

PGS Consensus Statement on management of Hepatitis B Virus Infection - 2003

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Introduction

Hepatitis B is a major health problem globally casting an enormous burden on health care system and a major source of patient's misery. Chronic hepatitis B is a serious clinical problem in Pakistan.^{1,2} It is also an important cause of hepatocellular carcinoma.³

Pakistan remains in the intermediate HBV prevalence area with a carrier rate of 3-4%.⁴ Encouraged by the recent developments in this field and appreciating in particular the limitation of resources, various social practices and reservations about the health care system, Pakistan Society of Gastroenterology and G.I. Endoscopy (PSG) organized a consensus conference in order to prepare guidelines to deal with this problem in the local perspective. The task was technically difficult as the primitive health care system and lack of research facilities and orientation preclude the collection of exact national data regarding various aspects of the disease. Limited studies were available which provided a hazy picture of the magnitude of the problem. However the team of experts tried its level best to bridge the inherent gaps with their vast experience and technical inputs from all the available resources.

An organizing committee developed an agenda and

selected the relevant topics for the development of guidelines. The topics include prevalence, mode of transmission, natural history of the disease, diagnosis, treatment and prevention of hepatitis B. Eminent experts from all over the country delivered their deliberations on the selected topics with an insight of local perspectives. The panelists were asked to critically analyze the scientific data and feed their input. Based on this work next day was devoted by all the participants to draft the consensus guidelines for the management of hepatitis B.

Prevalence of Hepatitis B - National Perspective

There are 400 millions HBV carriers worldwide, of which more than 250 million reside in Asia.⁵ In Pakistan, the estimate is 4.5 million carriers, with a carrier rate of 3-4%. As mentioned earlier, limited studies are available to have a clear picture of prevalence of hepatitis B at the national level. However small scale studies show the following figures.

In a study of 103858 blood donors, 3.3% (95% CI 3.20%-3.41%) were HBsAg, 4.0% (95% CI 3.91%-4.11%) were anti HCV and 0.007% anti HIV positive.⁶ In another study done on more than 50,000 blood donors, prevalence of HBsAg was 2.28%.⁷ In College going first time voluntary

blood donors, seroprevalence was 2.2%.⁸ In a community based study done at Hafizabad 31% percent had hepatitis B core antibodies, and 4.3% had hepatitis B surface antigen.⁹ In an older study the frequency of HBsAg in healthy subjects was 2.9% and HBs Ab 35%.¹⁰ A meta-analysis of published data about the serology of hepatitis B in the healthy carriers showed the following results:¹¹

· HBsAg	9159/295637	(3%)
· Anti HBc	338/1044	(32%)
· Anti HBs	135/541	(25%)
· HBeAg	197/733	(27%)
· Anti HBe	395/654	(60%)

An interesting feature that arises from the data is the low prevalence of HBeAg (27%) but a high prevalence of AntiHBe (60%) in HBsAg positive carriers. One possible explanation could be the high prevalence of so called healthy sero-converted carriers. Infection due to the variant of HBV which decreases or abolishes the production of HBeAg (precore mutants) could be another explanation but data of HBV DNA in these patients is not available. The predominant genotype in Karachi is genotype D.¹² Data from other parts of the country is not available.

In pregnant women 2.5% were HBsAg, out of these 17% HBeAg and 61% anti HBe positive.¹¹ Low frequency of HBsAg and HBeAg in pregnant women makes vertical transmission a less important cause of transmission. The most likely cause of HBV transmission in our setting appears to be horizontal transmission during childhood. In a cross sectional study done in children, 3% were HBsAg positive.¹³ In a study done few years back, HbsAg was positive in 42% cases hospitalized for acute viral hepatitis.¹⁴ Regarding coinfection 7.2% were anti-HCV and HBsAg positive while 35.1% were anti-HCV and anti-HBc positive.¹⁵

