitis E, and hepatitis G. Although these viruses all affect the liver, they are not otherwise related.

## **Hepatitis A: Key Points**

- *HAV is transmitted by the fecal-oral route.*
- *HAV resolves itself and does not become a chronic illness.*
- *Hepatitis A can be prevented with a vaccine.*
- *HAV Vaccine is recommended for all people with hepatitis C who do not have natural immunity to hepatitis A.*

## **Hepatitis A:**

### **General Information**

Hepatitis A is an inflammation of the liver caused by the hepatitis A virus (HAV); it was formerly known as infectious hepatitis. It is the most common type of viral hepatitis. The Centers for Disease Control estimates that there were approximately 22,000 new HAV infections in 2008 and that 33% of all people in the United States have been infected with HAV.

### **HAV Transmission and Prevention**

Hepatitis A is a highly infectious disease that is mainly spread through the fecal-

oral route, that is, virus contained in feces is transferred to a person's mouth. This can happen through ingesting contaminated food or water, household contact (especially with infants or young children), and some types of sexual contact (e.g., anilingus, or oral/anal sex). Workers in day care centers and long-term care facilities such as nursing homes have a higher risk of contracting HAV, as do international travelers to areas that do not have good sanitation or water processing facilities. Approximately 68% of HAV cases are of unknown origin.

New HAV infections in the U.S. are most commonly observed among:

- International travelers to areas with poor sanitation
- Employees of and children who attend daycare centers
- Employees of and people who reside in long-term care facilities
- Men who have sex with men
- People who practice oral/anal sex
- Injection drug users
- People who have household contact with an HAV-infected individual

To prevent transmission of HAV, wash hands thoroughly (for at least 20 to 30 seconds), especially after using the toilet or changing diapers. People with HAV should avoid preparing food for others. Clean up spilled blood or body fluids with a 10:1 bleach solution (10 parts water to 1 part bleach). Wear gloves when touching blood, body secretions, or any cuts or sores. Do not share razors, toothbrushes, or needles. Practice safer sex, including using latex condoms and latex or plastic barriers for oral/anal sex.

### ***HAV Symptoms and Progression***

Hepatitis A has an incubation period of about 10 days. People with acute HAV may experience mild flu-like symptoms, such as fever, fatigue, nausea, vomiting, loss of appetite, and general malaise. They may also have jaundice (yellowing of the skin and whites of the eyes), along with pale-colored stools and dark urine. Many people with HAV, especially children, exhibit no symptoms; however, asymptomatic HAV-infected people can still transmit the disease to others. Hepatitis A usually resolves completely on its own. Symptoms usually last a few weeks, although fatigue may linger for months. About 15-20% of people experience a relapse. There is no chronic or carrier state. Rarely, a person may develop fulminant hepatitis A, which is characterized by severe symptoms and may be fatal;

fulminant hepatitis A is more likely in people who already have chronic hepatitis B or C and in the elderly population.

### ***HAV Treatment***

Because hepatitis A typically resolves on its own, there is no standard treatment for HAV. During the acute period, general measures such as a healthy diet, plenty of fluids, avoidance of alcohol and adequate rest can help make a person feel better.

### ***The HAV Vaccine***

The HAV vaccine is considered safe and effective. The two-dose vaccine is administered by injection, with the second dose given 6 months after the first. The vaccine is recommended for anyone at risk of exposure to HAV, including men who have sex with men, daycare center workers, and certain international travelers. *People with hepatitis B or C or other types of liver disease should receive the HAV vaccine to prevent fulminant hepatitis A.* Routine mandatory vaccination of school age children in many states has reduced the incidence of outbreaks among children. Vaccination programs have the potential to reduce future outbreaks, if not eliminate the disease. An estimated 95-100% of people vaccinated develop protective antibodies against HAV one month after the initial dose. Some experts believe that people with compromised immune systems (such as people with HIV) may require more doses of the HAV vaccine. A combination HAV/HBV vaccine (Twinrix) was approved and an accelerated dosing of Twinrix (3 shots within 30 days followed by a booster in one year) was approved by the FDA in 2007. If a person has been exposed to HAV, an injection of HAV immune globulin (antibodies) may prevent the development of illness and lessen some of the symptoms, but it must be administered within two weeks of exposure to HAV. If a person has had hepatitis A once, they are immune to it and do not need the vaccine.

