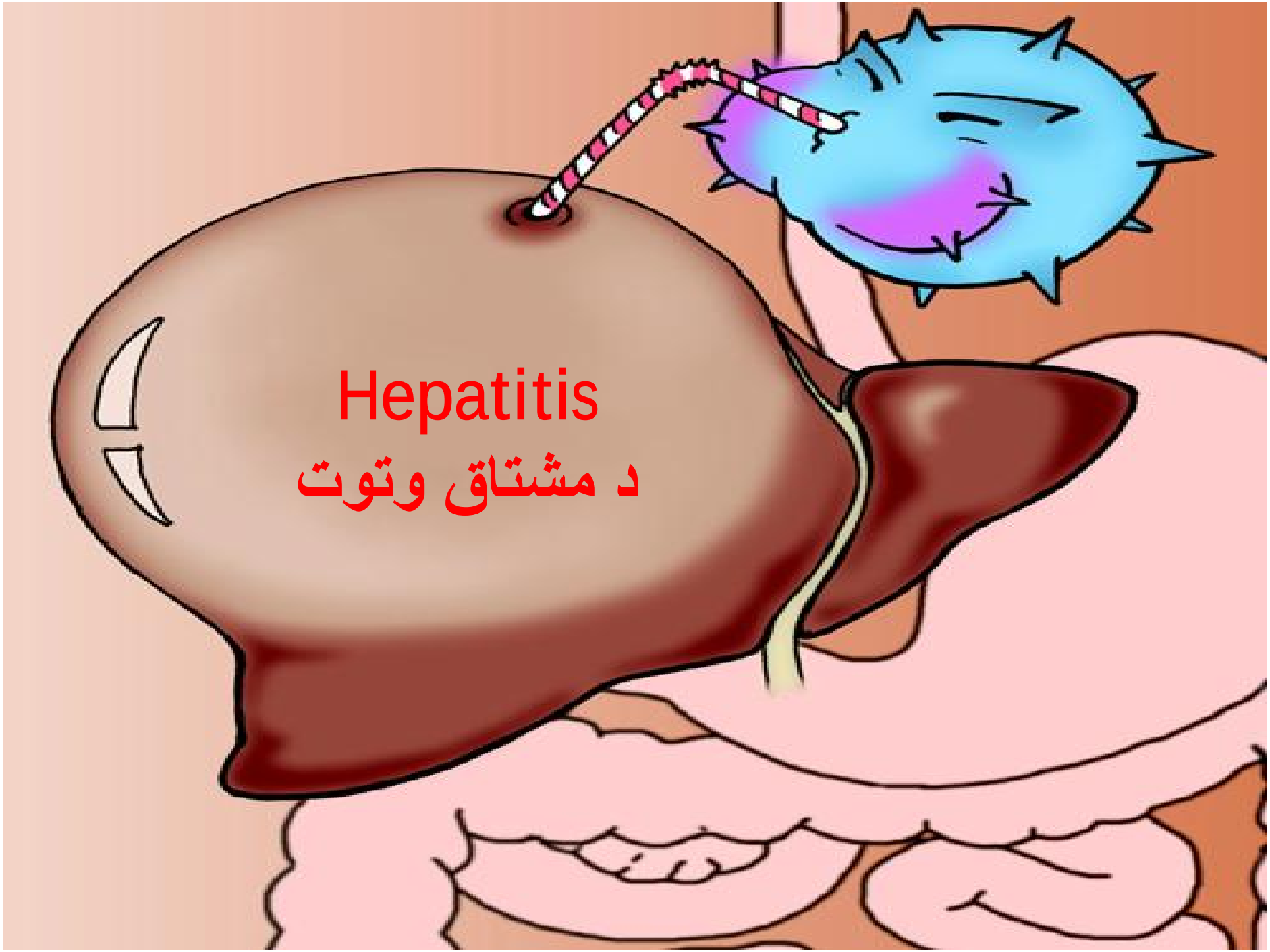
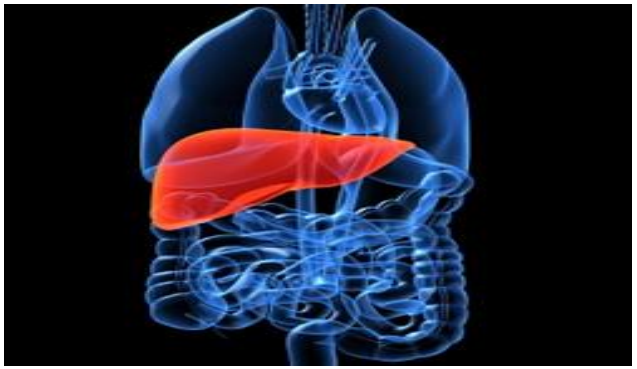


introduction



- ()Hepatitis means inflammation of the liver.
- Many illnesses and conditions can cause inflammation of the liver, for example, drugs, alcohol, chemicals, and autoimmune diseases.
- () There are several hepatitis viruses; they have been named types A, B, C, D, E, F (not confirmed), and G.
- () It is a common cause of jaundice
- () The viruses cause illnesses with similar clinical and pathological features and which are frequently anicteric or even asymptomatic.