Modes of Transmission

The mode of transmission of HBV varies in part with the prevalence of infection. Horizontal transmission, particularly in early childhood, accounts for most cases of chronic HBV infection in intermediate prevalence areas like Pakistan. Perinatal infection is the predominant mode of transmission in high prevalence areas.^{16,17} Unprotected sexual intercourse and intravenous drug use in adults are the major routes of spread in low prevalence areas.¹⁸

Perinatal Transmission

The infection rate among infants born to HBeAg-positive mothers is as high as 90 percent.¹ The high protective efficacy of (95 percent) of neonatal vaccination suggests that infection occurs predominantly at or after birth. There is no evidence that cesarean section prevents

maternal-infant transmission. Breast-feeding does not appear to increase the risk of transmission.¹⁹

The risk of maternal-infant transmission and the high frequency of perinatal transmission in endemic areas are related to the HBV replicative status of the mother. It is 85 to 90 percent in infants born to HBeAg positive mothers and 32 percent in infants born to HBeAg negative mothers.²⁰ A survey in an urban South-East Asia country estimated the overall risk of perinatal transmission in all HBsAg positive mothers to be 40 percent.²¹ Maternal serum HBV DNA levels correlate better with the risk of transmission.²²

Horizontal Transmission

Children may acquire HBV infection through horizontal transmission via minor breaks in the skin or mucous membranes or close bodily contacts with other children. Transmission via contaminated household articles such as toothbrushes, razors, and even toys, can occur. There is no firm evidence of HBV transmission via body fluids.

Transfusion Associated Transmission

The incidence of transfusion-related hepatitis B decreases significantly by excluding paid blood donors and screening hepatitis B surface antigen (HBsAg) of donors.²³ National legislation in Pakistan regulating blood banks has been introduced several times but has not been implemented. Nearly 50% of the facilities regularly utilize paid blood donors, while only 25% actively recruit volunteer donors. Facilities usually do not ask donors about injectable drug use, and any questions about high-risk sexual behaviour. Practices at most of the blood banks of Karachi fall well below WHO standards.²⁴

Sexual Transmission

Sexual transmission remains the major mode of spread of HBV in developed countries.^{25,26} In Pakistan, male sex workers are predominantly transvestites and transsexuals known as Hijras. A study done in 1998 in Karachi showed low prevalence of HBsAg positivity in transvestities of 3.4%.²⁷

Percutaneous Inoculation

Percutaneous transmission usually happens in Pakistan by reusing syringes and needles. Unsafe therapeutic injections appear to be the major risk factor for acute HBV infection and needs immediate focus from public health stand point.^{28,29} In a local study, 7.5% operation room personnel were positive for HBsAg infection and 25.43% for anti-HBc. Of these, 75% HBsAg-reactive personnel had received one to three needle-stick injuries per year. This study indicates a need for continued

efforts to minimize the risk of blood-borne infection by enhancing the compliance of operation room personnel with HBV vaccination and adherence to infection control measures.³⁰

Household contacts can also transmit hepatitis B through the sharing of razors or toothbrushes. Certain practices like acupuncture, tattooing, and body piercing and intravenous drug abuse have also been associated with transmission of hepatitis B.

Nosocomial Infection

HBV is an important transmitted blood-borne virus in the healthcare setting.³¹ Transmission generally occurs from patient to patient or from patient to health care personnel, via contaminated instruments or accidental needle stick. Healthcare workers, particularly surgeons, pathologists and physicians working in hemodialysis and oncology units, have the highest risks of HBV infection.³² Despite the publicity about hepatitis B transmission from healthcare workers to patients³³, this mode of spread is extremely rare. Transmission of hepatitis B from patients to healthcare workers is far more common.^{34,35}

Organ Transplantation

Organ donors are routinely screened for HBsAg. Transmission of HBV infection has been reported after transplantation of extrahepatic organs. The transplantation of liver from isolated anti-HBc positive donors may result in the conversion of HBsAg negative recipients to HBsAg positivity.³⁶

Safe Activities

Hepatitis B is not transmitted by hugging, shaking hands, preparing food or swimming in a pool.

