

Immunization: An Important Strategy to Control Hepatitis B

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Hepatitis B virus (HBV) is a serious public health problem world-wide and a major cause of chronic hepatitis, cirrhosis, and hepatocellular carcinoma (HCC). More than 350 million are chronic carriers of HBV⁽¹⁾ and approximately 75% of them live in Asia and Africa⁽²⁾. It was reported that 15-40% of HBV infected patients would develop cirrhosis, liver failure, or HCC⁽³⁾ and 500,000 to 1.2 million people die of HBV infection annually^(4,5). Because of the high HBV-related morbidity and mortality, the global disease burden of HBV infection is substantial.

The asymptomatic carrier status has far-reaching consequences particularly for pregnant women who have been shown to vertically transmit the virus to their fetuses. Thus, between 35 -40% of all the HBV infected cases diagnosed world-wide every year are resulted from this major mode of transmission⁽⁶⁾.

Transmission of HBV from carrier mothers to their babies can occur during the perinatal period, and appears to be the most important factor in determining the prevalence of the infection in high endemicity areas. Before integrating HBV vaccine into the routine immunization program, the proportion of babies that become HBV carriers was about 10-30% for mothers who were HBsAg-positive but HBeAg-negative. However, the incidence of perinatal infection is even greater, around 70-90%, when the mother is both HBsAg-positive and HBeAg-positive⁽⁷⁻⁸⁾. For neonates and children younger than 1 year who acquire HBV

infection perinatally, the risk of the infection becoming chronic is 90%⁽⁹⁾. The development of safe and highly effective hepatitis B vaccines now provides the means to confer long-term immunity against HBV infection⁽¹⁰⁾.

In May 1992, the World Health Assembly, the governing body of the World Health Organization, endorsed recommendations stating that all countries should have hepatitis B vaccine integrated into their national immunization programmes by 1997⁽¹¹⁾.

Since effective vaccines against hepatitis B became available in 1982, their widespread use in many areas of the world has dramatically reduced the carrier rate of HBV and significantly decreased the incidence of childhood HCC^(12, 13).

Following the neonatal vaccination programmes that were begun in 1989 in Saudi Arabia, the overall HBsAg carrier rate in children under 12 years old fell from 6.7% in 1989 to 0.3% in 1997⁽¹⁴⁾. Chen et al showed that 10 years after implementation of mass vaccination in Taiwan, the HBsAg seropositivity rate declined from 9.8% to 1.3%⁽¹⁵⁾.

A study carried out in Iran showed a significant reduction in the rate of HBsAg positivity in the subgroup of children aged 2-14 years after EPI. And postnatal horizontal transmission of HBV was prevented partly⁽¹⁶⁾.

Moreover, the children perinatally infected by their mothers may themselves be a source of horizontal transmission to their younger siblings and playmates, especially in overcrowded living conditions. Therefore, breaking the mother-to-

child transmission will interrupt most of the secondary routes of transmission, as well (17).

Giving vaccines to infants of HBeAg-positive mothers as soon as possible after birth is reasonable. In some countries, high protective efficacy rates have been reported without concomitant administration of hepatitis B immunoglobulin (HBIG) to high risk infants whose mothers were HBsAg-positive (18, 19).

The importance of hepatitis B immunoglobulin is overstated. It provides comparatively little additional protection to immunization in preventing infection in infants of HBeAg-positive mothers (20, 21).

Besides, the results of some studies in Taiwan and Hong Kong showed that the protective efficacy of vaccine alone was significantly low, especially when the mother is HBeAg-positive (17, 22).

Hepatitis B vaccination strategies may vary from one country to another, depending on HBV endemicity, predominant modes of the infection, age of contracting the infection, and available health care resources (23).

The rate of transmission and HBV carriage rates in high risk children strongly depends on HBeAg status of the mother. However, vaccination is stopping transmission in high risk groups partly, rather than completely (24). Thus, contriving a nationally accepted plan requires further analysis with attention to the efficacy of passive immunization, cost of prevention, the use of prenatal maternal screening, and costs of care for hepatitis B patients. Cost-effectiveness analysis of the hepatitis B vaccines and HBIG combination is likely to be a useful tool for this strategy. The global literature is relatively rich in economic evaluations of immunization against hepatitis B, especially studies from industrialized countries (25).

The overwhelming conclusion of these reviews is that the introduction of hepatitis B vaccine can be fully justified on economic grounds 'economic' grounds meaning either that the cost-benefit ratio is positive or that the cost-effectiveness ratio suggests the vaccine to be a good 'buy' for the public health services or both. A consensus statement in 2001 concluded that universal hepatitis B vaccination of infants is the most optimal strategy worldwide and the most cost-effective it becomes to vaccinate in the earlier years of life (26). For cost-effectiveness study of introducing the mother screening for HBsAg and addition of the HBIG to hepatitis B vaccine to high risk infants one needs to understand the premature deaths that can be prevented by this new strategy.

By the way, mass vaccination has been shown to be a safe and highly effective means for the control and prevention of HBV and protective efficacy following complete vaccination exceeds 95% (27, 28).

