Hepatitis B virus

Hepatitis B virus infections :

the viral Genome of hepatitis B virus consist of

1- a partially double stranded DNA usually with a short and a single stranded piece
2- it comprise usually 3,200 nucleotides making **it the smallest DNA virus.**
3-known it's from the family Hepadnaviridae viruses.

the main component of the virus:

1- the core Hepatitis B core antigen
2-the precore hepatitis B e antigen and that indicate usually infectivity and replication
3- the envelope of the virus contain the Hepatitis B surface antigen

Characteristics

1- Hepatitis B is usually asymptomatic or limited illness with fever and jaundice for days to weeks
2- it become chronic in up to 10% of patients and it might lead to liver cirrhosis and hepatocellular carcinoma
3- Hepatitis B virus has a DNA dependent DNA polymerase and it has only one serotype and there is a vaccine for Hepatitis B viruses
4- it usually has three different types of particles the Virion or Dane particle the Spheres and the filaments

Hepatitis B virus Epdimology

For epidemiological and medical purposes, there are four strains of hepatitis B virus based on the serological subtyping of hepatitis B surface antigens into groups, specific usually given the abbreviation a and two sets of mutually exclusive sets of epitopes: D or Y, as well as W or R. So that gives us four options. Speaking of hepatitis B virus, the epidemiology of hepatitis B virus distribution is worldwide, with an estimated two billion people — they have markers of infection.there is more than 400 million people who have chronic infection with hepatitis B virus so we have 400 million carriers worldwide and usually the **incidence of death from Hepatitis B virus infection is usually 1 million death per year**

Extra exp for better understanding

Hepatitis B virus is classified into four strains based on differences in its surface antigen (HBsAg). All strains share a common antigen called "a", and then differ by having one epitope from each of two mutually exclusive sets: either D or Y, and either W or R. This creates four possible subtype combinations: aDw, aDr, aYw, and aYr. These subtypes are important for understanding the virus's global distribution, tracking infections, and designing vaccines and diagnostic tools

Root of transmission

a hepatitis B virus as we said before it cause what is known as serum hepatitis so the spread of this virus is either by the intravenous route in other words the

1- transfusion of infected blood or blood products or by contaminated needles used by drug addicts tattooist aquapuncture
2- or by close personal contact such as during sexual intercourse particularly in male homosexuals the virus can be found in semen as well as the saliva
3- the vertical transmission have been documented from mother to child during birth or soon after birth the **usual mean of transmission worldwide needle stick injuries has resulted in higher risk of hepatitis B especially in the medical staff**

Hepatitis B virus can often lead to a type of liver cell damage known as piecemeal necrosis, now more commonly called interface hepatitis. This is a type of necrosis frequently seen in hepatitis and is characterized by inflammation that spreads from the portal tract into the periportal zone. It involves the death (necrosis) of periportal hepatocytes and disruption of the limiting plate — the boundary between the portal tract and the surrounding liver cells

incubation period

may be as brief as 7 days or as long as
160 days mean approximately usually 10 weeks Hepatitis B virus can cause acute or chronic symptomatic or asymptomatic disease which of these occur seems to be determined by the person immune response to the infection

Acute Hepatitis B

- Gradual onset of fatigue
- Loss of appetite ,Nausea
- Pain and fullness in the right upper abdominal quadrant
- Early in the course of the disease, pain and swelling of the joints and occasionally frank arthritis may occur (antigen-antibody complex-mediated)
- Some patients develop rash
- With increasing involvement of the liver, there is increased cholestasis (reduction or stoppage of bile flow.)
- Clay-colored stool
- Darkening of the urine
- Jaundice
- Symptoms may persist for several months

💗fulminant hepatitis leading to extensive liver necrosis and death develop in less than 1% of affected people with hepatitis B virus .

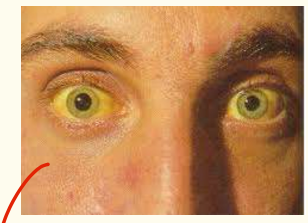
💗infection development of chronic hepatitis occur in approximately 10% of all patients with hepatitis B infection

💗the cellular carcinoma thereafter and up to 20% of the patient

💗progression to chronic disease is inversely related to the age of infection

💗approximately 90% of infected neonates they become chronic carriers of hepatitis B virus infection

Be aware that the hepatocellular injury is due to the cytotoxic T-cell, while the antigen–antibody complexes cause the arthritis and the vasculitis phenomena we talked about. As we said, about 5% become carriers. 90% of infected neonates become chronic carriers. There is a high risk of hepatocellular carcinoma, and the hepatocellular carcinoma with hepatitis B virus infection usually results from the integration of the viral DNA into the cellular DNA



Lifelong immunity from the hepatitis B virus can be confirmed by the detection of the hepatitis B surface antibody (anti-HBs).

