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Prevention and Control of HBV Infection

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HB Vaccine in Japan

In Japan, there are three companies which concern themselves in the development of HB Vaccine. Regarding the Vaccines developed by Kitasato Institute and Green Cross co., the licence was given by Ministry of Health and Welfare. After the safety test using Chimpanzees, these two HB Vaccines are going to be on the market and available around the end of 1985. The HB Vaccine developed by Kaketsuken Institute is now asking for the licence of it. Each Vaccine produced by three companies is made from e-Antigen negative Plasma, and it was inactivated by formaline after 10 hrs' heat sterilization at 60 degrees. The subtype of HBs Antigen of source plasma is adr, and 40μg of HBs Antigen is contained in 1ml of HB Vaccine. One dose of each Vaccine is 0.5ml for adult and 0.25 ml for babies and administrated subcutaneously. The producing method and Alminum content as an adjunct are different in these 3 Vaccines. (Table 1) The positive ratio of anti HBs reaches maximum point after 3rd vaccination, and the mean titer of anti HBs

Table 1 HB Vaccine in Japan

company	Kitasato Inst.	Green Cross Co.	Kaketsuken Inst.
purification	Ultracentrifuge KBr CsCl Sucrose	Absorb colloidal silicate Ultracentrifuge CsCl	Ion exchange chromatography Ultracentrifuge Sucrose
Al. content	300μg/ml	500μg/ml	200μg/ml
material	e Antigen negative sera		
inactivation	60°C 10hrs Formalin treatment 1/2000 37°C 96hrs		
subtype	ad(r)		
HBsAntigen	40μg/ml		
1dose	0.5ml (20μg)		

increases rapidly at that time, by those phase 3 study. In about 3 years observation of acquired anti HBs, anti HBs disappeared in a few cases, in almost all cases, anti HBs remains positive but the titer of anti HBs decreases with time. By these results, it is said that acquired anti HBs by the use of HB Vaccine remains positive for more than 3 years. HBV infection in adult is transient, and maternal infant transmission is persistent and infected babies become HBV carriers, so the main part of the prevention of HBV infection is in the prevention against maternal infant transmission.

Prevention for the maternal infant transmission of HBV

There are many reports for the prevention of maternal infant transmission of HBV, and the efficacy is clear. It is reported that the maternal infant transmission occurs only in the eAg positive mothers' deliveries in Japan. And the prevention was started 8 years ago. At the beginning, it was prevented only passive immunization with HB immunoglobulin, and in these 4 years, it is prevented by combination of passive and active immuni-

