HEPATITIS

What does the term hepatitis mean? What are the different types of hepatitis?

Hepatitis is a general term that means “inflammation of the liver.” There are many different causes of hepatitis – viral, bacterial, infectious and non-infectious.

There are five major hepatitis viruses globally (Hepatitis A, B, C, D, and E). Hepatitis A (HAV), Hepatitis B (HBV) and Hepatitis C (HCV) are the most common in the U. S.

How are the different forms of viral hepatitis similar and different?

They are all communicable, target the liver and can cause similar symptoms. However, they are not biologically related. They have different molecular structures, epidemiological patterns and natural histories.

All hepatitis viruses have similar symptoms that can include one or more of the following:

- Asymptomatic – Viral hepatitis in some adults and many children shows no signs or symptoms. Nevertheless, asymptomatic people can spread the disease.
- Fever
- Fatigue
- Loss of appetite
- Nausea
- Vomiting
- Abdominal pain
- Grey-colored bowel movements
- Joint pain
- Jaundice (yellow color in the skin, mucus membranes, or eyes)

Because of the similarity of symptoms, blood or serologic tests are necessary to determine the specific cause of hepatitis.

What are the functions of a healthy liver? What impairs its regeneration?

The liver regulates many important nutrients. It also cleanses the body and bloodstream of toxic and unneeded substances.

The liver’s ability to regenerate is impaired by repeated or extensive damage. For example, chronic heavy drinking of alcohol or viral hepatitis infection can cause irreparable damage to the liver.

What’s the difference between acute and chronic viral hepatitis?

Acute viral hepatitis is a short-term infection that occurs within the first six months after exposure. If not severe, the liver will heal without long-term damage. In severe acute hepatitis infection or acute fulminant hepatitis, the liver can be destroyed putting the person’s life in danger.
After acute hepatitis infection, chronic viral hepatitis can develop with hepatitis B (HBV) or hepatitis C (HCV) infection but not hepatitis A (HAV) which is acute only.

In most cases, chronic hepatitis infection causes continuing inflammation that damages the liver over a period of years. The normal hepatic tissue (liver tissue) is replaced gradually with scar tissue causing cirrhosis. Chronic liver failure begins when the liver is no longer able to perform its normal vital functions.

A liver transplant is the only option for long-term survival after chronic liver failure.

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**HEPATITIS A (HAV)**

**What’s the overall trend in hepatitis A rates in the U.S.**?

Rates have steadily declined.

HAV is still the most frequently reported type of acute viral hepatitis in the U.S.

**What’s the severity of HAV?**

The severity of disease varies widely from no symptoms to severe illness.

Most people feel sick for several months but usually recover completely without lasting liver damage.

Fewer than 20 people per year die from HAV in the U.S. People over 50 years of age and those with chronic liver disease or alcoholism are at greater risk for death.

**How is the hepatitis A virus transmitted?**

HAV is transmitted primarily by the fecal-oral route.

Close personal contact is the most frequently reported source of infection. For example, an infected person does not wash hands properly after going to the bathroom and touches other objects or food, or when a caregiver does not wash hands after changing diapers or soiled linens.

Sexual activity with an infected partner can transmit HAV even without direct oral-anal contact.

Sexual transmission can occur through anilingus, anal intercourse, and other fecal contamination.

Contaminated food or water can spread HAV. This is most common in countries with poor sanitary conditions. Clean water supplies prevent waterborne outbreaks in developed countries. Outbreaks in the U.S. can occur when infected food handlers contaminate food.

Blood-borne transmission of HAV is rare even though viremia (HAV in the bloodstream) occurs in the early stages of infection.

Transmission from saliva has not been demonstrated.
Which groups are at risk for HAV infection?

Almost half of reported HAV cases have no known risk factor identified.

Among adults with identified risk factors, men who have sex with men are the majority of cases. Others include:

- Users of illegal drugs
- International travelers in countries where HAV is endemic and families adopting children from those regions.
- Occupational risk occurs for persons working with nonhuman primates susceptible to HAV infection.
- People in close contact with an infected person – sexual and non-sexual.
- Medical risks include chronic liver disease and clotting factor disorders.

What is the course of the disease?

HAV has an incubation period of about 28 days (ranging from 15-50).

HAV replicates in the liver and is shed in high concentrations in the feces from two weeks before to one week after the onset of clinical illness. This period is highly infectious.

Symptoms, if present, usually last less than two months although 10-15% of cases are prolonged or relapse for up to six months.

Fatality from acute liver failure is rare (0.5%).

HAV is acute and self-limited and does not result in chronic infection or chronic liver disease.

Once HAV infection resolves, protective antibodies give lifelong immunity against reinfection.

How do hepatitis A symptoms vary by age?

