Hepatitis B

The causative agent is HBV, which is a DNA virus (*Hepadnaviridae*). Hepatocytes are broken down by the cytotoxic action of T and NK cells (they recognize the virus antigen bound to the surface of the hepatocyte). The virus is carried by 5% of the population. It is one of **the most serious viral diseases in humans** – one in five carriers dies of cirrhosis, one in nine from hepatocellular carcinoma. **It is transmitted through blood and bodily fluids** (sexual transmission). The incubation period is 30-180 days (most often 60-90 days)[1].

Antigens

- **HBsAg** (surface, Australian Ag) - 3 subtypes. It allows the virus to penetrate the hepatocyte. Its detection is a sign of the presence of the virus in the body (at any period of infection, in acute and chronic hepatitis - in the replication and integration phase).
- **HBcAg** (core antigen) - a protein that envelops the DNA of the virus. Present on the hepatocyte membrane (immunofluorescence in biopsy), where it is exposed to MHC I and recognized by TC and NK cells. Can be identified only in the period of replication (acute and chronic replication phase).
- **HBeAg** (envelope antigen) - part of HBcAg, which is secreted only during viral replication (in so-called wild type viruses), mutants that do not form HBeAg do exist. The antigen indicates active virus replication in the liver cell (in acute and chronic replication hepatitis). It is a sign of high infectivity of the patient.

Antibodies

- **Anti-HBs** – neutralizing (by binding to HBsAg on the surface of the virus prevents its entry into the cell), it is in the serum of people who have had HBV infection (then anti-HBc and anti-HBe are also present), or in people vaccinated (isolated anti-HBs positivity).
- **Anti-HBc** – the most specific and sensitive antibody in HBV infection - is present after any exposure to the virus (it is a trace that the virus leaves behind in the body).
- **Anti-HBe** – is usually present after the infection (not in the period of active replication of the virus, when HBeAg predominates).

In the serum of infected persons or persons after infection, either the relevant antigen or antibody is detected, always one which is in excess and not bound in the immunocomplexes.

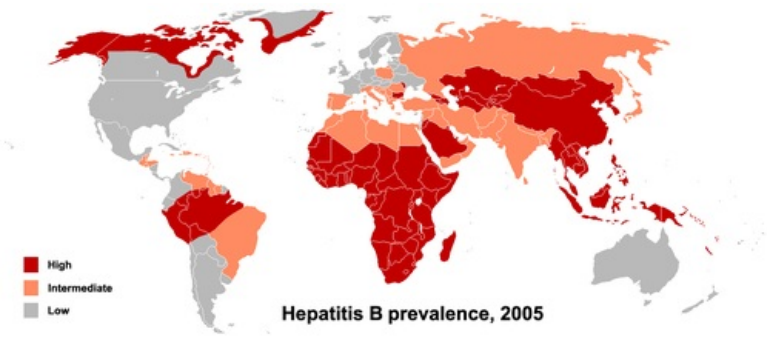
	HBsAg	anti-HBs	HBeAg	anti-HBe	IgG anti-HBc	IgM anti-HBc	HBV DNA
Acute VH B	+	–	+	–	+	+	+
Chronic VH B-active replication	+	–	+	–	+	+/–	+
Chronic VH B-inactive carrier	+	–	–	+	+	–	–
Past infection	–	+	–	+	+	–	–
Successful vaccination	–	+	–	–	–	–	–

Thus, in the period of active inflammation (acute hepatitis B and chronic hepatitis in the replication phase), HBsAg and HBV DNA (PCR) are detected as signs of the presence of virus and anti-HBc (with the presence of HBcAg in the hepatocyte membrane) and HBeAg. HBV DNA is not detectable in an inactive carrier, there are no HBcAg in the hepatocyte membrane, therefore no HBeAg is detected (however, there are anti-HBc and anti-HBe antibodies) - HBeAg seroconversion - anti-HBe. After infection, only antibodies are detected, not antigens (seroconversion HBsAg - anti-HBs, HBeAg - anti-HBe).