### ***Hepatitis B: Key Points***

- *HBV is transmitted through contact with infected blood and bodily fluids including sharing needles and works and through sexual contact.*
- *To prevent HBV transmission, do not share needles, practice safer sex, and clean up blood with a 10:1 bleach solution.*
- *Approximately 5-10% of adults who are infected with HBV become chronic carriers. The rate is much higher in children.*
- *Approximately 800,000 to 1.4 million Americans have chronic HBV.*

- *Approved treatment options for chronic HBV include interferon, lamivudine, adefovir, entecavir, telbivudine, tenofovir and pegylated interferon alpha 2a.*
- *Hepatitis B can be prevented with a vaccine.*

## **Hepatitis B:**

### ***General Information***

Hepatitis B is an inflammation of the liver caused by the hepatitis B virus (HBV); it was formerly known as serum hepatitis. HBV is highly infectious and is found in blood, semen, vaginal secretions, sweat, saliva, tears, and breast milk. The Centers for Disease Control estimates that there were approximately 38,000 new HBV infections in 2008, and that an estimated 800,000 to 1.4 million people have chronic hepatitis B. Over 5,000 individuals die annually of complications from HBV.

### ***HBV Transmission and Prevention***

HBV is a blood-borne virus that is spread when one person's blood or bodily fluids come into contact with another person's blood or mucous membranes. This may occur through sharing infected needles to inject drugs or sharing personal items such as razors or toothbrushes that may come into contact with blood. Healthcare workers may be infected through needle-stick accidents or other exposure to blood. HBV is present in semen and vaginal secretions, and it is estimated that as many as 50% of new infections in the United States may be sexually transmitted. Mothers can transmit HBV to their babies during birth; this is more likely if the mother has a high HBV viral load. Although HBV is found in breast milk, there is no evidence that breast-feeding transmits hepatitis B. New infections in the U.S. are most common among:

- Men who have sex with men
- Injection drug users
- Sex partners of HBV-infected individuals
- People who have household contact with HBV-infected individuals
- Healthcare workers
- Children born to HBV-infected mothers

To prevent transmission of HBV, do not share needles to inject drugs. Clean needles may be available from a local needle exchange. Do not share razors, toothbrushes,

or other personal items that may come into contact with blood. Use universal precautions in medical settings. Wear gloves when touching blood, body fluids, or cuts or sores. Properly dispose of bandages and used menstrual supplies. Clean up spilled blood or body fluids with a 10:1 bleach solution (10 parts water to 1 part bleach). Practice safer sex, including the use of latex condoms and barriers.

### ***HBV Symptoms and Progression***

The incubation period for HBV is 40 -180 days. During the acute phase, people may experience flu-like symptoms, fever, abdominal pain, fatigue, loss of appetite, and general malaise. Some people have jaundice, dark urine, and pale-colored stools. About a third of people with HBV have no symptoms. Often HBV resolves on its own, but becomes chronic in an estimated 5-10% of adults infected with the virus; the chronic rate is much higher in infants and children; up to 90% if the infant is not vaccinated at birth. People with chronic HBV can transmit the virus even if they have no symptoms. As with chronic HCV, people with chronic HBV may develop long-term liver damage including cirrhosis (in about 20-30%), liver cancer, and liver failure. **See Section VI: HCV Symptoms and Progression** for more on the long-term consequences of chronic hepatitis C.

### ***HBV Treatment***

There are currently seven FDA-approved treatments for chronic hepatitis B: interferon-alpha-2b (Intron-A), lamivudine (Epivir-HBV), adefovir (Hepsera), entecavir (Baraclude), pegylated interferon alfa 2a (Pegasys), telbivudine (Tyzeka) and tenofovir (Viread).

Due to the high rate of drug resistance that occurs in people who are treated with some HBV medications, it is generally recommended that the first line of treatment be entecavir, tenofovir and Pegasys. *See Table 1. Approved HBV Medications and Drug Resistance Profile at the end of this chapter.*

**Entecavir (Baraclude)** is a potent inhibitor of HBV replication that was approved to treat chronic HBV in 2005. Entecavir has shown the ability to reduce HBV viral DNA levels even when ALT levels were only slightly elevated. Entecavir resistance is rare in those who have never been treated with an antiviral; however, in patients who have already developed lamivudine resistance, entecavir resistance reaches 57 percent after just four years. **Caution:** entecavir has been shown to have antiviral properties against HIV so it is **not** recommended that people who are HIV/

HBV coinfecting use entecavir unless their HIV is well-controlled.