Causes

Common:

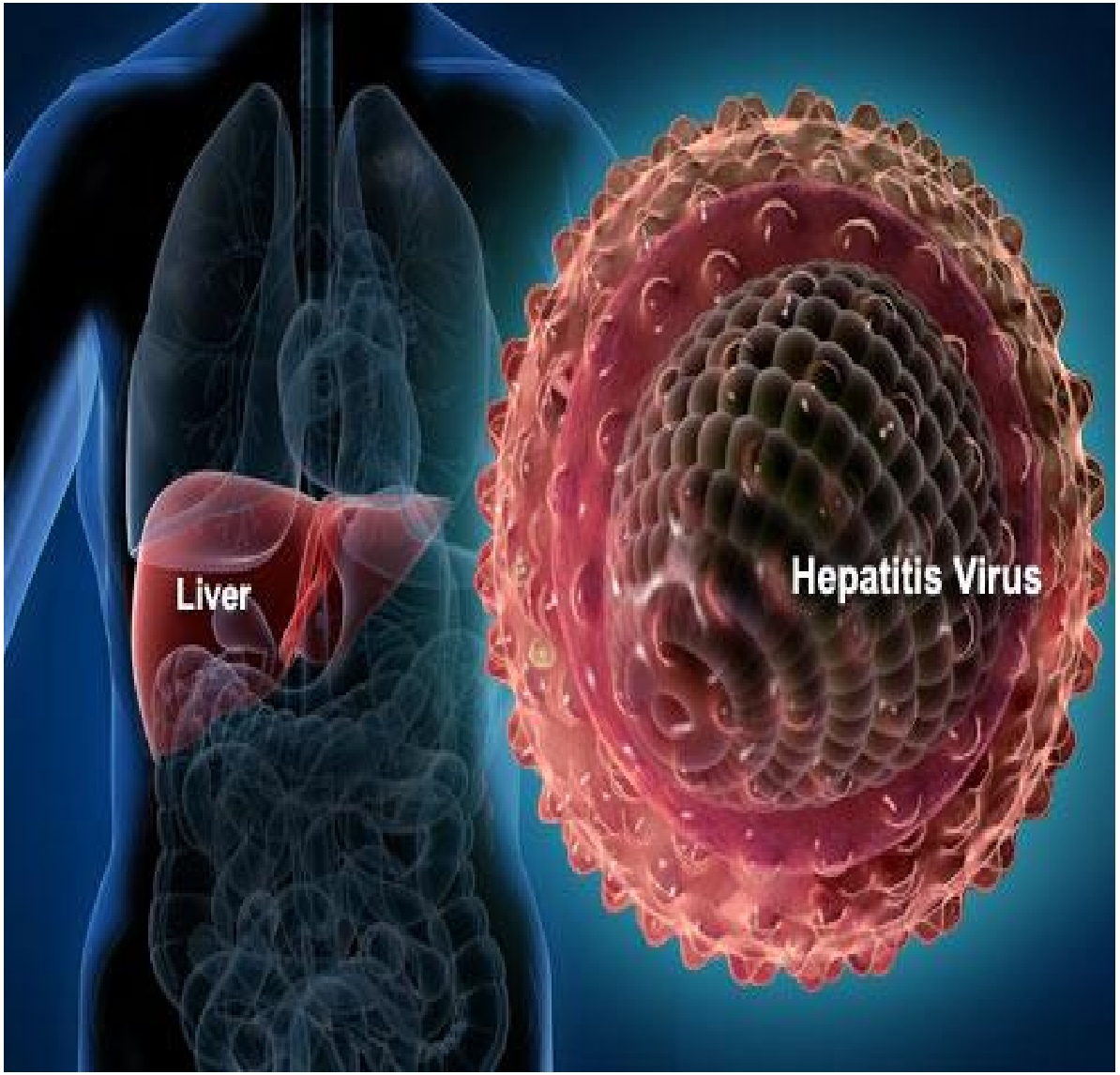
- Hepatitis A
- Hepatitis B ± hepatitis D
- Hepatitis C
- Hepatitis E

Less common:

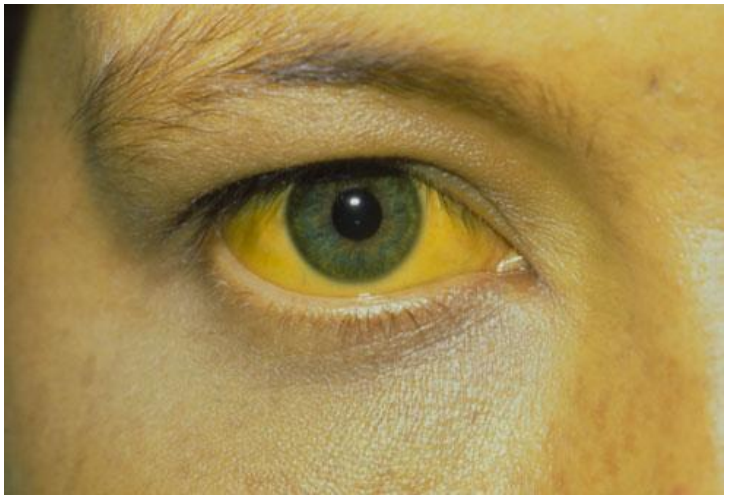
- Cytomegalovirus
- Epstein-Barr virus

Rare

- Herpes simplex
- Yellow fever



Clinical features



() A non-specific prodromal illness characterised by headache, myalgia, arthralgia, nausea and anorexia usually precedes the development of jaundice by a few days to 2 weeks.