In those pics , we see a hepatitis B patient in their icteric phase, where jaundice is visible.
With increasing involvement of the liver, there is rising cholestasis, which leads to clay-colored stool, darkening of the urine, and persistent jaundice.
These symptoms may last for several months before finally resolving.
The clinical presentation of hepatitis B virus in children is generally less severe than in adults, and the infection may even be asymptomatic in many pediatric cases

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Clinically apparent illness occurs in as many as 25% of those infected with hepatitis B virus. The majority, 90% of infected people, recover, and recovery is usually indicated by a decline in fever and renewed appetite.

Chronic hepatitis occurs, as we said, in 5% to 10% of people infected with hepatitis B virus, usually after mild or an apparent initial disease. Approximately one-third of these people will have chronic active hepatitis with continued destruction of the liver, leading to scarring of the liver and cirrhosis and liver failure or primary hepatocellular carcinoma.

The other two-thirds will have chronic passive hepatitis and are less likely to have problems.

Chronic hepatitis may be detected accidentally by finding elevated liver enzyme levels on a routine blood chemistry profile. Chronically infected people are the major source of spread of the virus, and they are at risk of fulminant disease if they become coinfected with hepatitis D virus.

Fulminant hepatitis occurs in approximately 1% of icteric patients, and it might be fatal in those patients

Testing Hepatitis B

In addition to the clinical picture described earlier and the liver chemistry tests — as we said, ALT, alkaline phosphatase, and total bilirubin — all of them can be found elevated.
Serology can be relied upon for the diagnosis of hepatitis B virus infection.
Almost all patients who develop jaundice show anti-hepatitis B core antigen IgM positive.
At the time of clinical presentation, hepatitis B surface antigen (HBsAg) may also be detected in the serum.
Past infection with hepatitis B is best determined by detecting IgG anti-hepatitis B core antigen, anti-hepatitis B surface antigen, or both.
HBV viral DNA is the most accurate marker of viral replication and can be detected by polymerase chain reaction (PCR).
Finally, a liver biopsy may be done to determine the grade of inflammation and the stage of fibrosis, especially in chronic hepatitis patients

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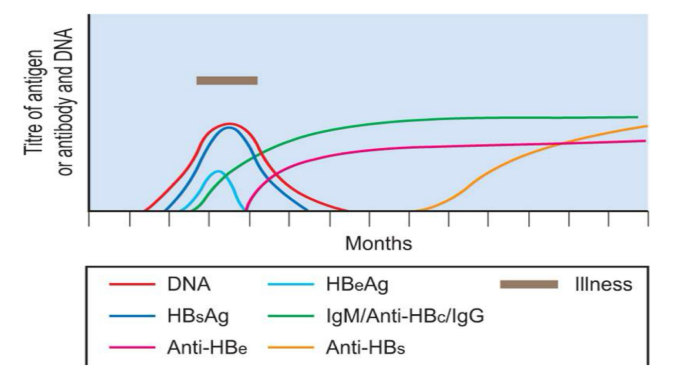


✅ **If we detect the hepatitis B surface antigen (HBsAg)**, it indicates a **current hepatitis B infection**.
If the antigen **persists for more than 6 months**, it suggests a **chronic hepatitis B infection**.

✅ **If we detect the antibody against the surface antigen (anti-HBs)**, it means the person has either **recovered from the infection** or has **developed immunity** — either from **past infection** or **vaccination**.

in this slide we could see the typical serology of HPV infection Where the laboratory diagnosis of acute hepatitis B is best made by demonstrating the **IgM** antibody to hepatitis B core antigen in the serum. In brief, hepatitis B surface antigen is used as a general marker of infection, **and if it stays high for more than six months**, it indicates chronic hepatitis. Hepatitis B surface antibody is used to document recovery and/or immunity to hepatitis B virus infection.

Hepatitis B core IgM antibody is a marker for acute infection, while anti-hepatitis B core IgG antibody is an indication of past or chronic infection. Finally, hepatitis B e antigen, the envelope antigen, indicates active replication of the virus, and therefore, infectivity.

