

Epidemiology and Clinical Course of Hepatitis C Infection

Michael Rigsby, MD
National Hepatitis C Program



Key points

- Approximately 85% of people infected with hepatitis C develop chronic infection (15% clear the infection spontaneously).
- The natural history of hepatitis C-related liver disease is long.
- The majority of those infected will never develop life-threatening complications.
- Approximately 10-20% of infected patients will eventually develop cirrhosis.
- Cirrhosis for Hepatitis C is the leading reason for liver transplantation in the US.

What is hepatitis C?

Hepatitis C is a virus that infects liver cells. Viruses are small packages of genetic material – DNA or RNA – that invade living cells and use the cell's biologic machinery to replicate – to make new copies of the virus. The cell is often destroyed in the process, or is attacked by the host immune system, which recognizes the virus as something foreign.

There are several different hepatitis viruses. Each is given its own alphabetical name (hepatitis A, hepatitis B, etc.). The only thing they have in common is that they infect the liver. They differ in many other ways, including their potential for causing chronic liver damage and the way that they are spread.

Hepatitis C was discovered in 1989. Prior to that, it was called non-A, non-B hepatitis. Tests to detect the virus and the antibodies that the body produces when infected with hepatitis C have made it possible to learn much more about the epidemiology and transmission of hepatitis C. These tests have shown that many people are infected without showing signs of illness.

There are several major sub-types of hepatitis C, known as genotypes. Genotype 1 is most common in the United States. The various genotypes do not differ in terms of how they affect the liver, but genotype 1 is more difficult to treat successfully than genotypes 2 and 3.

How common in hepatitis C infection?

Hepatitis C is the most common blood-borne infection in the United States. Approximately 4 million Americans are believed to be infected. Although most of them do not have severe liver disease, hepatitis C infection is currently the most common reason for liver transplantation.

	Type of Hepatitis Virus				
	A	B	C	D	E
Source of virus	feces	blood/ blood-derived body fluids	blood/ blood-derived body fluids	blood/ blood-derived body fluids	feces
Route of transmission	fecal-oral	percutaneous per mucosal	percutaneous per mucosal	percutaneous per mucosal	fecal-oral
Chronic infection	no	yes	yes	yes	no
Prevention	pre/post- exposure immunization	pre/post- exposure immunization	blood donor screening; risk behavior modification	pre/post- exposure immunization; risk behavior modification	ensure safe drinking water

Centers for Disease Control

New infections with hepatitis C have declined because of the screening of blood used for transfusion. However, because disease from hepatitis C often occurs decades after infection, the number of people with complications from hepatitis C continues to rise.

Transmission of hepatitis C

Hepatitis C is spread primarily by blood-to-blood contact. Historically, transfusion of blood or blood products was the most common means of infection. Injection drug use is another common mode of transmission, because blood can contaminate shared needles and other drug-use equipment. These two types of transmission account for the majority of known cases of hepatitis C.

Less frequently, hepatitis C can be spread in other ways. Sexual transmission is possible, but the chances are far lower for a single sexual exposure than for a single blood exposure. However, because sexual activity is much more common than transfusions or injection drug use, sexual transmission results in a significant number of hepatitis C infections. Infected mothers can pass the virus to their newborns, but this is not common.

Studies of large numbers of hepatitis C-infected individuals have produced some conflicting or confusing results about other possible modes of transmission. In some studies infection was associated with snorting cocaine, having tattoos, or excess alcohol use. Whether these are directly associated with transmission or are instead indicators of other high-risk behavior is not clear. These are probably best thought of as epidemiologic associations rather than proven methods of transmission.

The course of hepatitis C infection

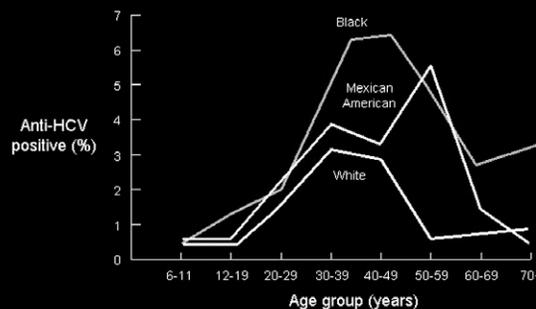
Most people do not get sick immediately when they are infected with hepatitis C. About 10-20 percent develop a mild case of acute hepatitis, usually 6-7 weeks after infection. Like other types of acute hepatitis, this phase may produce jaundice (yellowing of the skin and eyes), malaise, weakness, and loss of appetite. The acute phase resolves on its own.

About 15% of people who are infected with hepatitis C are able to eradicate, or clear, the infection. The body's immune response to hepatitis C is more effective in these people for reasons that are not known. The remaining majority develops chronic infection; that is, the virus continues to replicate and infect more liver cells. The virus also circulates in the bloodstream although the liver is the main target.

Everyone who is infected – whether they clear the virus or not – develops antibodies to hepatitis C. These antibodies are the basis for the blood test used to determine if a person has ever been infected. Only those who have chronic infection have the actual virus in their blood. PCR or other tests to detect the presence of the virus are used to determine whether infection is chronic. Successful treatment eliminates virus from the liver and the bloodstream.