() Vomiting and diarrhoea may follow, and abdominal discomfort is common.

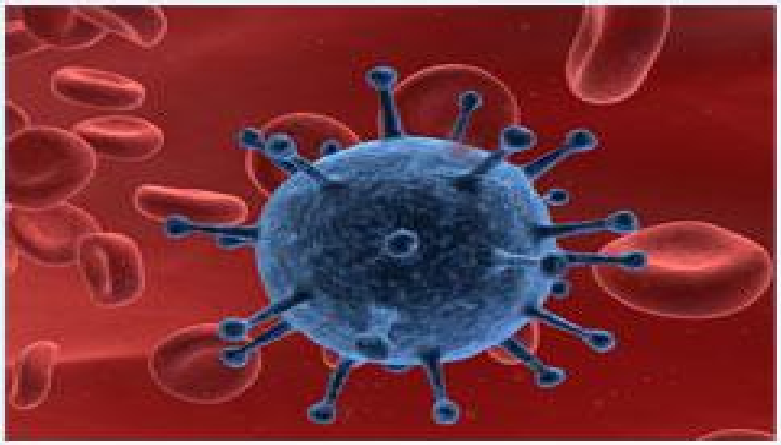
()Dark urine and pale stools may precede jaundice.

() There are usually few physical signs. The liver is often tender but only minimally enlarged. Occasionally, mild splenomegaly and cervical lymphadenopathy are seen. These are more frequent in children or those with Epstein-Barr virus infection.

() Jaundice may be mild and the diagnosis may be suspected only after finding abnormal liver blood tests in the setting of non-specific symptoms. Symptoms rarely last longer than 3-6 weeks.

Investigations

- A hepatitic pattern of LFTs develops, with serum transaminases typically between 200 and 2000 U/L.
- The ALP rarely exceeds twice the upper limit of normal.
- Prolongation of the prothrombin time indicates the severity of the hepatitis but rarely exceeds 25 seconds.
- The white cell count is usually normal with a relative lymphocytosis.
- Serological tests confirm the aetiology of the infection.



Management

- Most individuals do not need hospital care.
- Drugs such as sedatives and narcotics, which are metabolised in the liver, should be avoided.
- No specific dietary modifications are needed.
- Alcohol should be avoided during the acute illness.
- Elective surgery should be avoided in cases of acute viral hepatitis, as there is a risk of post-operative liver failure.
- Liver transplantation is very rarely indicated for acute viral hepatitis complicated by liver failure, but is commonly performed for complications of cirrhosis resulting from chronic hepatitis B and C infection.

Hepatitis A

- The hepatitis A virus (HAV) belongs to the picornavirus group of enteroviruses.
- HAV is highly infectious and is spread by the faecal-oral route. Infected individuals, who may be asymptomatic, excrete the virus in faeces for about 2-3 weeks before the onset of symptoms and then for a further 2 weeks or so.
- Infection is common in children but often asymptomatic, and so up to 30% of adults will have serological evidence of past infection but give no history of jaundice.
- Infection is also more common in areas of overcrowding and poor sanitation. In occasional outbreaks water and shellfish have been the vehicles of transmission.
- a chronic carrier state does not occur.

Investigations

- Anti-HAV is important in diagnosis, as HAV is only present in the blood transiently during the incubation period. Excretion in the stools occurs for only 7-14 days after the onset of the clinical illness.
- Anti-HAV of the IgM type, indicating a primary immune response, is already present in the blood at the onset of the clinical illness and is diagnostic of an acute HAV infection. Titres of this antibody fall to low levels within about 3 months of recovery.
- Anti-HAV of the IgG type is of no diagnostic value as HAV infection is common and this antibody persists for years after infection, but it can be used as a marker of previous HAV infection. Its presence indicates immunity to HAV.

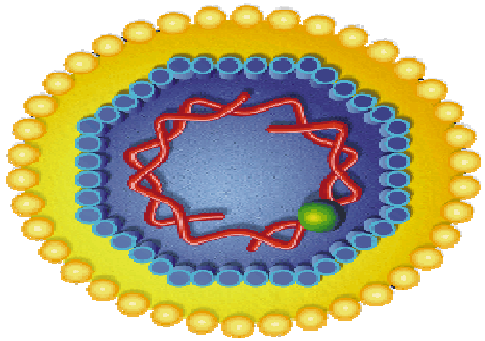
Managment

- Individuals can be given substantial protection from infection by active immunisation with an inactivated virus vaccine, which indicated in individuals with chronic hepatitis B or C infections.
- Immediate protection can be provided by immune serum globulin if this is given soon after exposure to the virus.
- Immune serum globulin can be effective in an outbreak of hepatitis, in a school or nursery, as injection of those at risk prevents secondary spread to families. People travelling to endemic areas are best protected by vaccination.
- Acute liver failure is rare in hepatitis A (0.1%) . However, HAV infection in patients with chronic liver disease may cause serious or life-threatening disease.