Anti-hepatitis B e antibody suggests the virus is no longer replicating, however, the patient can still be positive for hepatitis B surface antigen, which is made by the integrated hepatitis B virus DNA.

As we mentioned, the DNA of hepatitis B virus indicates active replication of the virus and is more accurate than the hepatitis B e antigen, especially in cases of escape mutants. It is used mainly for monitoring response to therapy

Even when the virus stops replicating (anti-HBe is positive), the person might still test **positive for HBsAg**. Why?

✅ Because **hepatitis B virus DNA can integrate** into the person's **own liver cell DNA**, and these infected liver cells can **continue producing surface antigen (HBsAg) — even without full viral replication**.

TABLE 41-4 Serologic Test Results in Four Stages of HBV Infection

Test	Acute Disease	Window Phase	Complete Recovery	Chronic Carrier State
HBsAg	Positive	Negative	Negative	Positive
HBsAb	Negative	Negative	Positive	Negative[1]
HBcAb	Positive[2]	Positive	Positive	Positive

We can see **four major clinical entities associated with typical Hepatitis B virus serology results**. In **acute infection**, the Hepatitis B surface antigen and the Hepatitis B core antibody of the IgM type become positive. During the **window period** (which is a short phase when the Hepatitis B surface antigen has disappeared from the blood, but the Hepatitis B surface antibody has not yet appeared), both the Hepatitis B surface antigen and the Hepatitis B surface antibody are undetectable. However, during this time, the Hepatitis B core antibody of the IgM type remains positive, and it is the **only reliable marker of infection during this phase**. In the **chronic carrier state**, the Hepatitis B surface antigen and the Hepatitis B core antibody of the IgG type are positive. In incomplete recovery, the Hepatitis B surface antigen becomes negative, while both the Hepatitis B core antibody and the Hepatitis B surface antibody are positive

	HBsAg HBeAg* HBV-DNA	HBcAb IgM	HBcAb IgG	HBeAb	HBsAb
Acute infection	+	+	–	–	–
Window period	–	+/–	+	+	–
Prior infection	–	–	+	+	+
Immunization	–	–	–	–	+
Chronic infection	+	–	+	+/–	–

Another table shows other interpretations of the typical serology of Hepatitis B virus infection. In post-Hepatitis B immunization, only the Hepatitis B surface antibody is positive, while all other markers are negative. In comparison, in the case of past infection, the pattern is different

- because the vaccine only contains the surface antigen (HBsAg).-

Treatment

There is no specific treatment for acute hepatitis B, and a high-calorie diet is desirable. Corticosteroid therapy has no value in uncomplicated acute viral hepatitis. For chronic hepatitis, interferon-alpha provides long-term benefit in about one-third of patients. Lamivudine is a potent inhibitor of HIV and is also active against hepatitis B virus, both in vitro and in initial clinical trials. However, resistance to this agent develops in approximately one-quarter of patients after 12 months of therapy

Because of that drug having resistance after 12 months of therapy, that leaves us with two other options of treatment. They are from the nucleotide analogue adenosine monophosphate, and they are newly approved for the treatment of chronic hepatitis. These are adefovir and entecavir

That leaves us with the safe practices and avoidance of needle stick injuries, especially for the medical personnel or injection drug abusers who use. They are the approaches that can be used to diminish the risk of Hepatitis B infection. Vaccination is highly effective against Hepatitis B virus infection. The available recombinar vaccines can be given to those who are at increased risk of Hepatitis B virus infection, such as healthcare workers. It's also given routinely to neonates, and in many countries. Hepatitis B immunoglobulin may be used t protect persons who are exposed to Hepatitis B. It's particularly efficacious within 48 hours of the incident Post-exposure prophylaxis may also be given neonates who are at increased risk of uh contracting hepatitis neonates

Measures include screening of blood donors as well as the blood itself and other body fluids. Here in Jordan, we have the hepatitis B virus as part of, المَطعوم السُداسي على ثلاث جُرعات، عادةً الشهر الثاني الثالث الرابعة. We check the response by measuring hepatitis B surface antigen antibodies. Usually, if it is more than 10 milli-international units, it is considered protective. So, we check the response post-vaccination for hepatitis B virus by measuring the antibody level.

hepatitis D virus, Delta hepatitis

This is a small **single-stranded RNA virus** that requires the presence of hepatitis B surface antigen for its transmission and is thus found only in persons with acute or chronic hepatitis B infection. Delta hepatitis is most prevalent in groups at high risk of hepatitis B, such as injection drug users, and as many as 50% of such individuals may have IgG antibody to the Delta virus antigen. Other risks include dialysis