References

1. World Health Organization. Hepatitis B: World Health Organization Fact Sheet 204.2000. <http://www.who.int/mediacentre/factsheet/fs204/en/>
2. Gust ID. Epidemiology of hepatitis B infection in the Western Pacific and South East Asia. *Gut* 1996; **38**: S18-S23
3. Lok AS. Chronic hepatitis B. *N Engl J Med* 2002; **346**: 1682-83
4. Mahoney FJ. Update on diagnosis, management, and prevention of hepatitis B virus infection. *Clin Microbiol Rev* 1999; **12**: 351-66
5. Lee WM. Hepatitis B infection. *N Engl J Med* 1997; **337**: 1733-45
6. Ghendon Y. Perinatal transmission of hepatitis B virus in high incidence countries. *J Virol Methods* 1987; **17**: 69-79
7. Sevens CE, Neurath RA, Beasley RP, Szmuness W. HBeAg and anti-HBe detection by radioimmunoassay. Correlation with vertical transmission of hepatitis B virus in Taiwan. *J Med Virol* 1979; **3**: 237-41
8. Xu ZY, Liu CB, Francis DP, Purcell RH, Gun ZL, Duan SC, et al. Prevention of perinatal acquisition of hepatitis B virus carriage using vaccine: preliminary report of a random double-blind placebo-controlled and comparative trial. *Pediatrics* 1985; **76**: 713-18
9. Hyams KC. Risks of chronicity following acute hepatitis B virus infection: a review. *Clin Infect Dis* 1995; **20**: 992-1000
10. Margolis HS, Coleman PJ, Brown RE, Mast EE, Sheingold SH, Arevalo JA. Prevention of hepatitis B virus transmission by immunization: an economic analysis of current recommendation. *JAMA* 1995; **274**: 1201-08
11. Maynard JE, Kane MA, Hadler SC. Global control of hepatitis B through vaccination: role of hepatitis B vaccine in the Expanded Program on immunization. *Reviews of Infectious Diseases* 1989; **11**: S574-78
12. Coursaget P, Yvonnet B, Chotard J, et al. Seven year study of hepatitis B vaccine efficacy in infants from an endemic area in Senegal. *Lancet* 1986; **2**: 1143-45
13. Chang MH, Chen CJ, Hsu HM, et al. Universal hepatitis B vaccination in Taiwan and the incidence of hepatocellular carcinoma in children. Taiwan Childhood Hepatoma Study Group. *N Engl J Med* 1997; **336**: 1855-59
14. Al-Faleh FZ, Al-Jeffri M, Ramia S, Al-Rashed R, Arif M, Rezeig M, et al. Seropositivity of hepatitis B virus infection in Saudi children 8 years after a mass hepatitis B vaccination programme. *JAMA* 1999; **38**: 167-70
15. Chen HL, Chang MH, Ni YH, Hsu HY, Lee PI, Lee CY, Chen DS. Seropositivity of hepatitis B virus infection in children: ten years of mass vaccination in Taiwan. *JAMA* 1996; **276**: 1802-03
16. Zali MR, Mohammad K, Noorbala AA, Noorinayer B, Shahrzad S. Rate of hepatitis B seropositivity following mass vaccination in the Islamic Republic of Iran. *East Mediterr Health J* 2005; **11**: 62-7
17. Beasley RP, Hwang LY, Lee GCY, et al. Prevention of perinatally transmitted hepatitis B virus infections with hepatitis B immune globulin and hepatitis B vaccine. *Lancet* 1983; **2**: 1099-102
18. Tsebe KV, Burnett RJ, Hlungwani NP, Sibara MM, Venter PA, Mphahlele MJ. The first five years of universal hepatitis B vaccination in South Africa: evidence for elimination of HBsAg carriage in under 5-year-olds. *Vaccine* 2001; **19**: 3919-26
19. Lolekha S, warachet B, Hirunyachke G. Protective efficacy of hepatitis B vaccine without HBIG in infants of HBeAg

- positive carrier mothers in Tailand. *Vaccine* 2002; **20**: 3739-43
20. Andre FE, Zuckerman AJ. Review: protective efficacy of hepatitis B vaccines in neonates. *J Med Virol* 1994; **44**: 144-51
 21. Poovorawan Y, Sanpavat S, Pongpunglert W, Chumdermpadetsuk S, Sentrakul P, Vandepapeliere P, *et al.* Long term efficacy of hepatitis B vaccine in infants born to hepatitis B e antigen-positive mothers. *Pediatr Infect Dis J* 1992; **11**: 816-21
 22. Wong VC, JP HM, Reesink HW, Lelie PN, Reerink-Brongers EE, Yeung CY, *et al.* Prevention of the chronic carriers state in newborn infants of mothers who are chronic carriers of HBsAg and HBeAg by administration of hepatitis B vaccine and hepatitis B immunoglobulin. Double-blind randomized placebo-controlled study. *Lancet* 1984; **1**: 921
 23. Ahn YO. Strategy for vaccination against hepatitis B in areas with high endemicity: focus on Korea. *Gut* 1996; **38**: S63-S66
 24. Adibi P, Ghassemian R, Alavian SM, *et al.* Effectiveness of hepatitis B vaccination in children of chronic hepatitis B mothers. *Saudi Med J* 2004; **25**: 1414-18
 25. Jefferson T, Demicheli V. Is vaccination against hepatitis B efficient: a review of world literature. *Health Economics* 1994; **3**: 25-37
 26. Beutels P, Edmunds WJ, Antonanzas F, *et al.* Economic evaluation of vaccination programmes: a consensus statement focusing on viral hepatitis. *Pharmacoeconomics* 2002; **20**: 1-7
 27. Tong MJ. Hepatitis B vaccination of neonates and children. *Am J Med* 1985; **87**: S33-S35
 28. Ghendon Y. WHO strategy for the global elimination of new cases of hepatitis B. *Vaccine* 1990; **8**: S129-S133, S134_S138