Hepatitis B

a hepadnavirus that can cause both acute and chronic hepatitis, chronic hepatitis develops in the 5-10% of adults

- Hepatitis B infection affects 300 million people and is one of the most common causes of chronic liver disease and hepatocellular carcinoma world-wide.
- The hepatitis B virus consists of a core containing DNA and a DNA polymerase enzyme needed for virus replication. The core of the virus is surrounded by surface protein .
- Humans are the only source of infection.
- Hepatitis B may cause an acute viral hepatitis; however, the acute infection is often asymptomatic, particularly when acquired at birth.
- Many individuals with chronic hepatitis B are also asymptomatic. Chronic hepatitis, associated with elevated serum transaminases, may occur and can lead to cirrhosis, usually after decades of infection .

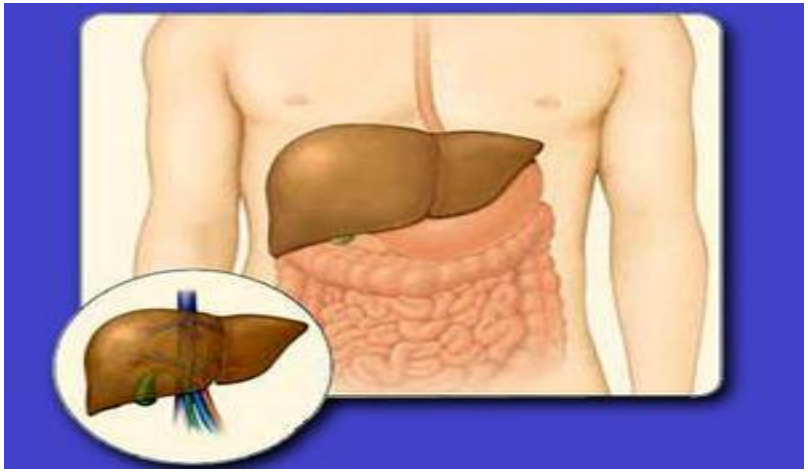


- Vertical transmission from mother to child in the perinatal period is the most common cause of infection world-wide and carries the highest risk.
- In this setting, adaptive immune responses to HBV may be absent initially. Several mechanisms contribute towards this:

1- the introduction of antigen in the neonatal period is tolerogenic.

2- the presentation of such antigen within the liver , promotes tolerance; this is particularly evident in the absence of a significant innate or inflammatory response.

3- very high loads of antigen may lead to so-called 'exhaustion' of cellular immune responses.



- () IP about 90 days.
- () Acute hepatitis B refers to newly acquired infections, Affected individuals notice symptoms approximately 1 to 4 months after exposure to the virus.
- () Chronic hepatitis B is an infection with HBV that lasts longer than 6 months.

Source of hepatitis B infection and risk of chronic infection

Horizontal transmission (10%):

- Injection drug use
- Infected unscreened blood products
- Tattoos/acupuncture needles
- Sexual (homosexual and heterosexual)
- Close living quarters/playground play as a toddler
- The virus may be transmitted when infectious fluids contact with broken skin or a mucous membrane.

Vertical transmission (90%):

- HBsAg-positive mother
- Breast feeding

People who are at an increased risk of being infected with the hepatitis B virus include the following:

1- Men or women who have multiple sex partners, especially if they don't use a condom •

2- homosexual •

3- Men or women who have sex with a person infected with hepatitis B virus •

4- People with other sexually transmitted disease. •

5- People who inject drugs with shared needles •

6- People who receive transfusions of blood or blood products •

7- People who undergo dialysis for kidney disease

8- mentally handicapped people and their attendants, caregivers, and family members

9- Health care workers who are stuck with needles or other sharp instruments contaminated with infected blood

10- Infants born to infected mothers

11- In some cases, the source of transmission is never known.

