LEADING ARTICLE

HEPATITIS B VACCINATION - THE PRESENT STATUS

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Hepatitis B virus (HBV) infection is endemic locally. Neonatal and childhood infections occur frequently [1]. When infection is acquired early in life, persistence of the disease is the rule. Chronic infection can progress to chronic hepatitis, cirrhosis and hepatocellular carcinoma (which is a very common cancer in this region). There is no effective treatment for chronic HBV infection to date. The only sure way to prevent the development of the carrier state and its chronic sequela is to immunise all newborns, children and susceptible young adults.

Presently two types of Hepatitis B vaccines are available. The plasma-derived vaccine has been in the market since 1982. Recombinant yeast vaccines became available in 1986. Early concern regarding transmission of the human immunodeficiency virus (HIV) by the plasma-derived vaccine has proved to be unfounded [2].

Screening prior to vaccination is recommended in areas of high prevalence of HBV infection because of the high costs of vaccines. Although no conceivable harm could occur when a carrier is vaccinated, this is probably a wasteful procedure as it offers no protection. Besides, these carriers may be misled to believe that they have been protected while they continue to be a source of infection to others. For those already immune, vaccination would boost their antibody levels. Hepatitis B surface antigen (HBsAg) and antibodies to HBsAg (AntiHBs) are widely adopted as screening tests. Antibody to HB-core antigen (AntiHBc) when present indicates previous infection but does not differentiate carriers from those who have recovered from an acute infection. Besides, low levels are unreliable and the test is expensive. A recent study showed that the pick-up rate of patients with previous exposure to HBV was similar whether anti-HBc was measured alone or when HBsAg and anti-HBs were measured together [3].

Recommended vaccine doses for healthy subjects vary among different makes of vaccines. Some manufacturers recommend different doses for different age groups. Table I summarizes the different doses of the more commonly available vaccines. Conventional doses of these vaccines have been found to protect up to 60% of infants of HBeAg positive (actively replicating and therefore infectious) mothers, if given at birth. The protection rate is increased to 95% when HB immune globulin is given together with the first dose of vaccination to such infants [4].

Table I
Common vaccines in current use - dosage for different age groups (recommended by manufacturers) for vaccination at month 0, 1, 6.

	<10 yrs	10 - 19 yrs	> 20 yrs
Plasma Vaccine MSD (B-HepVac I)	5 µg	10 µg	10 µg
Yeast Vaccine MSD (B-HepVac II)	2.5 µg	5 µg	10 µg
Engerix-B (SKF)	20 µg	20 µg	20 µg

This regime is also recommended for post-exposure prophylaxis (eg. needle prick injuries) although the protection rate in such instances has not been assessed. A recent study from Thailand using a yeast-derived vaccine alone has shown a protective efficacy of 95% in infants of HBe positive mothers [5]. The site of injection has been found to affect the absorption and ultimately, the antibody response of the vaccinee. Injections should be given into the deltoid muscle in children and adults and in the thigh muscles anterolaterally in neonates [6].

Because of high cost of vaccines, and in order to bring vaccination to the masses in endemic but developing countries, the effectiveness of reduced doses was investigated. Reduction in doses of certain vaccines

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has been found to be as immunogenic as the full recommended dose among young adults in Greece, Singapore and New Zealand [7-10].

The actual protective level of anti-HBs has not yet been established although levels in excess of 10 IU/L (EIA) are generally considered adequate. The overall antibody response rate to HB vaccination is about 95%. Response among young healthy adults is excellent and the majority of them will develop high antibody levels [7,9,10]. This is also evident in a recent study from Malaysia [11]. Antibody response decreases with increasing age and lower levels of anti-HBs are achieved among older people. Immunosuppressed patients including those with renal failure on chronic haemodialysis respond suboptimally and doubling the dose increases anti-HBs response in these individuals [12]. Non-responders are individuals who are completely negative for anti-HBs one to three months after completing a standard regimen. Hyporesponders are those who have a low titre of anti-HBs (<10 IU/L) one to three months after completion of vaccination. The actual incidence of non-responsiveness is rather low and non-responders/hyporesponders eventually respond to repeated booster doses of vaccines. Pre-S vaccines (still under clinical evaluation), are thought to be more immunogenic and may be useful to non-responders and hyporesponders. Immune manipulation eg. giving vaccines together with low doses of interferon, has been found to increase the antibody response rate in non-responders/hyporesponders [13].

Although no data is available on the safety of the vaccine in the developing foetus, the risk is minimal as both plasma and yeast vaccines are inactivated and do not contain live virus particles. Pregnancy should therefore not be considered a contraindication for women in the high risk group [12].

The duration of immunity after successful vaccination is unknown. Available data indicate that vaccine-induced antibody levels decline significantly with time [14]. The duration of antibody persistence is directly related to the peak level achieved after the third dose of vaccine [15]. Studies in adults have demonstrated that in spite of declining levels of antibody, protection against clinical (or viremic) HBV infection persists for more than 5 years [14]. It appears that vaccinees, once responded, are likely to develop anamnestic responses on subsequent exposure to the virus [16]. Booster doses may not be routinely required for healthy children and adults who had good initial response to vaccination. The situation with booster doses after long intervals will become clearer when additional information becomes available.

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EDITOR'S NOTE

In the Epidemiological News Bulletin of Singapore, published in February 1990 [1], it was stated that both the 5 µg and 10 ug were equally efficacious in producing seroconversion in babies given the Merck plasma-based vaccine at birth (with HBIG), one month and 2 months who were born to HBeAg carrier mothers. The seroconversion also prevented clinical hepatitis B and the chronic carrier state. In Taiwan, it is not the recommendation to use lower than 10 ug doses for vaccination since the chronic carrier state was dependent on the dose of antigen given but it is important to note that the vaccine used was "Heptavax", Merck, Sharp and Dohme, and the regimen was different - at birth, one month and 6 months [2-4].

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