In children six years or younger, 70% have no symptoms. They are an important source of HAV transmission.

Older children and adults are typically symptomatic and have jaundice 70% of the time.

Signs and symptoms, when present in young children, usually occur abruptly and last less than two months.

Signs and symptoms are similar to other types of viral hepatitis. Blood or serologic tests are necessary to determine the specific virus.

What measures are recommended to prevent and control the spread of hepatitis A?

Vaccination with two doses six months apart is the best preventative measure. Vaccinations are recommended for:

- All children at the age of twelve months
- Adults with identified risk factors (see above)
- Any person desiring immunity.
Immune globulin (IG) provides short-term protection for approximately three months. It must be administered within two weeks after exposure for maximum protection.

Good hygiene including hand washing/hand sanitizer after using the bathroom, changing diapers and before preparing food prevents fecal-oral contamination.

Clean water and sewage systems prevent water contamination.

**What are the recommendations for post-exposure prophylaxis (PEP) to hepatitis A?**

The hepatitis A vaccine is recommended for healthy persons aged 1-40 years old who have been exposed recently and who have not been previously vaccinated.

Immunoglobulin (IG) is recommended for:

- Children under one year of age
- Immunocompromised persons
- Persons with chronic liver disease
- Persons allergic to vaccine
- Persons over 40 years old. (Vaccine may be used if IG not available.)

**For whom is post-exposure prophylaxis (PEP) recommended?**

PEP is recommended for

- Close personal contacts – household or sexual
- Persons who have shared illegal drugs with an HAV-infected contact
- Food handlers working with an HAV-infected food handler.

**How should hepatitis A be tested and diagnosed?**

Use the clinical case definition developed by CDC.

Confirm the hepatitis A diagnosis with a serologic test unless the case meets the case definition and has an epidemiologic link to a laboratory-confirmed case.

Pre-vaccination testing is not generally recommended unless it can reduce the costs of vaccinating people who are already immune and not interfere with initiation of vaccination.

Post-vaccination testing is not recommended.

**How is hepatitis A treated?**

There is no medication. Supportive treatment of rest, nutrition and fluids is recommended.

Hospitalization is required for patients with signs or symptoms of acute liver failure.

Use caution with medications that might cause liver damage or that are metabolized by the liver.

Consumption of alcohol should be avoided.
HEPATITIS B (HBV)

How is hepatitis B transmitted?

Sexual transmission accounts for most U.S. cases. HBV is passed primarily through the exchange of body fluids. It is 50-100 times more infectious than HIV.

Perinatal transmission from mother to child during birth is common in many parts of the world. In the U.S. routine testing of pregnant women and vaccination at birth have greatly reduced perinatal transmission.

Percutaneous transmission (puncture through the skin) occurs from sharing needles or drug paraphernalia, needle sticks, splashing of blood, and chronic hemodialysis.

Parenteral or horizontal transmission is not well understood. The majority of cases are in developing countries. It can result from daily family contact and sharing contaminated fluids through items such as toothbrushes and razors.

Which groups are at highest risk of HBV infection?

Developing countries, especially Southeast Asia and Africa have high rates of chronic HBV.

Other risk groups are: infants born to infected mothers, sex partners, sexually active persons not in long-term mutually monogamous relationships, persons with sexually transmitted disease, men who have sex with men, injection drug users, workers exposed to blood and blood-contaminated body fluids, hemodialysis patients, residents and staff of facilities for the developmentally disabled, and travelers to regions with higher rates of hepatitis B.

What is the natural history of HBV infection?

The incubation period averages 90 days after exposure to HBV with a range from 6 weeks to 6 months. HBV can be a self-limited, acute illness, or it can develop into a lifelong chronic infection. 90% of adults recover completely from the acute infection. The risk for chronic infection is greatest among infants (90%) and children under five (25-50%).

If the HBV infection resolves, protective antibodies give lifelong immunity.

Chronic HBV infection can lead to premature death from cirrhosis or liver cancer (25% of those infected in childhood and 15% infected in adulthood).

What are the signs and symptoms of hepatitis B?

Most children under age 5 and newly infected immunosuppressed adults are asymptomatic.

30-50% of persons five years and older have initial signs and symptoms.

Signs and symptoms are same for all viral hepatitis (see above).

When symptoms of acute hepatitis B occur, they typically last for several weeks but can persist for up to 6 months.
Persons with chronic HBV infection might be asymptomatic, or have a spectrum of disease ranging from chronic hepatitis to cirrhosis or hepatocellular carcinoma.

**What does CDC recommend for prevention and control of hepatitis B?**

Vaccine is the best prevention – 3 shots over 6 months for adults and 3 to 4 shots over 18 months for infants and children.