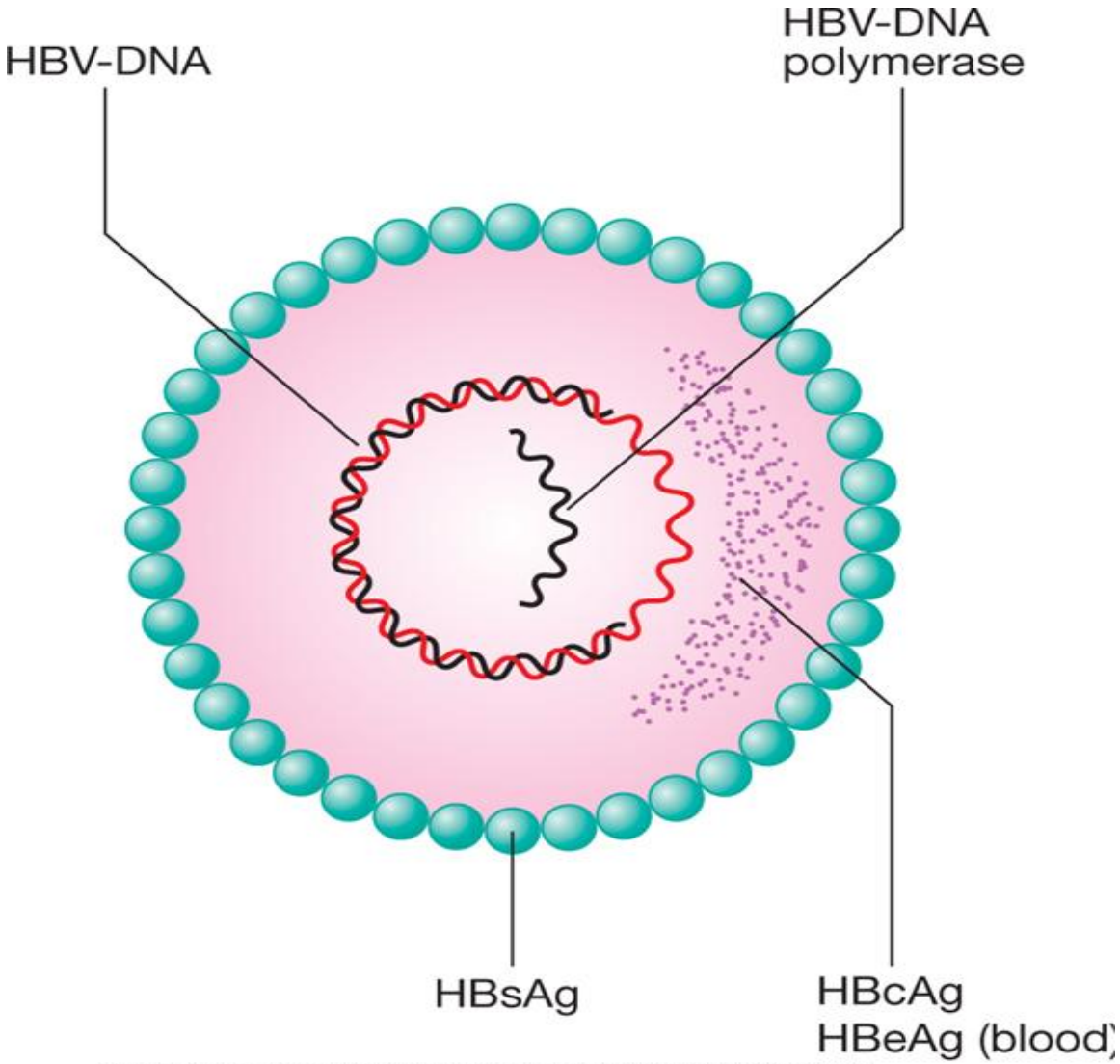
investigations

Serology: •

1-HBsAg •

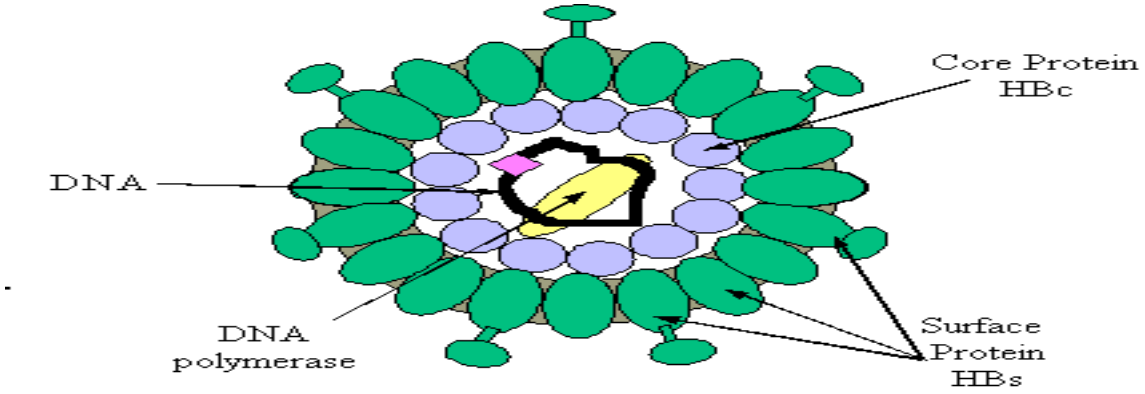
2-HBcAg •

3-HBeAg •



Colledge et al: Davidson's Principles and Practice of Medicine, 21st Edition

- *The hepatitis B surface antigen* (HBsAg) :
- () is an indicator of active infection, and a negative test for HBsAg makes HBV infection very unlikely.
- () HBsAg appears in the blood late in the incubation period . it may be present for a few days only, disappearing even before jaundice has developed, but usually lasts for 3-4 weeks and can persist for up to 5 months.
- () The persistence of HBsAg for longer than 6 months indicates chronic infection.
- () Antibody to HBsAg (anti-HBs) usually appears after about 3-6 months and persists for many years or perhaps permanently.
- Anti-HBs implies either a previous infection or previous vaccination, in which case anti-HBc is not present.