Etiopathogenesis

Hepadnavirus, has reverse transcriptase. Its genome is a partial double helix of circular DNA.

The genome is unique, each piece of DNA encodes something (even more than one thing).

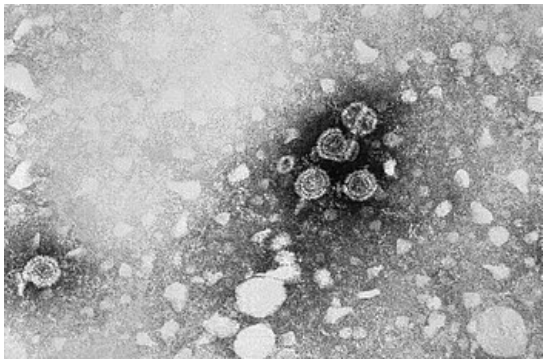


The global prevalence of hepatitis B

- HBcAg ("core") - a nucleocapsid protein, it still has a part of the DNA called pre-core, when it is translated in its entirety (pre-core + core), HBeAg is formed.
- HBsAg ("surface") - is put on the membrane of hepatocytes, it is on the envelope of the virus and much of this antigen is produced by the hepatocytes and freely released into the circulation.
- DNA polymerase – reverse transcriptase, occupies most of the genome.
- HBX - a protein from the X region, is essential for viral replication, acts as a transcriptional transactivator of viral genes, and also as a transactivator of many host promoters. It is thought to play a role in the development of hepatocellular ca.

The course of infection

It often occurs inapparently, especially in children and immunodeficient patients.


Hepatitis B: virions

Acute infections

Elimination by the immune system in 85-90% of the cases. The virus enters the liver through the bloodstream. Through HBsAg, it enters the cell, where it replicates in the nuclei of hepatocytes. HBsAg and HBeAg are released into the serum. HBcAg is bound to the cell surface, which is recognized by immunocompetent cells that induce lysis of affected hepatocytes. Release of virions into the circulation and attack of other hepatocytes, the release of enzymes (transaminases - increase of **ALT** and **AST** in serum), decreased ability of the liver to secrete bilirubin (hyperbilirubinemia to hepatocellular jaundice). In case of an excessive immune response, fulminant hepatitis with acute liver failure.

Chronic stage

10-15%. Depending on the success of the immune response, two situations occur. **Replication** - constant inflammatory activity (multiplication of the virus with HBcAg on the surface of hepatocytes, which are lysed by lymphocytes) - can progress to liver cirrhosis to cancer. At this stage the patient is highly infectious, JT levels are elevated. Furthermore, **integration** - decrease in inflammatory activity (stopping the multiplication of the virus, HBcAg disappears from the hepatocyte membrane, viral DNA integrates into the hepatocyte genome) - so-called carrier, infectivity is less but not zero, liver tests (transaminases) are normalized.

During perinatal transmission, due to the immature immune system, the child always develops chronic infection with the risk of developing carcinoma after the age of 20. It must be vaccinated passively after birth (applies to all newborns of HBsAg positive mothers), actively vaccinated after one week, and only then can the mother breastfeed the baby.

Acute hepatitis B

The prodromal stage lasts up to several weeks, and arthralgia or rash often occurs. Jaundice lasts longer than in the case of the VHA. **Arthralgia and pruritic rash** due to circulating immunocomplexes may be present. The worst complication is the **development of liver failure** - especially in the elderly and exhausted.

90% of neonates, 30–40% of children, 5–10% of adults lead to chronicity. Fulminant form - in about 1 in 1,000, mostly women, the patient dies within 10 days of hepatic coma caused by very rapid destruction of hepatocytes by cytotoxic T lymphocytes.

Chronic hepatitis B

It manifests itself either as a consequence of the acute or primarily - without an obvious acute phase.

Histologically we distinguish:

- **benign form** - persistent hepatitis (patient has mild clinical difficulties, slightly elevated liver tests, not infectious);
- **progressive form** - aggressive hepatitis (the patient has significant clinical difficulties, impaired liver function, has HBsAg and HBeAg in the blood, but lacks antibodies, the virus multiplies and is in the blood, the course and prognosis are serious, the risk of cirrhosis and hepatocellular carcinoma, is infectious).