According to the CDC's National Health and Nutrition Examination Survey (NHANES) of 1988-1994, 3.9 million Americans were infected with HCV, and of this group, 2.7 million were estimated to have chronic infection. Because NHANES is a population-based household survey, it does not include certain groups with a substantially increased prevalence of infection, such as persons who are incarcerated, homeless, or institutionalized.

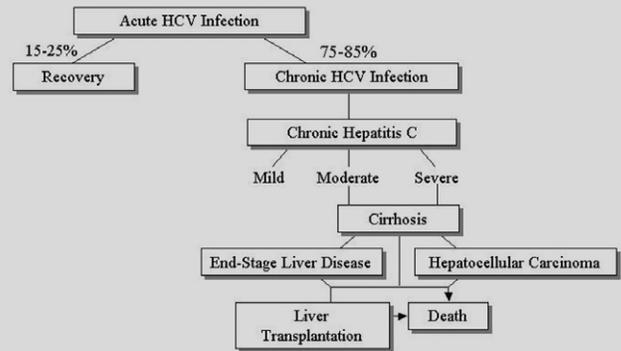
Prevalence of HCV Infection, United States, 1990



Over time, the liver is damaged by the effects of the virus and by the attempts of the immune system to kill the virus by attacking infected cells. The damage to the liver is called fibrosis, which is a kind of scarring. The normal, healthy liver tissue is replaced by fibrous scar tissue. Eventually, the scarring may become severe. This is known as cirrhosis.

The course of hepatitis C disease is variable. The large majority of infected individuals never develop severe manifestations of liver damage. Estimates of the proportion of chronically infected persons who develop cirrhosis 20 years after initial infection vary widely from 2 to 4 percent in studies of children and young women to as high as 20 to 30 percent in middle-aged transfused subjects. The actual risk is likely intermediate between these two ranges, on the order of 10 to 15 percent. All of the factors that contribute to whether the disease progresses rapidly, slowly, or not at all are not known. In general, being male and being infected at an older age seem to accelerate disease progression. Alcohol consumption and infection with HIV also accelerate the course of hepatitis C infection.

Hepatitis C Infection: Spectrum of Disease



The clinical manifestations of hepatitis C infection

The most important clinical manifestations of hepatitis C infection are those that result from liver cirrhosis. The cirrhotic liver cannot perform its vital functions, which include cleaning the blood of toxins and producing important proteins such as those that help the blood to clot. The consequences can include confusion and eventually coma, bleeding, infections, and accumulation of fluid in the abdominal cavity. Liver cancer (known as hepatocellular carcinoma) can develop within the cirrhotic liver.

In the United States, deaths related to hepatitis C are more likely to be due to complications of cirrhosis than to liver cancer. The only effective long-term treatment for those who have developed decompensated cirrhosis is liver transplantation. Currently, hepatitis C is the primary reason for liver transplantation in the United States.

Hepatitis C accounts for approximately one-third of hepatocellular carcinoma (HCC) cases in the United States. The rate of hepatitis C-HCC continues to rise in United States and worldwide, in part because of the increasing numbers of persons who have been chronically infected for decades, the presence of co-morbid factors, and the longer survival of persons with advanced liver disease due to improved management of complications.

There are other complications outside the liver, known as extra-hepatic manifestations. These include skin and joint problems, diabetes and kidney failure, and cancer of the lymph nodes. These are all less common than the liver complications.

Prevention and treatment

There is no vaccine available to prevent hepatitis C infection. Those who are at risk from injection drug use should be counseled about risk and assisted with reducing their risk by referral to drug treatment programs. Because the incidence of transmission between monogamous sexual partners is low, the CDC does not recommend that such couples change sexual practices if one partner is infected. The already low risk of sexual transmission can be further reduced by limiting the number of sexual partners and using condoms. While household transmission of hepatitis C is rare, individuals who are infected should not share razors, toothbrushes, or other

items that can become contaminated by blood with others. Blood products and donated organs for transplantation are screened for hepatitis C, but those who know they are infected should voluntarily refrain from donating blood, blood products, or organs for transplant.

Preventing the adverse health consequences of hepatitis C is sometimes referred to as secondary prevention. There are many things patients and their health care professionals can do to limit the morbidity and mortality related to hepatitis C.

Current treatment for hepatitis C consists most commonly of the combination of interferon and ribavirin. This treatment is given for 6 to 12 months and led to viral eradication in up to half of patients treated in clinical trials. A full discussion of treatment is available in the VA "Treatment Recommendations for Patients with Chronic Hepatitis C," available in electronic format at www.va.gov/hepatitisc.

Preventing morbidity and mortality in those infected

- Identification and treatment
 - Screening and testing
 - Evaluation and monitoring
 - Antiviral therapy when appropriate
- Reduce the risk of disease progression
 - Avoiding alcohol and liver-toxic drugs
 - Maintaining healthy lifestyle
- Prevention of complications from cirrhosis
- Screening for liver cancer
- Early identification of candidates for transplant

