Prevention of Hepatitis B Virus Infections

Infants born to mothers who are hepatitis B surface antigen (HBsAg) positive are frequently infected with hepatitis B virus (HBV). Many of these newborns will become chronic carriers of HBV and will subsequently develop chronic liver disease. Recent studies have demonstrated that perinatal transmission can be prevented by immunization of the newborn. Recommendations for the management of infants at risk are presented.

PERINATAL TRANSMISSION OF HBV INFECTIONS

Perinatal infection of infants by mothers who are HBsAg positive is most likely to occur if mothers are also hepatitis B antigen positive. About 90% of infants whose mothers are positive for both markers will become infected and most will become permanent carriers. Infants whose mothers are HBsAg negative or who have antibody to HBsAg are at lesser risk, but can still be infected.

Infected infants usually will not become HBsAg positive until several weeks after birth. Although clinical jaundice or acute hepatitis are rare in infected infants, elevations in transaminase levels are frequent. It is estimated that about one in four infants who become chronic carriers following perinatal infection will develop cirrhosis or hepatocellular carcinoma later in life. As they are persistent carriers, later in life they may transmit infection to other family members, to sexual contacts, or to others by transfusions or inoculation of their blood. Infection of female infants may eventually result in transmission of HBV to their own infants. Indeed, transmission from mother to infant is a major method of perpetuation of this virus in hyperendemic areas, eg, the Far East.

SCREENING OF WOMEN FOR HBsAg

Pregnant women who are HBsAg positive should be identified prior to delivery. This is essential to enable those who are to attend her at delivery to minimize the risk of exposure to her blood. It is urgent, moreover, that passive immunization of infants of mothers who are HBsAg positive be accomplished promptly after birth in order to prevent infection in the infants.

It has been estimated that certain ethnic groups account for approximately two thirds of infants at risk of HBV infection in the United States. In a study in New York City, San Francisco, and Los Angeles approximately 8.6% of all women of Asian descent, including 2.4% of those who were native born, were found to be HBsAg positive. Nearly 40% of these women will also be positive for HBsAg. Other women may be at increased risk of being HBsAg positive because of occupation, life-style, exposure to an infected sexual partner, or health-related reasons. Infants of these mothers should be immunized regardless of HBsAg status; therefore, testing for HBsAg only is recommended. In order to identify women who are HBsAg positive, it is recommended that the following be included in a screening program: (1) women of Asian, Pacific Islander (Polynesian, Micronesian Melanesian) or of Alaskan Eskimo descent; (2) women born in Haiti or Sub-Saharan Africa; and (3) women with a history of (a) acute or chronic liver disease, (b) having worked or been treated in a hemodialysis unit, (c) having household or sexual contact with a hemodialysis patient, (d) having occupational or residential exposure in an institution for the mentally retarded, (e) having been rejected as a blood donor, (f) receiving blood transfusions on repeated occasions, eg, for thalassemia, (g) frequent occupational exposure to blood in medicodental settings, (h) household contact with an HBV carrier, (i) multiple episodes of venereal disease, and (j) percutaneous use of illicit drugs.

IMMUNIZATION OF INFANTS

The greatest protection of infants is achieved by using a combination of active immunization of infants with three doses of hepatitis B vaccine and passive immunization with hepatitis B immune globulin (HBIG). HBIG should be administered as soon after birth as possible, but vaccine adminis-
tration may be delayed if necessary. However, giving the first dose of vaccine prior to discharge from the hospital eliminates an additional return visit. Infants should be immunized whether delivered vaginally or by cesarean section.

The administration of 0.5 mL of HBIG intramuscularly should be incorporated into routine procedures for newborn care of these infants, eg, administration of vitamin K and prophylaxis of ophthalmia neonatorum. In studies evaluating the effectiveness of HBIG in preventing HBV infection, most infants received HBIG within a few hours after birth. Although delay is not recommended, it is believed that HBIG would still be effective when given up to 48 hours after birth. Even if mothers are found to be HB,Ag positive after this time, HBIG should be given as it might still be of some value. HBIG given at birth should not interfere with the response to DTP (diphtheria-pertussis-tetanus) or polio vaccine given at 2 months of age.