According to the activity of the virus, we distinguish:

- **replication phase** - multiplies in hepatocytes;
- **integrated phase** - latent storage in the genome.

During replication, various mutants of the virus are created:

- pre-core mutant - does not form HBe antigen - more often liver failure, faster cirrhosis, less sensitive to interferon;
- then only the defective mutant is selected during treatment, starting treatment as soon as possible before the mutant is formed.

Asymptomatic carrier of VHB

They have no **clinical, biochemical or biopsy** symptoms. **Only the presence of HBsAg in the serum** is evident. It may disappear spontaneously, rarely it may develop into chronic VHB. Therefore, if such a patient emerges, they are dispensarized. We detect HBeAg and anti-HBe to detect active virus replication, we detect ALT.

Pregnancy hazard - 90% risk of infecting a baby during childbirth, therefore HBsAg examination is performed on all pregnant women. In the case of positivity, the newborn must be passively immunized within 12 hours.

Diagnostics

Prior to the development of jaundice, transferases are elevated. **Serology is performed by ELISA**. As the first sign of infection, HBsAg appears in the serum (a few weeks before the others), which disappears from the serum during recovery. When HBs cannot be detected (in small amounts of HBV), we detect IgM against HBc. Examination of the replication or integrated phase of chronic HBV is an antigen - HBe and IgM against it indicate a replication phase.

If HBeAg disappears, the patient's infectivity decreases. There is an increase in viral DNA polymerase in serum. Anti-HBc remains for life and are markers of past infection. Anti-HBs occur during acute infection, but mainly after vaccination. The most sensitive marker of infection is **PCR**.

Therapy

- IFN-α (necessity of s.c. application, for so-called pegylated IFNs once a week is enough);
- lamivudine (viral DNA synthesis blocker, p.o application);
- adefovir dipivoxil (indicated for lamivudine resistance).

Treatment is indicated for chronic infection (over 6 months) and viremia over 100,000 copies/ml.

Immunisation

The principle is the binding of the antibody to HBsAg, which aims to prevent the virus from penetrating the hepatocyte:

- **active (prophylactic)** - administration of an immunogenic fragment of HBsAg leading to the formation of anti-HBs;
- **passive (post-exposure)** - administration of anti-HBs from the serum of immunized donors.

Links

Related articles

- Viral hepatitis
- Jaundice (icterus)
- Jaundice
- PCR
- Immunisation

External links

- HUSA, Petr – PLÍŠEK, Stanislav – ŠPERL, Jan, et al. *Diagnostika a léčba chronické hepatitidy B : Doporučený postup České hepatologické společnosti a Společnosti infekčního lékařství* [online]. Společnost infekčního lékařství ČLS JEP, ©2009. The last revision 2009-04-09, [cit. 2011-04-09]. <https://www.infekce.cz/DoporVHB09.htm>.
- Hepatitis B (czech wikipedia)
- Hepatitis B (english wikipedia)

Sources

- PASTOR, Jan. *Langenbeck's medical web page* [online]. [cit. 2010]. <http://langenbeck.webs.com>.
- BENEŠ, Jiří. *Studijní materiály* [online]. [cit. 2010]. <http://jirben.wz.cz>.

References

1. Doporučené postupy pro praktické lékaře. *Virové hepatitidy*. 2001. reg. č. o/020/016. Autoři: Stanislav PLÍŠEK a GALSKÝ Jan. Available from <http://www.cls.cz/dokumenty2/postupy/r016.rtf>.

Literature used

- HAVLÍK, Jiří, et al. *Infektologie.* 2. edition. Praha : Avicenum, 1990. pp. 393. ISBN 80-201-0062-8.
- LOBOVSKÁ, Alena. *Infekční nemoci.* 1. edition. Praha : Karolinum, 2001. pp. 263. ISBN 80-246-0116-8.