Dietary Measures

There are no specific dietary measures that have been shown to have any effect on the progression of chronic hepatitis B. However, heavy use of alcohol (>40 g/d) has been associated with higher ALT levels^{37,38} and development of cirrhosis.³⁹ In addition, the development of cirrhosis and HCC occurs at a younger age in heavy drinkers with chronic hepatitis B.^{40,41}

Natural History Of Hepatitis B

Chronic hepatitis B virus infection generally consists of an early replicative phase which is characterized by presence of hepatitis Be antigen (HBeAg) and high levels of serum HBV DNA. Alanine aminotransferase (ALT) may be normal or abnormal in this phase.⁴² A late phase involves immune clearance of HBV and destruction of infected hepatocytes which may be manifested by more marked increases of aminotransferase levels and spontaneous, as well

as treatment related, HBeAg sero-conversion is common. This sero-conversion is generally related to extent of elevation of aminotransferase levels prior to start of treatment.⁴²

The outcome of HBV infection depends upon various factors such as age at which the infection occurs, viral factors, host factors and exogenous factors such as alcohol. The possible outcomes are acute hepatitis, fulminant hepatitis, HBsAg carrier state, chronic hepatitis and cirrhosis (15-40% of chronic hepatitis cases). Perinatal and childhood HBV infection are usually asymptomatic while adult HBV infection is icteric in 30-50% cases. Fulminant hepatic failure occurs in 0.1-0.5 % cases. Co-infection with HCV or HDV increases the risk of fulminant hepatic failure.

Cumulative risk of progression to cirrhosis in untreated HBeAg +ve chronic hepatitis is 8-20% at 5 years. Progression to cirrhosis is faster in HBeAg negative chronic hepatitis.⁴³⁻⁴⁵ Factors that influence the progression to cirrhosis are, age of patients, ongoing HBV replication, stage of fibrosis at diagnosis, genotype of virus, concurrent HDV, HCV and HIV infections and heavy alcohol intake.^{46,47}

Clinical Spectrum and Diagnosis of Hepatitis B Infection

Acute Hepatitis B Viral Infection

A diagnosis of acute HBV infection can be made on the basis of high ALT and the detection of IgM class antibody to hepatitis B core antigen (IgM anti HBc) in serum; IgM anti-HBc is generally detectable at the time of clinical onset and declines to sub-detectable levels within 6 months. IgG anti-HBc persists indefinitely as a marker of past infection. HbsAg is usually positive at the time of diagnosis of acute hepatitis B. Prothrombin time may be prolonged and is the best marker of the extent of acute liver dysfunction.

Acute Liver Failure

Clinically this is characterized by jaundice, encephalopathy and coagulopathy associated with raised aminotransferases and bilirubin, and prolonged prothrombin time. Anti-HBc IgM is reactive while HBsAg may not be reactive at times.

Chronic Hepatitis B

The diagnostic criteria for CBH are as follows:

1. HBsAg positive >6 months
2. Serum HBV DNA >105 copies/mL
3. Persistent or intermittent elevation in ALT/AST levels
4. Liver biopsy showing chronic hepatitis (different grades of necroinflammation and various stages of fibrosis), not mandatory.

HBeAg is reactive in wild type virus but is absent in pre-core mutants where anti-HBe antibody appears in the presence of detected HBV DNA.⁴⁸

Inactive HBsAg Carrier State

This state is characterized by persistence of HBV infection of the liver without significant, ongoing necro-inflammatory disease and the following criteria

1. HBsAg positive >6 months
2. HBeAg negative, anti-HBe positive
3. Serum HBV DNA <10⁵ copies/mL
4. Persistently normal ALT/AST levels
5. Liver biopsy confirms absence of significant hepatitis (necroinflammatory score <4)

Cirrhosis

Patients might present with cirrhosis for the first time (compensated or decompensated).