CDC recommends routine screening of all pregnant women and immunoprophylaxis of infants born to HBsAg-positive mothers.

Routine infant vaccination and vaccination of previously unvaccinated children and adolescents is recommended.

Unvaccinated adults at increased risk for infection should be vaccinated. (See list above.)

- These groups account for 95% of all new HBV infections.
- Also recommended is universal vaccination of adults who receive care in STD treatment facilities, HIV testing and treatment, drug abuse treatment programs, correctional facilities, healthcare settings targeting men who have sex with men, chronic hemodialysis facilities and end-stage renal disease programs, facilities for the developmentally disabled,

Booster shots are recommended only for hemodialysis patients and other immunocompromised persons. These patients should be tested regularly to see if booster shots are warranted.

**What are the recommendations for HBV post-exposure prophylaxis (PEP)?**

Hepatitis B immunoglobulin (HBIG) and hepatitis B vaccine are highly effective after exposure. HBIG is typically used as an adjunct to vaccination to provide increased protection. Guidelines vary by exposure source.

Persons exposed to HBsAg-positive source should receive:

- If they have written documentation of complete hepatitis B vaccine series – one booster dose.
- If they are in the process of being vaccinated – one dose of hepatitis B immune globulin (HBIG) plus completion of the vaccination series.
- If they are unvaccinated – both HBIG and hepatitis B vaccine as soon as possible after exposure (preferably with 24 hours).

Exposure to a source with unknown HBsAg status requires:

- No further treatment for someone with written documentation of a complete hepatitis B vaccine series.
- Completion of the vaccine series for persons not fully vaccinated.
- For unvaccinated persons – the hepatitis B vaccine series with the first dose administered as soon as possible after exposure, preferably within 24 hours.
How and why is HBV tested and diagnosed?

Testing is the best way to determine whether a person is infected with HBV since many people with acute and chronic hepatitis B are asymptomatic and don’t know that they are infected.

Testing for HBsAg is the first line of screening.

Different serologic markers can identify different phases of HBV infection; determine whether a patient’s infection is acute or chronic; and determine if a patient is immune due to prior infection or vaccination.

For whom is HBV testing recommended?

Testing is not recommended pre-vaccination.

Post-vaccination testing is not necessary after routine vaccination. Serologic testing for immunity is advised only for persons whose subsequent clinical management depends on knowledge of their immune status.

Testing for chronic hepatitis B infection is recommended for:

- Pregnant women
- Persons born in regions with intermediate or high HBsAg prevalence.
- Unvaccinated U.S.-born persons born to parents from countries with high rates of hepatitis B
- Infants born to HBsAg-positive mothers
- Household, needle-sharing, or sex contacts of HBVsAg-positive persons
- Men who have sex with men
- Injection drug users
- Patients with elevated liver enzymes (ALT/AST) of unknown etiology
- Hemodialysis patients
- Persons needing immunosuppressive or cytotoxic therapy
- HIV-infected persons
- Sources of blood involved in potential HBV exposure such as needle sticks.
- Donors of blood, plasma, organs, tissues, or semen

What is the treatment for acute and chronic hepatitis B?

For acute HBV infection, no specific medication is available. Supportive treatment with rest, nutrition, and fluids is used.

For chronic HBV infection:

- Antiviral drugs such as adefovir dipivoxil, interferon alfa-2b, pegylated interferon alfa-2a, lamivudine, entecavir, and telbivudine are available.
- Medical evaluation and regular monitoring are necessary to determine whether the disease is progressing.
HEPATITIS C (HCV)

Why is hepatitis C called a “silent epidemic?” What is the trend in the U.S.?

HCV is a silent epidemic because acute infection is usually asymptomatic and chronic symptoms usually do not become evident for decades. Few people are tested or diagnosed.

75% of those infected develop chronic hepatitis C. Of those, 20% develop advanced liver disease.

Rates are leveling off in the U.S.

Hepatitis C is the leading indication for liver transplants in the U.S.

How is HCV transmitted?

The hepatitis C virus is highly infectious and most efficiently transmitted through percutaneous (skin puncture) exposure to infected blood or blood-containing body fluids.

In about 20% of cases there is no known cause of transmission.

In the U.S. the most common means of transmission comes from injection drug use and sharing of injection equipment.

Donated blood, blood products, organs and tissues were a common source of transmission until 1992 when screening for HCV began in the U.S.

Other, less common sources of blood transmission are:

- Occupational injuries (needle sticks)
- Unsafe injection practices, lapses in infection control in healthcare settings
- Sharing of personal items contaminated with infectious blood (not an efficient mode of transmission)
- Unprofessional tattooing and body piercing

Sexual transmission is uncommon. Outbreaks have occurred in HIV-infected men having sex with men. Long-term sex partners of people with chronic HCV infection with no other risk factors have a very low prevalence (average 1.5%) of HCV.