Two major types of Delta infection have been noted simultaneously:

1- Delta and hepatitis B infection. Simultaneous infection with both Delta and hepatitis B results in clinical hepatitis that is indistinguishable from acute hepatitis A or B. However, fulminant hepatitis is much more common than with hepatitis B virus alone

2- Delta superinfection in those with chronic hepatitis B: persons with chronic hepatitis B who acquire infection with hepatitis D suffer relapse of jaundice and have a high likelihood of developing chronic cirrhosis. Diagnosis is made most commonly by demonstrating IgM or IgG antibodies, or both, to the Delta antigen in the serum. IgM antibodies appear within three weeks of infection and persist for several weeks . IgG antibodies persist for years.

Response to treatment with interferon alpha in patients with Delta hepatitis and hepatitis B is less than those with hepatitis B alone. The recommended doses are higher and may produce sustained improvement in only a quarter of patients

Because the capsid of Delta hepatitis is hepatitis B surface antigen, measuring it aids in limiting the transmission of hepatitis B. To prevent transmission of Delta hepatitis, individuals infected with hepatitis B or D should not donate blood, organs, tissues, or semen. Methods of reducing transmission include decreased use of contaminated needles and syringes by injection drug users and use of needle safety devices by healthcare workers.

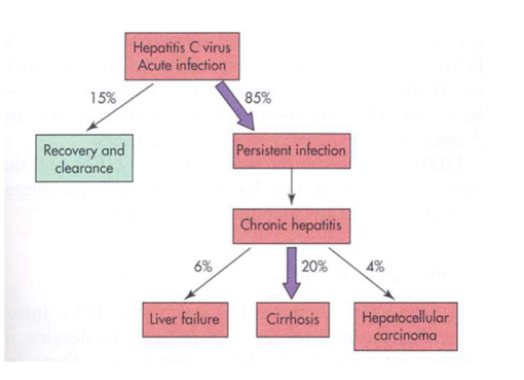
hepatitis C virus

Hepatitis C virus is an RNA virus in the Flaviviridae family. It has a very simple genome consisting of just three structural and five non-structural genes. Hepatitis C is an insidious disease in that it does not usually cause a clinically evident acute illness. Instead, its first manifestation in about one quarter of those infected may be the presence of symptoms during chronic hepatitis that may ultimately lead to liver failure

Transmission is less well understood than for hepatitis A, B, and D. Hepatitis C was the major cause of post-transfusion hepatitis until a serologic test for screening blood donors was developed. Hepatitis C virus has at least six genotypes and multiple subtypes, hypervariable regions in the envelope glycoprotein, and it is calledQuasispecies

Transmission of hepatitis C by blood is well documented. Indeed, until screening blood for transfusions was introduced, it caused the great majority of cases of post-transfusion hepatitis. Hepatitis C may be sexually transmitted but to a much lesser degree than hepatitis B. Needle sharing accounts for up to 40% of the cases, for example in the United States.

Five million people have antibodies to hepatitis C, and screening of donor blood for antibodies has reduced post-transfusion hepatitis C by 80 to 90%. Other individuals considered at risk for hepatitis C include chronic hemodialysis patients as well as spouses. In this slide, we can see the outcome of hepatitis C virus infection



First of all, the incubation period of hepatitis C averages between 6 to 12 weeks. The infection is usually asymptomatic or mild and anicteric (no jaundice) , but results in a chronic carrier state in up to 85% of adult patients. The average time from infection to the development of chronic hepatitis is 10 to 18 years, and cirrhosis and hepatocellular carcinoma are late sequelae of chronic hepatitis. Antigens of hepatitis C are not detectable in blood, so diagnostic tests attempt to demonstrate antibodies in hepatitis C virus infection. Unfortunately, the antibody response in acute disease remains negative for 1 to 3 weeks after clinical onset and may never become positive in 10 to 20% of patients with acute resolving disease. Current tests measure antibodies to multiple hepatitis C antigens by either enzyme immunoassay or immunoblot. Even with newer assays, IgG antibody to hepatitis C may not develop for up to four months, making the serodiagnosis of acute hepatitis C very difficult. Quantitative assays of hepatitis C RNA may be used for diagnosis, estimating prognosis, predicting interferon responsiveness, and monitoring therapy, but there is not a very good correlation between viral load and histology. **Combination therapy with interferon alpha and ribavirin** is the current treatment of choice for patients with evidence of hepatitis due to hepatitis C. Corticosteroids are not beneficial in hepatitis C infection.

