Hepatitis B Progression

Soon after the hepatitis B virus (HBV) enters the body, it infects cells in the liver called hepatocytes. In response to this infection, the immune system tries to destroy the virus. The liver participates in this fight by increasing the amount of enzymes it manufactures, which causes inflammation of the liver (hepatitis).

The initial infection is known as acute hepatitis B, meaning short-term inflammation of the liver. Most people are able to clear hep B from the body within six months of becoming infected. If they clear it, they are no longer infected, nor can they infect others. Additionally, they now have hepatitis B antibodies, which will protect them from future reinfection.

Chronic Hepatitis B Virus Infection

A chronic hepatitis B infection means that the immune system is not able to get rid of the virus within six months after infection. In other words, the virus continues to reproduce in the person’s liver for several months or years after infection. This can increase the risk of liver damage and liver cancer. What’s more, someone with chronic HBV infection can transmit the virus to others. The risk of chronic infection is higher in infants and children than it is in adults.

Most adults who are infected with hepatitis B clear the virus during the acute phase of the infection. People who have impaired immune responses have a higher risk of not clearing hep B on their own and are more likely to develop chronic HBV infection. Examples are:

- People living with HIV
- Organ transplant recipients
- Those undergoing chemotherapy
- People on dialysis for kidney problems
- Anyone on steroid therapy to suppress the immune system.

Phases of Chronic Hepatitis B Infection

Chronic hepatitis B infection is characterized by four phases. Not everyone will experience all four phases, and the lengths of the phases vary among people. Your medical provider will order lab tests regularly to monitor changes in your condition. The phase you are in is determined by multiple lab tests, not by a single result. To learn more about these tests, visit Hepatitis B Lab.
Immune-Tolerant Phase

In this phase, HBV is replicating, or multiplying, quickly, but inflammation is low. People who contracted hep B during birth may be in this phase for decades before progressing to the next phase. Key characteristics are:

- Normal ALT (liver enzymes)
- HBV DNA (viral load) > 1 million IU/ml
- Positive HBeAg (hepatitis B e antigen)
- Minimal liver inflammation
- Minimal liver fibrosis

HBeAg-Positive Immune-Active Phase

In this phase, HBV is beginning to do significant damage to the liver, both in terms of inflammation and fibrosis. People who contracted hep B in infancy or childhood typically transition to this phase in their thirties. In this stage, people are monitored for the loss of HBeAg and the development of antibodies called anti-HBe. This process is called seroconversion. HBeAg seroconversion marks a transition from the immune-active phase to the inactive carrier state (see “Inactive Chronic Hepatitis B Phase”). HBeAg seroconversion is associated with lower rates of disease progression to cirrhosis and hepatocellular carcinoma, and improved survival rates. Key characteristics are:

- Elevated ALT
- HBV DNA (viral load) ≥ 20,000 IU/ml
- Positive HBeAg
- Moderate to severe liver inflammation
- Moderate to severe liver fibrosis

Inactive Chronic Hepatitis B Phase

This is also called the inactive carrier state. In this phase, HBe antibodies (anti-HBe) are present. ALT is normal, and HBV DNA may be low or undetectable. Inflammation is minimal, and fibrosis level can vary depending on how much liver damage occurred in the previous stage. Around 67 to 80 percent of people will remain in this inactive stage; 4 to 20 percent may revert one or more times to the HBeAg-positive phase. Key characteristics are:

- Normal ALT
- HBV DNA (viral load) undetectable or < 2,000 IU/ml
- Negative HBeAg
- Minimal liver inflammation
Variable liver fibrosis

HBeAg-Negative Immune Reactivation Phase
In this phase, people have seroconverted to anti-HBe positive, but their chronic HBV is very active. ALT and HBV viral loads are elevated. Liver inflammation and fibrosis levels are moderate to severe. In this phase, HBV has usually mutated to a variant. Key characteristics are:

- Elevated ALT
- HBV DNA (viral load) $\geq$ 2,000 IU/ml
- Negative HBeAg
- Moderate to severe liver inflammation
- Moderate to severe liver fibrosis

Resolved Chronic Hepatitis B Virus Infection
Every year, approximately 0.5 percent of people will clear HBsAg (hepatitis B surface antigen); most will also acquire HBs antibodies. When this occurs, it means their chronic hepatitis B infection is resolved. Some will continue to have low levels of HBV DNA. A resolved chronic hep B infection reduces the risk of liver failure and death.

Risks
Here are some of the factors that increase the risk of cirrhosis (scarring of the liver) and/or hepatocellular carcinoma (HCC), a type of liver cancer:

- Over age 40
- Male
- Immune compromised
- HBV DNA (viral load) $> 2,000$ IU/ml
- Elevated ALT
- Prolonged time to HBeAg seroconversion
- HBeAg-negative
- Genotype C chronic HBV
- Presence of other viral infections, such as HCV, HDV or HIV
- Heavy alcohol use
- Metabolic syndrome (diabetes, obesity)

Additionally, adults from sub-Saharan Africa and those with a family history of HCC are at
increased risk of developing HCC. Other factors that increase HCC risk are smoking and consuming aflatoxin, a mold found in peanuts, corn and cottonseed.

Among 100 untreated adults with chronic hepatitis B infection, in five years roughly:

- Eight to 20 people will develop cirrhosis; of those,
- 20 people will go on to experience severe liver failure known as hepatic decompensation,
- and/or two to five people will go on to develop HCC.

About 15 percent of adults who develop chronic hepatitis B after childhood—along with 25 percent of those who became chronically infected as children—die prematurely from cirrhosis HCC. In the United States, approximately 2,000 to 4,000 people die every year from chronic hepatitis B–related causes.

For those wanting complete and technical information, click here to read about the prevention, diagnosis, and treatment of chronic hepatitis B published by the American Association for the Study of Liver Diseases (AASLD), February 2018

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