**Tenofovir (Viread)**, the newest antiviral, was approved by the FDA in August 2008. It has been used successfully against HIV for years. Viread (tenofovir disoproxil fumarate) is a nucleotide analog reverse transcriptase and HBV polymerase inhibitor that blocks an enzyme that the hepatitis B virus needs to replicate in liver cells. The recommended dose for chronic hepatitis B is one 300-mg tablet a day. Two Phase III clinical trials comparing Viread with Hepsera found that chronic hepatitis B patients on Viread achieved a higher rate of complete treatment response compared with patients taking Hepsera, according to the company, which says the two drugs should not be used together.

**Pegylated interferon alfa-2a (Pegasys)** is a longer acting form of interferon that was approved to treat chronic HBV in 2005. In the group of 537 HBeAg-negative patients treated with Pegasys monotherapy, 36% were able to lower their HBV viral loads below 20,000 cp/mL and achieve ALT normalization after 48 weeks of treatment. HBeAg clearance increased from 3% at 1 year post treatment to 12% at 5 years post treatment. In a study of 814 HBeAg-positive patients treated with Pegasys, 27% achieved HBeAg seroconversion at end of treatment and 42% at 1 year post treatment (in the 271 patients who remained in the study).

*Other medications to treat chronic hepatitis B include:*

**Interferon-alpha-2b (Intron-A)** is an injectable medicine that has been shown to have limited success in treating chronic hepatitis B.

**Lamivudine (also known as 3TC; Epivir-HBV)** is an oral nucleoside analog drug that inhibits HBV replication. Lamivudine monotherapy leads to the development of drug-resistant HBV with long-term use or prolonged treatment (resistance developed in 60 – 70% of patients who were treated over a 5-year period).

**Adefovir (Hepsera)** is a nucleotide analog drug, which requires one less processing step within the body than a nucleoside analog. Several recent studies have yielded promising results, with adefovir producing substantial decreases in HBV DNA viral load, reductions in ALT level, and improvements in liver damage. Adefovir appears to work well against both wild-type and lamivudine-resistant HBV. Adefovir's 5-year resistance rate is 29% when used as a monotherapy.

**Telbivudine (Tyzeka)**, approved by FDA in October 2006, is a nucleoside analog that has shown similar success as lamivudine in suppressing viral load and improvement of liver inflammation. One 52-week study that compared telbivudine to adefovir in 135 patients with HBeAg-positive hepatitis B and elevated ALT found it produced more significant declines in HBV DNA than adefovir. The daily dose is 600 mg/day. The most common side effects were elevated CPK (creatinine phosphokinase), an enzyme that is present in muscle tissue and is a marker for breakdown of muscle tissue, upper respiratory tract infection, fatigue, headache, abdominal pain and cough. Health officials have warned that *telbivudine should not be taken in combination with pegylated interferon*. After two years telbivudine use leads to the development of drug resistance in 25% in HBeAg positive patients and 57% in HBeAg negative patients.

### ***Future HBV Treatment Options***

*Research is underway to develop new and better HBV treatments for the future including emtricitabine (FTC, Emtriva) listed below.*

**Emtricitabine (FTC, Emtriva)**, already approved by the FDA for treatment of HIV, has been found to be effective in lowering HBV viral DNA and improving liver histology. Emtricitabine are currently in phase III studies. It appears that emtricitabine is more effective in combination with another antiviral medication.

Combination therapies with newer agents are under study. Some people with chronic hepatitis B (especially asymptomatic carriers) do not require treatment. Certain alternative and complementary therapies may also be used to help improve the health of the liver – for example, milk thistle (*silymarin*), licorice root (*glycyrrhizin*), and vitamin E. For more information, see **Section IX: Alternative and Complementary Therapies**.