Perinatal transmission during birth occurs less than 5% of the time.

Co-infection with HIV increases the transmission rate.

Which groups are at risk of HCV infection?

- Injection drug users – including those who injected only once many years ago
- Recipients of clotting factor concentrates made before 1987
- Recipients of blood transfusions or organ transplants before July 1992
- Chronic hemodialysis patients
- Healthcare workers after needle stick or sharps injury exposure to HCV-positive blood
• Persons with HIV
• Children born to HCV-infected mothers

What is the significance of the different HCV genotypes?
There are 6 genotypes and over 50 subtypes. Genotype 1 is the most common in the U.S. Genotype information is helpful in defining the epidemiology and making recommendations for treatment.

What is the natural history of HCV? What is the progression of hepatitis C? What are contributing factors? What is the immune response?
The incubation period averages 45 days and ranges from 14 to 180 days. The progression of the disease varies. Of 100 people infected with HCV:

- 15-25 will clear the virus without developing chronic infection.
- 75-85 will develop chronic infection of which:
  - 60-70 will develop chronic liver disease.
  - 5-20 will develop cirrhosis over a period of 20-30 years.
  - 1-5 will die of liver cancer or cirrhosis.

Contributing factors that hasten the progression of chronic HCV infection are:

- HIV/HCV co-infection resulting in cirrhosis nearly twice as fast.
- Other contributing factors include: increased alcohol intake, alcoholic liver disease, age of 40 or older at time of infection, being male.

If some changes evade immune response during replication, no protective antibodies develop and no lifelong immunity is created.

What are the signs and symptoms of acute and chronic hepatitis C?
Very few cases of acute hepatitis C are ever diagnosed or reported. Only 20-30% of newly infected persons develop symptoms, usually 4-12 weeks after exposure (ranging from 1-14 weeks). Symptoms are similar to all types of viral hepatitis. Fatigue is a common symptom.

In chronic hepatitis C, some people remain asymptomatic. Those who develop advanced liver disease may take 20-30 years for symptoms to develop. Disease can include cirrhosis or hepatocellular carcinoma. Some people are identified as HCV-positive when blood screening indicates elevated levels of alanine aminotransferase (ALT).
**How can hepatitis C be prevented and controlled?**

There is no vaccine or post-exposure prophylaxis.

Primary prevention requires keeping people from becoming infected.

Secondary prevention involves early detection and treatment to reduce complications.

CDC guidelines are under revision.

Routine testing of high risk groups (defined above) can help identify asymptomatic people and provide them with information to prevent transmission. People with persistently abnormal alanine aminotransferase levels should also be tested.

**What tests are available to identify hepatitis C?**

Anyone infected with HCV will develop antibodies to hepatitis C (anti-HCV) and will always test positive for anti-HCV. The first screening test for anti-HCV antibodies is a serological assay such as enzyme immunoassay (EIA) or enhanced chemiluminescence immunoassay (CIA).

The nucleic acid test is the second recommended test if the immunoassay detected anti-HCV antibodies.

The most commonly used test for HCV RNA is a polymerase chain reaction (PCR) test.

Quantitative PCR tests provide information about viral load.

A positive PCR indicates that a person is presently infected.

HCV RNA can be detected as early as two to three weeks after infection.

Recombinant immunoblot assay (RIBA) is a sensitive, but infrequently used, supplemental test.

**What are the treatment guidelines for hepatitis C?**

Persons with chronic HCV infection should be monitored for chronic liver disease, including assessment of liver function tests and evaluation of the severity of liver disease for possible treatment with antiviral medication.

Acute HCV infection, when recognized, may be treated with antiviral medication to prevent chronic infection in some cases.

The current standard of treatment is the immune booster pegylated interferon and the antiviral ribavirin. New oral treatments are forthcoming.

Treatment of HCV in HIV co-infected persons is still investigational. Anti-HCV treatment might improve tolerance to highly active antiretroviral therapy (HAART).
How should HC-infected patients be counseled?

Patients who test positive for anti-HCV should know about:

- The need for RNA testing.
- How to protect their liver from further harm by:
  - Avoiding drinking alcohol.
  - Checking with their doctor before taking any new medicines including OTC and herbal supplements.
- How to reduce the risk of transmission of HCV by:
  - Not donating blood, body organs, tissue, or semen.
    - Not sharing personal items that might have blood (toothbrushes, razors, etc.)
    - Covering cuts and sores.
  - The need for medical evaluation for chronic liver disease and possible treatment.

HCV-positive persons with one, long-term steady sex partner do not need to change their sexual practices although they should discuss the low but present risk for transmission.

HCV-positive women do not need to avoid pregnancy or breastfeeding.