

# Perinatal transmission of hepatitis B virus infection and vaccination in China

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## Abstract

**Hepatitis B remains one of the most important infectious diseases in China. In 1980, an overall hepatitis B virus (HBV) infection rate of 42.6% was reported and a hepatitis B surface antigen (HBsAg) carrier rate of 10.3%. HBsAg positivity among children under 1 year of age ranged from 5.1% in Beijing to 7% in Guangdong. A peak in carrier rate was observed in 7 to 14 year olds, reaching 24% in Guangdong. During the past decade, there has been no significant change in overall HBV carrier rates. However, in areas where hepatitis B vaccination for all neonates has been introduced, a decline in HBsAg positivity in lower age groups has been observed. Perinatal transmission is believed to account for 35–50% of carriers although horizontal transmission is also important, particularly within families. Infants born to HBeAg positive carrier mothers are at even greater risk of infection. HBV infection during childhood leads to an increased risk of serious longterm sequelae, including hepatocellular carcinoma (HCC). It is hoped that universal childhood immunisation will allow control of HBV infections in China within a few generations.**

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TABLE I HBsAg positivity according to age in Beijing, 1980 and 1990<sup>2</sup>

Age (y)	HBsAg+ve (%)	
	1980	1990
0-	5.1	3.1
3-	4.7	3.7
7-	7.1	3.6
10-	5.8	5.4
15-	8.1	6.5
20-	6.2	7.7
25-	5.5	7.3
30-	5.9	5.1
Total	6.1	5.4

China is among the areas of the world with the highest prevalence of chronic hepatitis B virus (HBV) infection. It represents a vast area containing a number of densely populated cities as well as an enormous rural population. The prevalence of hepatitis B surface antigen (HBsAg) carriage varies not only between rural and urban areas but also between one city and another. As shown in more detail below, hepatitis B remains one of the most important infectious diseases in China. Control of HBV infection has therefore been a priority for public health care managers for many years now.

TABLE II HBV markers according to age in Guangzhou, 1986<sup>3</sup>

Age (y)	Number studied	HBsAg+ve n (%)	Anti-HBs+ve n (%)
0-	185	13 (7.0)	21 (11.3)
1-	847	94 (11.1)	84 (9.9)
3-	1484	205 (13.8)	328 (22.1)
7-	1405	342 (24.3)	494 (35.2)
14-	7278	1165 (16.0)	3251 (44.7)
30-	4651	641 (13.8)	2131 (45.8)
50-	855	82 (9.5)	359 (41.9)

## Prevalence of HBV infection

A general population sampling study carried out in 1980 showed that the overall HBV infection rate was 42.6% (range 35.5–61.6%), with an HBsAg carrier rate of 10.3% (range 7.4–15.4%).<sup>1</sup> Both rates were found to be higher in south China and in rural areas compared with north China and urban areas. The HBsAg positive rate among children under 1 year of age was found to be 5.1% in Beijing in 1980, reaching a peak level of 7–8% in children aged 7 to 15 years (Table I).<sup>2</sup> Figures reported for Guangdong in 1986 were considerably higher than this, with 7% of infants less than a year old testing HBsAg positive and as many as 24% of those aged 7 to 14 (Table II).<sup>3</sup>

During the eight year period from 1986 to 1994, there was no significant change in the overall HBsAg carrier rate, as indicated by data from Guangzhou (Table III).<sup>3</sup> However, figures from Beijing for 1990 do show a considerable decline in HBsAg positivity for children up to around 7 years of age (Table I),<sup>2</sup> which probably reflects the initiation of infant vaccination programmes.

Investigators have also shown that there is a high rate of family clustering of HBsAg carriers in China, as discussed by Professor Yao Guangbi elsewhere in these proceedings (pages S39–S42).<sup>4</sup> HBsAg positive mothers are believed to account not only for mother to child transmission at birth but also for much of the intrafamilial horizontal transmission of HBV during infancy and early childhood.

## Perinatal transmission of HBV

It has been estimated that 35–50% of HBsAg carriers in China result from perinatal transmission of HBV.<sup>2</sup> This is supported by the lower HBsAg carrier rates in infants in Beijing, where only 2.5% of pregnant women (2389 of 96 950 tested in 1988) were found to be HBsAg positive,<sup>2</sup> and the higher infant carrier rates in Guangzhou, where 11.3% of pregnant women (440 of 3895 tested in 1986) were HBsAg positive (J L Yao, unpublished data). There was no difference in HBsAg carrier rates between pregnant and non-pregnant women in each city. Similarly, the HBeAg positive rate among the HBsAg carrier women was approximately 40–45% in each case. The risk of perinatal transmission of HBV is increased considerably in infants born to HBeAg positive carrier mothers compared with those born to HBeAg negative carriers. In one study, 50–60% of babies born to mothers with both HBsAg and HBeAg positivity were infected and subsequently became HBsAg positive if

TABLE III *HBV markers in Guangzhou from 1986 to 1994*<sup>3</sup>

Year	Number studied	HBsAg+ve n (%)	Anti-HBs+ve n (%)	% HBsAg+ve in HBsAg carriers
1986	3576	533 (15.0)	1405 (39.3)	51.2
1988	7192	1041 (14.5)	3108 (43.2)	29.1
1990	1207	178 (14.7)	616 (51.0)	24.7
1992	4328	724 (16.7)	2400 (55.5)	31.4
1994	2459	366 (14.9)	1490 (60.6)	29.8

hepatitis B vaccine was not given within 24 hours of birth (J L Yao, unpublished data).