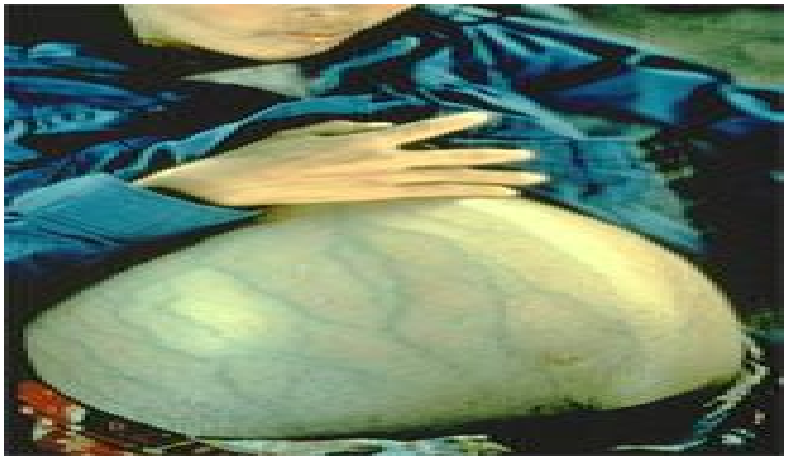
- *The hepatitis B core antigen* (HBcAg):
- () is not found in the blood, but antibody to it (anti-HBc) appears early in the illness and rapidly reaches a high titre, which subsides gradually but then persists.
- () Anti-HBc is initially of IgM type with IgG antibody appearing later.
- Anti-HBc (IgM) can sometimes reveal an acute HBV infection when the HBsAg has disappeared and before anti-HBs has developed.

The hepatitis B e antigen (HBeAg): •

() is an indicator of viral replication. •

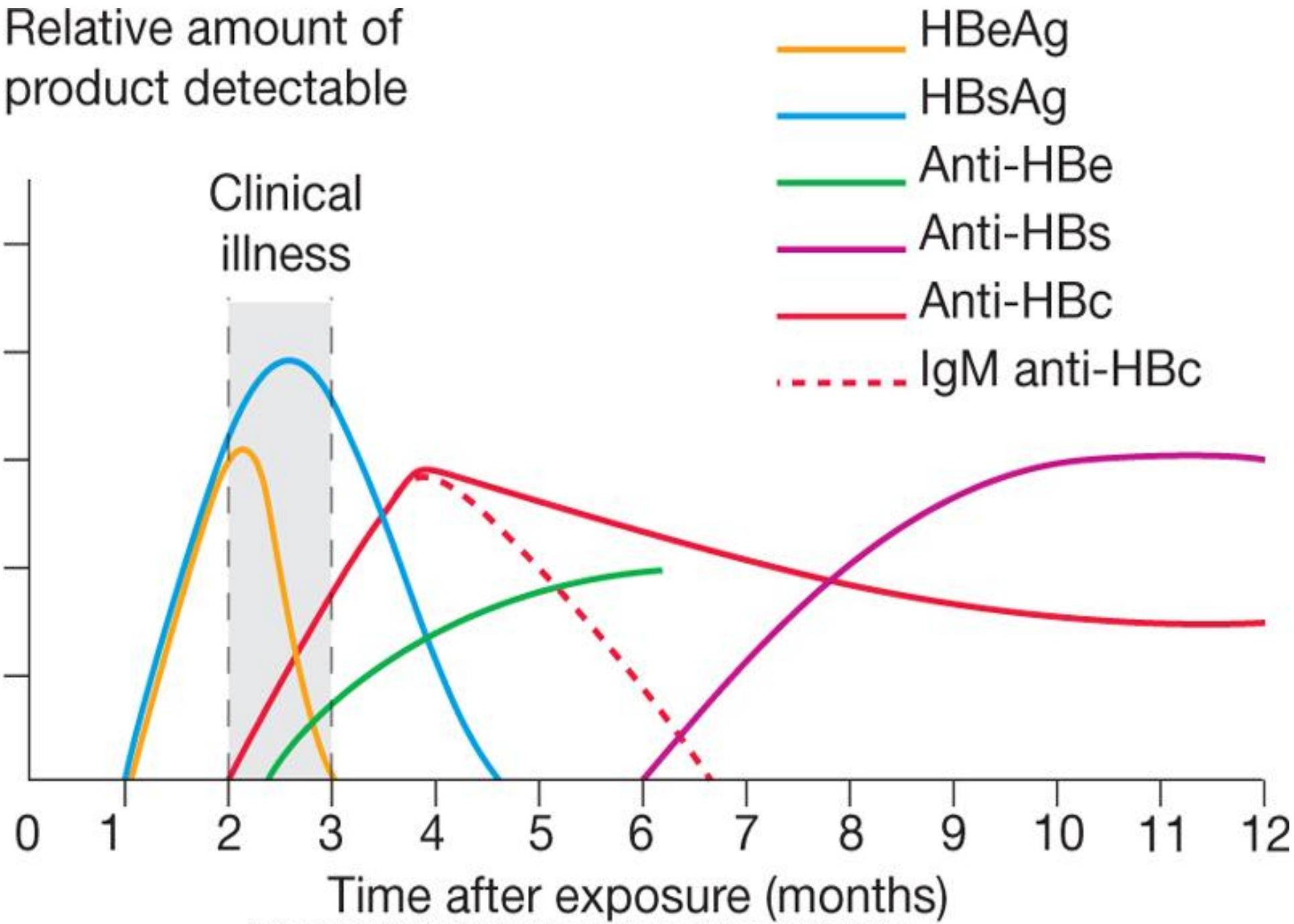
() In acute hepatitis B it may appear only • transiently in the illness; its appearance is followed by the production of antibody (anti-HBe).