The first dose of hepatitis B vaccine can be given at the same time as HBIG using a different site and a separate syringe. Data on the effectiveness of hepatitis B vaccine are not available for infants with birth weight less than 2,000 g. If necessary, vaccine but not HBIG administration can be delayed. If hepatitis B vaccine must be delayed until 3 months of age, a second dose of HBIG, 0.5 mL, should be given. A dose of 10 μg of hepatitis B vaccine (0.5 mL or half the adult dose) is administered, followed by similar doses 1 and 6 months after the first. Simultaneous administration of hepatitis B vaccine with DT-polio vaccine has not led to increased reactions. Antitetanus antibody in infants immunized with DT-polio vaccine was similar in infants who did or did not receive hepatitis B vaccine. Antibody to hepatitis B antigens was similar in infants who received hepatitis B vaccine with or without DT.

The presence of anti-HB, after 9 months of age is indicative of successful immunization. In one study, 94.3% of infants immunized with HBIG and hepatitis B vaccine were anti-HB, positive when tested; 2.5% of the infants were persistently HB,Ag positive from birth and could not have been successfully immunized. Children should be tested for HB,Ag and anti-HB, at 9 months of age or later. Those who are found to be negative for anti-HB, and anti-HB,Ag should receive another dose of hepatitis B vaccine and retested. Those who are HB,Ag positive are infected, and they should be tested periodically as they are likely to become chronic carriers. Infants who are found to be HB,Ag positive at any time should not receive additional doses of HBIG or hepatitis B vaccine.

The following schedule is recommended: (1) at birth, 0.5 mL of HBIG as soon as possible and 10 μg of hepatitis B vaccine (0.5 mL or half the adult dose) before discharge; (2) 1 and 6 months, after the first dose, 10 μg of hepatitis B vaccine; and (3) 9 months of age or later, test for anti-HB,Ag.

**PRECAUTIONS FOR INFANTS OF HB,Ag POSITIVE MOTHERS**

Infants born to mothers who are HB,Ag positive should be cleansed by a gloved attendant. There is no need to isolate such infants. As a small number of these infants will be HB,Ag positive at birth, their blood should be handled with appropriate precaution. Infants who are to have surgical procedures, eg, circumcision, or who are to remain in the hospital for additional treatment, eg, premature infants, should have venous blood tested for HB,Ag. Testing of cord blood is unreliable and is not recommended. There appears to be no reason to withhold breast-feeding. In two studies in which infants were not protected by immunization, there was no increased risk of HBV infections in those who were breast-fed.

**IMMUNIZATION OF CONTACTS OF CARRIER MOTHERS OR INFANTS**

Susceptible personnel who are likely to be exposed to the blood of infants or mothers with HBV infection should be considered at increased risk of contracting hepatitis and should be immunized with 20-μg (1-mL) doses of HBV vaccine. Household members and sexual contacts of those who are HB,Ag positive should receive hepatitis B vaccine if testing indicates they are negative for antigen and antibody. Dose is 10 μg for those less than 10 years of age; others should receive 20 μg. Immunization requires a series of three doses. The second dose is 1 month after the first, and the third dose should be 6 months after the first.

**SAFETY OF HEPATITIS B VACCINE**

To date, approximately 1.5 million doses of hepatitis B vaccine have been distributed; it is estimated that about .5 million individuals have received two or more doses. Approximately 35 significant reactions have been recorded following receipt of the vaccine. These have included arthritis and arthralgia, some neurologic reactions, and others. The rate of Guillain-Barré syndrome following administration of hepatitis B vaccine does not appear to be increased above the expected level. It cannot be determined whether such temporally associated reactions are etiologically related to hepatitis B vaccine.
Although the vaccine is prepared from material obtained from the blood of HBV carriers, it is treated with urea, formalin, and pepsin, substances known to inactivate viruses of all known classes including retroviruses. To date, there have been no cases of acquired immune deficiency syndrome (AIDS) in vaccine recipients who are not also in established groups at high risk for developing AIDS.

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