Acute Exacerbation or Flare of Hepatitis B

Intermittent elevations of aminotransferase activity to more than 10 times the upper limit of normal and more than twice the baseline value.

Reactivation of Hepatitis B

Reappearance of active necro-inflammatory disease of the liver in a person known to have inactive HBsAg carrier state or resolved hepatitis.

Resolved Hepatitis B

Previous HBV infection without further virologic, biochemical, or histologic evidence of active virus infection or disease.

1. Previous known history of acute or chronic hepatitis B or the presence of anti-HBc ± anti-HBs antibodies
2. HBsAg negative, undetectable serum HBV DNA, Normal ALT

Recommendations

Evaluation of Patients with Chronic HBV Infection

Initial evaluation includes history and physical examination and laboratory tests to assess liver disease i.e. complete blood counts with platelets, hepatic panel and prothrombin time.

Further test includes

- Tests for HBV replication: HBeAg / anti-HBe, HBV DNA
- Tests to rule out other cause of liver disease: anti-HCV, anti-HDV
- Tests to screen for HCC: AFP and, in high risk patients,

- Ultrasound
- Test to grade and stage liver disease: Liver biopsy for patients who meet criteria for chronic hepatitis.

Suggested follow-up for patients not considered for treatment

- a) HBeAg-positive chronic hepatitis with HBV DNA >10⁵ copies/mL and normal ALT
 - ALT every 3-6 months
 - If ALT >1-2 X ULN, recheck ALT every 1-3 months
 - If ALT > 2 X ULN for 3-6 months and patient is HBeAg positive, HBV DNA >10⁵ copies/mL, consider liver biopsy and treatment
 - Consider screening for HCC in relevant population
- b) Inactive HBsAg carrier state
 - ALT every 6-12 months
 - If ALT > 1-2 X ULN, check serum HBV DNA level and exclude other causes of liver disease
 - Consider screening for HCC in relevant population.

Treatment of Chronic Hepatitis B

Goals of Treatment

The primary goal of treatment in chronic hepatitis B is to eliminate or permanently suppress HBV replication. The short term goal is to ensure the loss of HBeAg (with appearance of anti HBe and /or loss of HBV DNA or significant suppression with ALT normalization at the end of the treatment. This will decrease pathogenicity and infectivity of hepatitis B virus and will reduce hepatic activity and necro-inflammation. The ultimate goal of treatment is to decrease progression to cirrhosis and /or hepatocellular carcinoma and thus improve ultimate survival.^{42,49}

Current available Treatments

Most frequent treatment of chronic hepatitis B has been with interferon alpha (INF-a) and nucleoside analogue lamivudine. However, pegylated interferon and other nucleosides, in particular, adefovir dipivoxil and entecavir are also being used.

Alpha Interferon

Alpha Interferon given 5 MU subcutaneously daily or 10 MU subcutaneously every other day for 4-6 months has given a seroconversion rate of 35-40% compared to 10-20% of controls.⁴⁹ In those patients who achieve HBeAg sero-conversion, more than 80% cases are sustained and may be followed by loss of hepatitis B surface antigen (HBsAg). However, loss of HBsAg has been rare in Asian

patients.⁵⁰ A biochemical "flare up" evidenced by a rise in serum aminotransferase levels often coincides with a fall in HBV DNA and is mostly observed near the end of treatment in responders to INF- α .⁵¹

Patients treated with interferon have significant side effects and hepatitis flares may lead to hepatic decompensation in some patients with cirrhosis.^{49,50} INF is contraindicated in patients with uncontrolled seizures, autoimmune disease, cardiac arrhythmias and decompensated cirrhosis.⁵¹ Patient with high ALT and high HIA score and low HBV DNA level respond better to INF.^{50,51} Patients with lower ALT, high HBV DNA and immunosuppression have poorer response.⁴⁹ Long term follow up studies from Asia, Europe and USA have shown better survival in CHB patients with compensated cirrhosis⁵¹ especially if they seroconvert.