Although perinatal transmission is considered to be a major risk factor for HBV infection in this country, horizontal transmission during childhood is also important and probably occurs through close contact with other HBV infected family members or schoolmates. The crucial importance of HBV infection at such an early age is that it increases the likelihood of chronic infection and associated chronic liver disease. It also makes treatment more difficult, with poor responses to interferon, and increases the risk of developing hepatocellular carcinoma (HCC) in later adult life.

#### Hepatocellular carcinoma

There is a high incidence of HCC in China compared with some other parts of the world and HBsAg positivity has been identified as the most important associated factor.<sup>5</sup> In a study carried out in Guangzhou in 1985, 87% of patients with HCC were found to be HBsAg positive.<sup>5</sup> Chronic carriers of HBsAg should therefore be screened regularly by ultrasonography and serum  $\alpha$  fetoprotein testing, which has been shown to increase the possibility of early detection, early treatment, and therefore increased survival time.

#### Vaccination strategy

Although there have been no significant changes in overall HBV infection and HBsAg carrier rates during the 10 years since initiation of vaccination programmes for all newborns in a number of cities, decreasing HBsAg positivity rates have been seen among the lower age groups. As reported earlier, the HBsAg carrier rate in children under 1 year of age fell from 5.1% to 3.1% in Beijing.<sup>2</sup> Even better results were reported for Shanghai, with a decrease from 9.3% to 0.9% (G B Yao, personal communication), and similar results were reported for Guangzhou (J L Yao, unpublished data).

In view of the importance of both perinatal and horizontal transmission of HBV, a nationwide hepatitis B immunisation programme for

all neonates, whether or not their mothers are HBsAg positive, was started in China in the late 1980s. Babies born to mothers who are positive for both HBsAg and HBeAg are given three 30  $\mu$ g doses of hepatitis B vaccine. All other babies are given 30  $\mu$ g for the first vaccine dose followed by 10  $\mu$ g and 10  $\mu$ g for the two subsequent doses. The vaccination programme has produced encouraging initial results in the cities and will be extended to other regions. Table IV shows the anti-HBs response to two different hepatitis B vaccine dosage schedules in a study of 486 infants, of whom approximately two thirds achieved titres of 10.1 IU/l or greater.<sup>3</sup> Many doctors in China believe that all children under the age of 7 years should also be vaccinated if their HBV markers are negative.

#### Conclusions

Hepatitis B remains a serious health problem in China at present, with higher carrier rates in the general population and serious longterm sequelae resulting from infection at an early age. A universal childhood immunisation programme is therefore necessary in this hyper-endemic area to block both perinatal and horizontal transmission during the early stages of life. It is hoped that such a strategy will allow control of HBV infections in China within a few generations.

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#### Discussion

*Kiire:* In the International Task Force on Hepatitis B Immunisation, we have been very concerned about the issue of charging for hepatitis B vaccine because of its implications for the overall EPI programme. In China, it may have been practical to charge for this vaccination, but it does raise the issue that poorer members of your society may not be able to afford it. If we treat hepatitis B vaccine differently from the other EPI vaccines then obviously it will be looked at quite differently. As a result, I think it will be much more difficult to achieve control and eventual eradication of hepatitis B. *Yao:* The situation in China is changing. In the past, all vaccines were free and were paid for by the government. Currently, the government cannot afford to provide hepatitis B vaccine to so many people, so they have to charge for it. The economic situation is improving, however, and many parents can now afford to pay for their children to be vaccinated against hepatitis B. All the other vaccines are free in China, as are most other forms of medication, but not interferon!

TABLE IV *Anti-HBs response to hepatitis B vaccination*<sup>3</sup>

Anti-HBs titre (IU/l)	0, 1, 6 Monthly total n (%)	0, 1, 2 Monthly total n (%)	Total n (%)
<2	32 (10.6)	15 (8.6)	48 (9.9)
3-1	20 (6.4)	22 (12.6)	42 (8.6)
8-1	52 (16.7)	34 (19.4)	86 (17.7)
10-1	96 (30.9)	71 (40.6)	167 (34.4)
20-1	110 (35.4)	33 (18.8)	143 (29.4)
Total	311 (100)	170 (100)	486 (100)