()The HBeAg reflects active replication of the • virus in the liver.



Chronic HBV infection :

- () is marked by the presence of HBsAg and anti-HBc (IgG) in the blood. Usually, HBeAg or anti-HBe is also present; HBeAg indicates continued active replication of the virus in the liver.
- () Although the presence of anti-HBe usually implies low viral replication, the exception is HBeAb-positive replicating chronic hepatitis B in which high levels of serum HBV-DNA are seen, despite negative HBeAg



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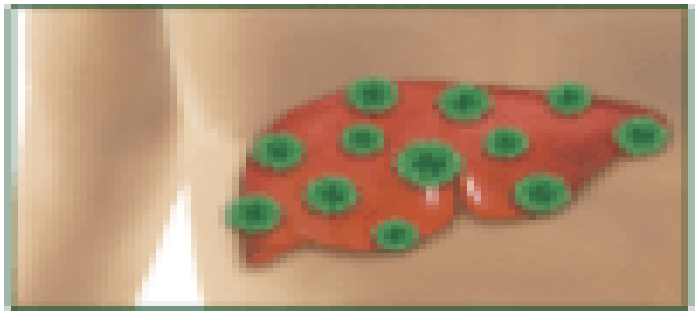
Viral load

- HBV-DNA can be measured by polymerase chain reaction (PCR) in the blood. Viral loads are usually in excess of 10^5 copies/mL in the presence of active viral replication, as indicated by the presence of e antigen.
- Measurement of viral load is important in monitoring antiviral therapy and identifying patients with pre-core mutants. Specific HBV genotypes can also be identified using PCR. Genotypes B and C appear to have more aggressive disease that responds less well to interferon.



High viral load

How to interpret the main investigations used in the serological diagnosis of hepatitis B virus infection

	HBsAg	Anti-HBc IgM	Anti-HBc IgG	Anti-HBs
• Incubation period	+	+	-	-
• Acute hepatitis				
• Early	+	+	-	-
• Established	+	+	+	-
• Established (occasional)	-	+	+	-
• Convalescence				
• (3-6 months)	-	±	+	±
• (6-9 months)	-	-	+	+
• Post-infection				
• > 1 year	-	-	+	+
• Chronic infection				
• Usual	+	-	+	-
• Occasional	-	-	+	-
• Immunisation without infection	-	-	-	+

Management

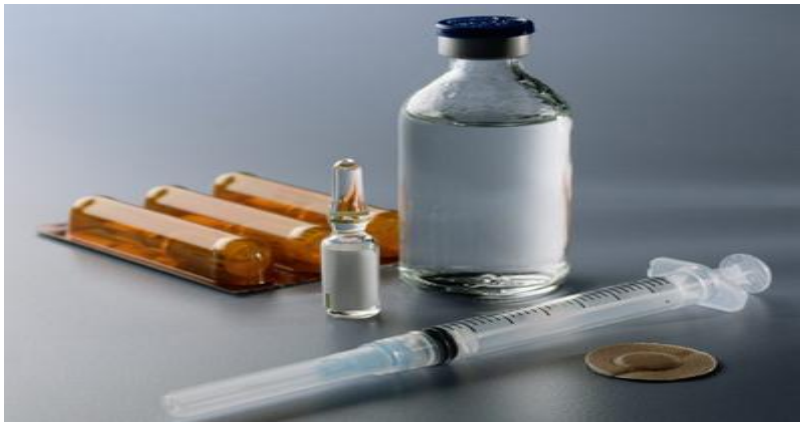
Acute hepatitis B

- Treatment is supportive with monitoring for acute liver failure, which occurs in less than 1% of cases.
- There is no definitive evidence that antiviral therapy (e.g. lamivudine) reduces the severity or duration of acute hepatitis B.

- Full recovery occurs in 90-95% of adults following acute HBV infection. The remaining 5-10% develop a chronic infection which usually continues for life.
- Infection passing from mother to child at birth leads to chronic infection in the child in 90% of cases and recovery is rare. Chronic infection is also common in immunodeficient individuals, such as those with Down's syndrome or HIV infection.
- Fulminant liver failure due to acute hepatitis B occurs in less than 1% of cases.
- Recovery from acute HBV infection occurs within 6 months and is characterised by the appearance of antibody to viral antigens. Persistence of HBeAg beyond this time indicates chronic infection. Combined HBV and HDV infection causes more aggressive disease.

Chronic hepatitis B

- Treatments are still limited. The goals of treatment are HBeAg seroconversion, reduction in HBV-DNA and normalisation of the LFTs.
- *The indication for treatment* is a high viral load in the presence of active hepatitis, as demonstrated by elevated serum transaminases and/or histological evidence of inflammation and fibrosis. The oral antiviral agents are more effective in reducing viral loads in patients with e antigen-negative chronic hepatitis B than in those with e antigen-positive chronic hepatitis B.
- Most patients with chronic hepatitis B are asymptomatic and develop complications such as cirrhosis and hepatocellular carcinoma only after many years
- Cirrhosis develops in 15-20% of patients with chronic HBV over 5-20 years. This proportion is higher in those who are e antigen-positive.