Lamivudine

A dose of 100 mg per day produces HBeAg seroconversion in proportion to pre treatment ALT levels. A response of 65% in patients with ALT >5 x ULN and 25% in patients with ALT 2-5 x ULN and only 5% in those with ALT <twice ULN has been noted.^{50,51} Lamivudine has been found to be effective in Asian patients with chronic hepatitis B when used for extended period of time.⁵² Its efficacy has been demonstrated in patients with HBeAg-positive and HBeAg-negative chronic hepatitis B.⁵³ Patient with elevated ALT and active histologic disease were most important factor in prediction of HBeAg loss after lamivudine therapy.⁵⁴ Prolonged therapy with Lamivudine increases the proportion of HBeAg seroconversion and those patients who achieve this have more than 80% sustained responses.^{50,54} Lamivudine has been well tolerated but prolonged use has resulted in emergence of YMDD mutations and reappearance of HBV DNA and frequent ALT elevation.⁵⁵ After one year of lamivudine therapy, 14 to 32% of individuals have genotypic resistant mutation.⁴⁹⁻⁵¹

Other Promising Therapies

Adefovir depivoxil in a dose of 10 mg per day causes significant suppression of HBV DNA and results in improved histology.⁵⁶ It effectively suppresses the YMDD mutants. It has been approved by FDA and under the process of registration in Pakistan. Entecavir is another nucleoside analogue which is showing promising results in early trials especially in lamivudine - resistant strains.⁵⁶ Other agents under trial include thymosine alpha, monoclonal antibodies, therapeutic vaccines, interleukin-12 and Chinese herbal medicines.

Combination Therapy

Interferon alpha given 9 MU three times a week with

lamivudine 100 mg daily for 52 weeks is more effective than interferon monotherapy.⁵¹

Special Groups

Children can be treated with lamivudine and interferon. Pregnancy is not a contraindication for lamivudine. Patients with HIV can also have lamivudine included in their therapy and has been helpful for effective HBV suppression in these patients.⁵⁰

Role of Liver Biopsy

Liver biopsy is recommended before the treatment to determine the fibrosis stage and extent of necro-inflammation which may be helpful in guiding the anti-viral treatment⁵⁰ and may help to rule out other causes of liver disease.⁵⁷

Recommendations

Who To Treat and How to Treat

- Patient with normal ALT respond poorly and should not be treated.
- Patient with elevated ALT at least twice the upper limits of normal and HBeAg-positive with or without detectable HBV DNA should be considered for treatment.
- Patient with HBeAg-negative (pre core mutant) should be considered for treatment if ALT is elevated and HBV DNA is present.
- Patient with ALT level more than two times ULN should be started on either lamivudine 100 mg daily or interferon alpha (5 MU daily or 10 MU thrice weekly or 6MU/m² (children).
- Patient with positive HBeAg and ALT levels of 1-2 times upper limits of normal are difficult to treat and observation with monitoring of ALT, HBeAg / HBV DNA and serial liver biopsies may be recommended in these patients.

How to Monitor

- Patients on lamivudine should have ALT, HBeAg and /or HBV DNA at least every 2-3 months. After seroconversion, they should be monitored every 3 months with ALT, HBeAg and HBV DNA.
- Patient on interferon should be monitored with CBC, ALT, HBeAg and/or HBV DNA every 1-2 months.
- After the end of the therapy, patient's ALT and HBV DNA and HBeAg should be checked every 2-3 months.

When to Stop Therapy

- Recommended duration of interferon therapy is 4-6 months irrespective of response. Subsequent follow up may

show sero-conversion even at a later date.