### ***The HBV Vaccine***

The HBV vaccine is considered safe and effective. Adults are given three injections. The second injection is given one month after the first injection, and the third is given six months after the first. The HBV vaccine is recommended for healthcare workers, sexually active adults, injection drug users, and household contacts of HBV-infected individuals. Today, the HBV vaccine is part of the standard childhood vaccination series, and is also given to adolescents who were not vaccinated as children. In addition, people with chronic hepatitis C and other types of liver

disease are encouraged to receive the HBV vaccine if not previously infected with HBV. The FDA has approved a combination HAV/HBV vaccine (Twinrix) and recently approved accelerated dosing of Twinrix (3 shots within 30 days followed by a booster in one year). If a person has been exposed to HBV, an injection of HBV immune globulin or HBIG (antibodies) may help reduce the severity and length of illness. HBIG plus the HBV vaccine can also prevent hepatitis B in infants born to HBV-positive mothers. *If a person has had hepatitis B before and has successfully cleared the virus, they are immune and do not need the vaccine.*

## **HDV, HEV, and GBV-C:**

### ***General Information***

Other forms of viral hepatitis include hepatitis D, and hepatitis E. Hepatitis D is not very common in the United States. Another virus, GBV-C, was initially thought to cause hepatitis (hepatitis G), but this has been challenged since evidence to date has not shown that infection with GBV-C results in liver disease.

### ***HDV, and HEV: Key Points***

- *HDV is transmitted in similar ways to HBV, but is not very common in the U.S.*
- *Active HBV infection is required in order to become infected with HDV.*
- *HEV is transmitted in similar ways to HAV.*

## **Hepatitis D:**

### ***General Information***

Hepatitis D, formerly known as delta hepatitis, is caused by the hepatitis D virus (HDV). The virus is not prevalent in the U.S., but is common in the Mediterranean, South America, and northern Africa. Its transmission routes are similar to those of HBV: primarily contact with infected blood or contaminated needles. In order to become infected with HDV, a person must also have active HBV infection. People coinfecting with HBV and HDV are more likely to have severe acute symptoms, develop chronic disease and have more severe and faster disease progression than those with HBV alone. The symptoms of HDV are similar to those of HBV, including flu-like symptoms, fever, fatigue, jaundice, dark urine, and pale-colored stools. Because HDV infection only occurs in people with active HBV, the HBV vaccine prevents HDV as well. Treatment of HDV with interferon has had limited success.

## Hepatitis E:

### General Information

Hepatitis E, also known as enteric hepatitis, is caused by the hepatitis E virus (HEV). The recent NHANES study estimated that 21% of Americans have HEV antibodies, which is an indication of prior infection. HEV transmission routes are similar to those of HAV, primarily the fecal-oral route, but it may also be transmitted by consuming raw or under cooked meat especially pork. Symptoms of acute hepatitis E are also similar to those of HAV. The disease is usually mild, but 20% of pregnant women with HEV experience severe, potentially fatal fulminant (acute liver failure) hepatitis. The virus is typically cleared by the body and does not become chronic. Currently there are no approved treatments for HEV. A vaccine to protect against HEV has been developed by China and hopefully it will be mass produced to protect people from the worldwide pathogen.

## GBV-C:

### General Information

Hepatitis G is an RNA virus that is very similar to hepatitis C. However, it has not been associated with any chronic liver disease. In fact, it seems to be a benign flavivirus that is widely present throughout the world. There has been no association between poor outcomes of patients who are infected with hepatitis C and hepatitis G at the same time. However, there is some evidence that, in people who are coinfecting with HIV and GBV-C, there is a slower HIV disease progression and lower transmission rate of HIV from mother to child.

Drug/Brand name	Resistance
Interferon alfa-2a (Intron A)	None
Lamivudine (Epivir-HBV)	14 - 32% at Year 1; 60 - 70% at year 5
Adefovir (Hepsera)	0% at year 1; 29% at year 5
Entecavir (Baraclude)	1.2% in treatment naïve at year 6; 57% in lamivudine resistant at year 6
Peginterferon alfa-2a (Pegasys)	None
Telbivudine (Tyzeka)	25% in HBeAg positive at year 2; 11% in HBeAg negative at year 2
Tenofovir (Viread)	0% at year 4; adefovir resistant HBV should be treated with tenofovir and another HBV antiviral

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