Prevention of hepatitis C relies upon avoidance of injection drug use and screening blood products, which are important preventive measures. It is not clear whether prophylactic immune serum globulins protect against hepatitis C. In addition, it is questionable whether a vaccine will be effective; there is none yet for hepatitis C virus, and patients may be reinfected by the wild-type virus.

Here are preventive measures that should be taken when dealing with patients with hepatitis C virus. This table could be of high value, especially for you as a medical personnel, as it explains post-exposure prophylaxis for different scenarios.

Post exposure prophylaxis

جدول رقم (9) الاجراءات الفورية بعد اصابة عمل

المريض مصدر الاصابة	الوضع التطعيمي للموظف	الاجراء
التهاب الكبد (B) موجب HBsAg (positive)	- لم يتم تطعيمه - غير مكتمل الجرعات - ثلاث جرعات من التطعيم	-اعطاء التطعيم فورا + جرعة جلوبيولين مناعي* - إكمال كل الجرعات و اعطاء جلوبيولين مناعي* - فحص الاجسام المناعية (اذا كان أكثر أو يساوي 10 وحدة دولية لا شيء) **
التهاب الكبد (B) سالب HBsAg (negative)	- لم يتم تطعيمه - تم تطعيمه	- يتم تطعيمه - لا شئ
غير معروف اصابته بالتهاب الكبد ب	- لم يتم تطعيمه - غير مكتمل الجرعات - ثلاث جرعات من التطعيم	- يعامل كما لو كان مصدر الاصابة ايجابيا - يعامل كما لو كان مصدر الاصابة ايجابيا - يعامل كما لو كان مصدر الاصابة ايجابيا
حامل لمضاد فيروس التهاب الكبد (C)	لا يوجد لقاح للالتهاب الكبد (C)	فحص الموظف بعد الاصابة مباشرة ثم بعد اسبوعين و بعد شهر ثم بعد 3 اشهر بطريقة HCV-Abو PCR و اذا ظهرت بوادر اصابته يحول الى أخصائي جهاز هضمي
غير معروف اصابته بالتهاب الكبد (C)	لا يوجد لقاح للالتهاب الكبد (C)	فحص الموظف بعد الاصابة مباشرة ثم بعد اسبوعين و بعد شهر ثم بعد 3 اشهر بطريقة HCV-Abو PCR و اذا ظهرت بوادر اصابته يحول الى أخصائي جهاز هضمي
حامل لفيروس العوز المناعي البشري HIV	لا يوجد لقاح لفيروس العوز المناعي البشري HIV	- مدة اربعة اسابيع يتم فيه تناول ثلاثة ادوية مضادة للفيروسات (مثل زيدوفودين ولاميفودين) ويجب الرجوع الى البرنامج الوطني لمكافحة الايدز*** - يبدأ العلاج فوراً(خلال ساعات)

* يتم ذلك خلال 24 ساعة من التعرض للعدوى

* *تقاس الاستجابة المناعية لمطعوم الكبد (B) بفحص الاجسام المضادة (Hbs Ab) وتعتبر ايجابية اذا كانت أكبر أو يساوي 10 وحدة دولية

Table 1 summary

Comparison of A, B, D (Delta), C, and E Hepatitis

Feature	A	B	D	C[a]	E
Virus type	Single-stranded RNA	Double-stranded DNA	Single-stranded RNA	RNA	RNA
Percent of viral hepatitis	50	41	<1	5	<1
Incubation period (days)	15–45 (mean, 25)	7–160 (mean, 60–90)	28–45	15–160 (mean, 50)	?
Onset	Usually sudden	Usually slow	Variable	Insidious	?
Age preference	Children, young adults	All ages	All ages	All ages	Young adult
Transmission					
Fecal–oral	+++	±	±	–	+++
Sexual	+	++	++	+	+?
Transfusion	–	++	+++	+++	–
Severity	Usually mild	Moderate	Often severe	Mild	Variable
Chronicity (%)	None	10	50–70	>50%	None
Carrier state	None	Yes	Yes	Yes	?
Immune serum globulin protective	Yes	Yes[b]	Yes[c]	Uncertain	?

Abbreviation: Plus and minus signs indicate relative frequencies.

[a] Many individuals with hepatitis C virus are also infected with the hepatitis G virus, which is similar to hepatitis C.

[b] Hyperimmune globulin more protective.

[c] Prevention of hepatitis B prevents hepatitis D.