- Patients treated with lamivudine can be advised to stop treatment after one year or when there is normal ALT, HBeAg sero-conversion with HBV DNA loss on two consecutive measurements at least three month apart.
- Longer treatment is required for HBeAg negative HBV DNA positive mutants (IFN for one year or lamivudine >one year)
- To cover YMDD variants consider adding adefovir in patients with disease breakthrough or in HBeAg negative patients for whom long term therapy is required.

Prevention of hepatitis B virus infection

In 2001-2002 Pakistan received a major grant from the Global Alliance for vaccines and Immunization (GAVI) that has enabled the introduction of Hepatitis B in routine EPI vaccination.⁵⁸

Currently available hepatitis B vaccines are extremely safe. Unfortunately, vaccination coverage is low in Pakistan because of the lack of funding and infrastructure to purchase and deliver the vaccines. There is a misconception that vaccination is only necessary in high-risk groups.

Neonatal Vaccination

The global advisory group of the Expanded Program on Immunization (EPI) recommended integration of hepatitis B vaccine into all national immunization programs. Universal vaccination of all newborns regardless of maternal HBsAg status is necessary for global eradication of HBV infection. HBIG and concurrent hepatitis B vaccine have been shown to be 95 percent efficacious in the prevention of perinatal transmission of HBV from HBsAg positive mothers.⁵⁹

Catch-up Vaccination

It refers to vaccination of children who were born before universal neonatal vaccination was implemented. Most of these children are school-age

High-risk Groups Vaccination

Every effort should still be made to vaccinate high-risk individuals. These include homosexual or bisexual males⁶⁰, household contacts of patients with hepatitis B, intravenous drug users, healthcare workers, patients on chronic hemodialysis, sexually active individuals with multiple sex partners and patients requiring repeated blood or blood product transfusion .

In a local study, only 49% health care workers and 42.20% medical students were vaccinated. The main reasons for non-vaccination (47.7%) among health care

workers was the high cost of vaccination, while the most often cited reason (33.7%) among medical students was the belief that they were not at risk. This belief was also prevalent among nurses (36.4%), laboratory workers (38.6%) and paramedics (33.2%).⁶¹

Seroprotection

Using the definition of >10 IU/L anti-HBs as a positive response, the overall seroconversion rate is about 95 percent in healthy adults. The rate decreases with increasing age.⁶² The response rate is significantly lower in patients with cirrhosis or chronic renal failure, organ transplant recipients, and immunosuppressed patients.

Duration of Protection

Although anti-HBs titers decrease with time, the duration of protection is prolonged.^{63,64} The long duration of protection despite low or undetectable anti-HBs levels is probably due to the priming of memory cells, which are capable of eliciting anamnestic response when challenged. Protection appears to extend beyond 12 to 15 years in vaccinees who have a high titer anti-HBs response (>100 IU/L) after the initial course of vaccination.⁶⁴⁻⁶⁶ Thus, regular booster injections are not required except for patients on hemodialysis in whom vaccine-induced protection may persist only as long as the antibody level is above 10 IU/L.⁶⁷

Pre-vaccination Screening

Pre vaccination screening is unnecessary in children. Screening should be performed in Pakistani adults since there is a high prevalence of past and current infection. Screening may be performed by a single test for anti-HBc alone, which will detect individuals with past and current infection, or by a combination of tests for HBsAg and anti-HBs. Administration of hepatitis B vaccine to individuals who are infected or immune will not result in any adverse outcome but screening would help in case identification.

Dose and Frequency

The recommendation for dose of the vaccine depends upon the availability of the studies of that vaccine. For adults, it is 20 µg in three doses at months 0, 1 to 2, and then 6 to 12, for most of the vaccines available in Pakistan. A recent study done in Pakistan using a Cuban vaccine showed two doses of 20µg in adults and 10 µg in subjects up to 20 years given at 0 and 1 month give adequate protection. Three doses of 10 µg of this vaccine given to adults at at 0, 1 and 6 months also achieved the comparable seroprotection.⁶⁸

