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Failure of neonatal hepatitis B vaccination: the role of HBV-DNA levels in hepatitis B carrier mothers and HLA antigens in neonates

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In a hepatitis B vaccination program (1982–1992), 705 infants born to HBsAg-positive mothers received HBIg within 2 h of birth and were vaccinated according to a three- or four-dose vaccination schedule, starting either at 3 months or directly after birth. Eight children became HBsAg-positive during the first year of life (group 1: infected nonresponders). To determine whether failure of the hepatitis B vaccination was due to perinatal high-level maternal viraemia or genetically determined infant nonresponsiveness to the vaccine, we measured HBsAg and anti-HBs levels in infants and HBeAg and hepatitis B virus-DNA levels in maternal serum, and determined the HLA type of the infants. Controls included 14 infants with a normal anti-HBs response 1 year after vaccination (group 2: noninfected responders) and all eight infants without HBsAg and anti-HBs 1 year after vaccination (group 3: noninfected low responders). HBsAg, HBeAg and anti-HBs were measured by radioimmunoassay (Abbott Laboratories), hepatitis B virus-DNA was measured quantitatively by solution hybridization for groups 1, 2, and 3 (Abbott hepatitis B virus-DNA assay, Abbott Laboratories), and HLA was characterized by

microcytotoxicity test for groups 1 and 3. All infants in groups 1 and 2 were born to HBeAg carrier mothers, and those in group 3 to HBeAg-negative mothers. Hepatitis B virus-DNA levels in maternal serum in group 1 were significantly higher than in group 2 (Wilcoxon rank-sum test: $p<0.01$). Hepatitis B virus-DNA was not observed in group 3 maternal serum samples. HLA B8 and DR3 were not found in group 1 but were present in 4/8 and 2/8 infants of group 3, respectively. Failure of current passive-active hepatitis B immunization appears to be related not to genetic nonresponsiveness in infants but rather to perinatal high-level maternal viraemia. Hepatitis B virus-DNA assay of HBeAg-positive mothers may identify those infants in need of additional action to lower the risk of vertically transmitted hepatitis B virus infection.

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Key words

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