Interferon-alfa :

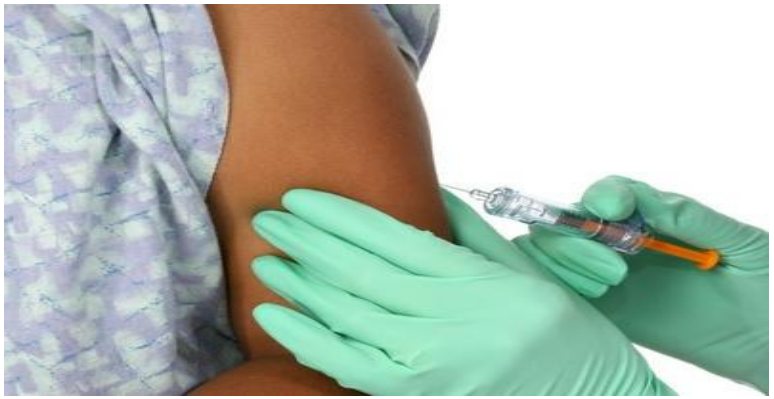
- This is most effective in selected patients with a low viral load and serum transaminases greater than twice the upper limit of normal, in whom it acts by augmenting a native immune response.
- In HBeAg-positive chronic hepatitis, 33% lose e antigen after 4-6 months of treatment, compared to 12% of controls. Response rates are lower in HBeAg-negative chronic hepatitis, even when patients are given longer courses of treatment.
- Interferon is contraindicated in the presence of cirrhosis, as it may cause a rise in serum transaminases and precipitate liver failure.
- Longer-acting pegylated interferons which can be given once weekly
- Side-effects are common and include fatigue, depression, irritability, bone marrow suppression and thyroid disease. The drug appears to be better tolerated in patients with hepatitis B compared to those with hepatitis C.

Lamivudine :

- This is a nucleoside analogue which inhibits DNA polymerase and suppresses HBV-DNA levels.
- It is effective in improving liver function in patients with decompensated cirrhosis and may prevent the need for transplantation.
- Complicated by mutation of virus after 9 monts

Adefovir

- This is a nucleotide analogue that is phosphorylated to yield active drug which inhibits HBV-DNA polymerase.
- enhances the frequency of HBeAg seroconversion and leads to histological improvement, but is contraindicated in renal failure.
- Relapse occurs on stopping treatment, and the optimum length of treatment remains unknown.
- Adefovir is effective in suppressing most of the lamivudine-induced DNA polymerase mutant viruses.



Entecavir and telbivudine :

- These drugs are more effective than lamivudine and adefovir in reducing viral load in HBeAg-positive and HBeAg-negative chronic hepatitis
- Antiviral resistance mutations occur in only 1% after 3 years of entecavir drug exposure. Entecavir, unlike telbivudine, may have anti-HIV action and is contraindicated in HIV patients who are not on antiretroviral therapy.

Tenofovir and other drugs :

- Other drugs which also have action against chronic hepatitis B include tenofovir and emcitabine; these also have anti-HIV efficacy. Tenofovir has recently been shown to be superior to adefovir in the treatment of chronic hepatitis B .
- The role of combination antiviral therapy, as used in HIV infection, is still unclear.

Liver transplantation :

- Historically, liver transplantation was contraindicated in the presence of hepatitis B because infection often recurred in the graft. However, the use of post-liver transplant prophylaxis with lamivudine and hepatitis B immunoglobulins has reduced the reinfection rate to 10% and increased 5-year survival to 80%, making transplantation an acceptable treatment option in selected cases.

Prevention :

- HBV-DNA can be found in saliva, urine, semen and vaginal secretions. The virus is about ten times more infectious than hepatitis C, which in turn is about ten times more infectious than HIV.

- A recombinant hepatitis B vaccine containing HBsAg is available (Engerix) and is capable of producing active immunisation in 95% of normal individuals. The vaccine gives a high degree of protection and should be offered to those at special risk of infection who are not already immune, as evidenced by anti-HBs in the blood The vaccine is ineffective in those already infected by HBV, indicated in :
- Parenteral drug users
- Men who have sex with men
- Close contacts of infected individuals
  - Newborn of infected mothers
  - Regular sexual partners
- Patients on chronic haemodialysis
- Patients with chronic liver disease
- Medical, nursing and laboratory personnel

- Infection can also be prevented or minimised by the intramuscular injection of hyperimmune serum globulin prepared from blood containing anti-HBs. This should be given within 24 hours, or at most a week, of exposure to infected blood in circumstances likely to cause infection (e.g. needlestick injury, contamination of cuts or mucous membranes).
- Vaccine can be given together with hyperimmune globulin (active-passive immunisation
- Neonates born to hepatitis B-infected mothers should be immunised at birth and given immunoglobulin. Hepatitis B serology should then be checked at 12 months of age.

Thank you•