In infants, children and adolescents up to the age 19, three shots of half the normal adult dose of a particular vaccine are required to complete the course.⁶⁶⁻⁶⁹ An optional

two dose regimen of an American vaccine has also been approved for adolescents aged 11 to 15 using the adult dose with a second shot given four to six months after the first dose.^{70,71}

Efficacy of low-dose, intra-dermal hepatitis B vaccination has also been assessed in Pakistan with comparable efficacy, although technical difficulties do exist in this method.⁷²

Recommendations

- Patients with chronic HBV infection should be counseled regarding lifestyle modifications and prevention of transmission.
- Abstinence or only limited use of alcohol is recommended in hepatitis B carriers.
- Nosocomial transmission can be prevented by
 - screening of blood and blood products,
 - use of disposable needles and equipment,
 - proper sterilization of surgical instruments,
 - enforcement of infection control measures and
 - vaccination of healthcare workers.
- Compliance with universal precautions for infection control in the health care setting should be ensured
- Healthcare workers who are positive for hepatitis B surface antigen (HBsAg) and HBV DNA or hepatitis B e antigen (HBeAg) should stop "exposure-prone" procedures. Those who are HBsAg positive but HBV DNA negative may continue their usual work.
- Program of HBV vaccination of neonates should be strictly implemented.
- Carriers should be counseled regarding prevention of transmission of HBV. Carriers should be advised to cover open cuts and scratches and clean up blood spills with bleach, because HBV can survive on environmental surfaces for at least one week.⁷³
- Public health education and the use of disposable needles or equipment are important in preventing this mode of transmission.
- Healthcare workers should be screened for Hepatitis B and vaccinated.
- Sexual and household contacts of carriers should be tested for HBV (HBsAg and anti-HBs) and if negative receive hepatitis B vaccination. For sex partners who have not been tested or have not completed the full immunization series, barrier protection methods should be employed.
- Maternal carrier testing should be performed on all

women at the first prenatal visit

- Newborns of HBV-infected mothers should receive HBIG and hepatitis B vaccine at delivery and complete the recommended vaccination series.
- Greater flexibility is permitted in the vaccination schedule for infants born to mothers with negative HBsAg status. The first dose can be administered up to two months of age, the second dose at four months, and the third dose up to 18 months.
- Two dose regimens may be followed where the clinical data is available of that particular vaccine.
- Vaccines should be administered intramuscularly since deposition of the vaccine into adipose tissue result in a lower seroconversion rate.⁷⁴ Thus, the deltoid is the preferred site in adults while the vastus lateralis is preferred in infants. Longer needles should be used in overweight individuals.
- Cesarean section should not be routinely recommended for carrier mothers.
- Infants who have been vaccinated may be breast-fed.⁷⁵
- Regular booster injections are not required in ordinary risk individuals.
- Persons who remain at risk for HBV infection such as infants of HBsAg-positive mothers, health care workers, and dialysis patients should be tested for response to vaccination. Infants of carrier mothers should be tested at age nine to fifteen months, and health care workers one to two months after vaccination, and dialysis patients should be tested annually.²⁵
- Patients undergoing hemodialysis should receive double the standard dose⁷⁶ as well as annual booster doses
- Nonresponders should complete a second three-dose vaccine series or undergo testing to determine whether they are positive for HBsAg. Retesting for anti-HBs should be repeated after the second vaccination series.²⁰
- As many as 80 percent of these individuals with isolated anti-HBc developed a primary anti-HBs response to hepatitis B vaccine, suggesting that these individuals should be vaccinated.⁷⁷

Postexposure Prophylaxis

- Postexposure prophylaxis is recommended for all nonvaccinated individuals who are exposed to blood or infectious secretions. The first dose vaccine should be given as early as possible within 12 hours of exposure while administering one dose of HBIG at the same time in another site.
- Individuals who have no post-vaccination testing will require a second course of vaccination unless anti-HBs is

detectable at the time of exposure.

- Individuals who are documented to be non-responders will require two doses of HBIG given one month apart.

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