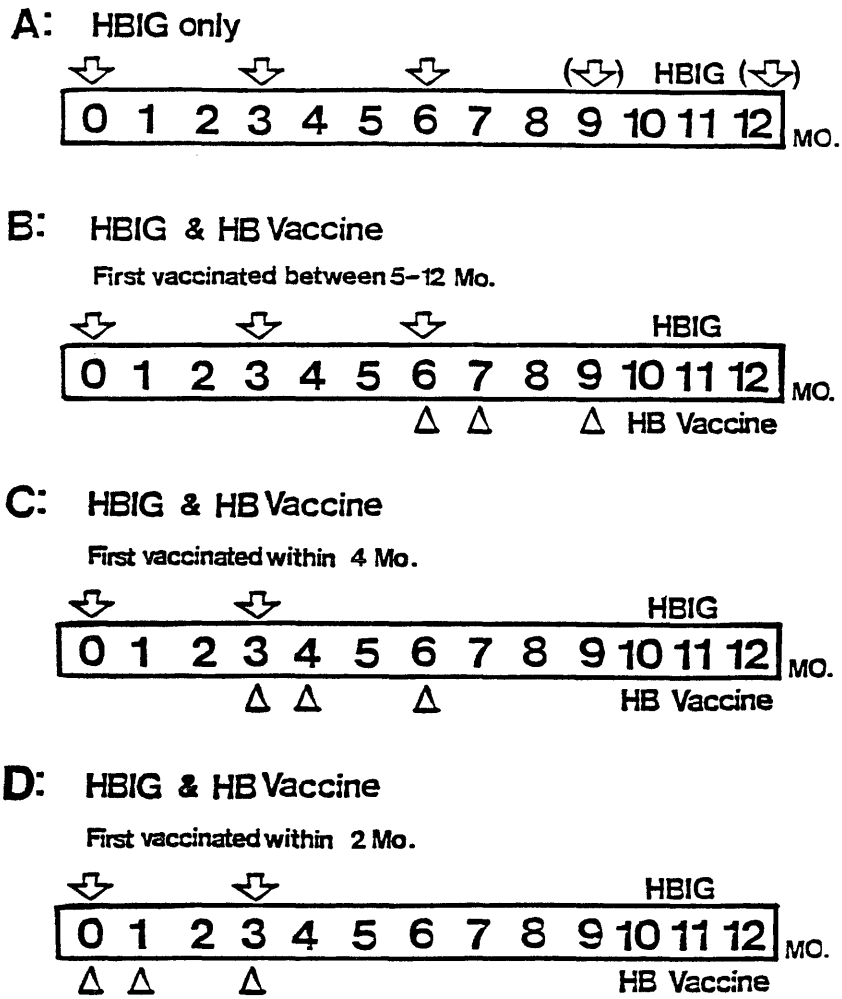


Fig. 1 Schedules lof the prevention for HBV vertical transmission

zation. It is supposed that more than 10,000 babies born to eAg positive mothers were treated by passive or passive active immunization in Japan. We have treated 1,102 babies born to eAg positive mothers. Preventive efficacy is 94.3% in all cases. Of those, 569 babies are observed more than 12 months of age. Preventive efficacy is also 93.1%. We have tried 4 different schedules of prevention to those babies. (Fig. 1) In each preventive schedule, 1ml of HB immunogloblin is given to babies as early as possible within 24 hrs after birth and same dose of HBIG is given 3 months of age. In schedule A, with some additional shots of HBIG, babies were treated only by passive immunization by the use of HB immunogloblin. Babies were kept positive to anti HBs at least for one year. Schedule B, C and D are the combined treatment with HB immunogloblin and HB Vaccine. In addition to passive immunization, in schedule B, C and D, each start of HB Vaccine is 6 months, 3 months after birth and just after birth. One dose of HB Vaccine contains 10μg of HBs antigen. 1,102 babies born to e-Antigen positive mothers have been prevented in those schedule. Out of them, 63 babies become carriers, giving the carrier rate is 5.7%. (Table 2) In each schedule, the carrier rates are 14.3%, 9.9%, 4.0% and 1.8%. This result explains that babies acquire a sufficient amount of anti HBs even by the administration of HB Vaccine just after birth. Early administration of HB Vaccine prevents to development carrier more effectively than the late administration of HB Vaccine.

Table 2. Development to carrier state in each preventive schedule

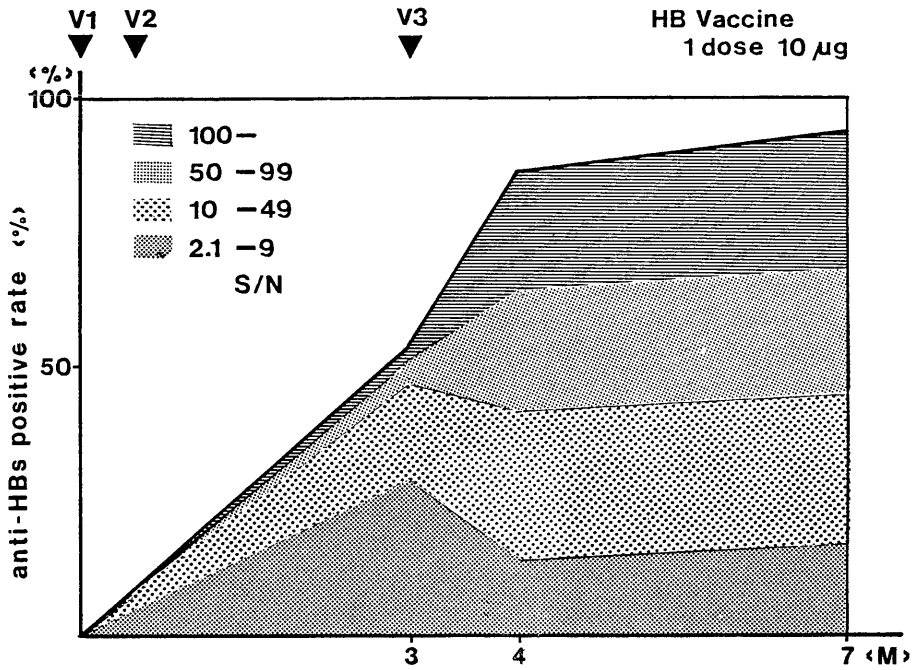
Group	Cases	Carrier
A	147	21 (14.3)
B	91	9 (9.9)
C	808	32 (4.0)
D	56	1 (1.8)
Total	1102	63 (5.7)

( ) %

HB Vaccine response in new borns

80 babies born to e-Antigen negative mothers were administrated HB Vaccine. HB Vaccine is also given 3 times such as just after birth, 1 and 3 months of age. Positive rate of anti HBs reaches 86.1% at 4 months of age and 93.6% at 7 months of age. The new born babies are getting anti HBs same titer and same positive rate in adult. (Fig. 2)

The Ministry of Health and Welfare appropriates about one and half million U. S. dollars for the prevention of maternal infant transmission of HBV in the budget of 1985 in Japan. In this project, all pregnant women will be tested for HBsAg, and if they are positive, they will be tested for eAg, the babies born to eAg positive mothers will be treated by HBIG and HB Vaccine with public expense. In Japanese national project of the prevention against maternal infant transmission of HBV will be started at June, 1984.



	T 3	T 4	T 7
cases	80	72	47
positive cases	43	62	44
positive rate (%)	53.8	86.1	93.6
average (S/N)	20.5	66.2	69.0

Fig. 2 Anti-HBs Response and the Titer of Acquired of Anti-HBs in Newborns

Anti viral therapy for chronic hepatitis type B

Recently, there is a remarkable progress in the treatment of chronic hepatitis type B by the development of anti-DNA viral agent. There are 3 kinds of anti-viral therapy such as therapy with interferon, with Ara-A and corticosteroid withdrawal therapy (CWT). Compared with CWT and interferon and Ara-A by the level of DNA-Polymerase are the marker of HB viral replication, in the duration of administrating interferon and Ara-A, the level of DNA-P is reduced and re-elevated after the treatment. On the contrary, DNA-P level is elevated with administration of CWT and it decreases after the treatment. CWT forms the contrast with the treatment with the use of interferon and Ara-A. In the CWT, the host immunity is suppressed by the administration of corticosteroid, then the replication of HBV in hepatocytes is accelerated. The immuno-suppression is released by the withdrawal of corticosteroid and intense immuno-response to replicated HBV is evoked. In this way, HBV is cleared out with the remarkable exacervation of liver function tests.

Out of 37 patients treated with CWT, 21 patients (56.8%) are continuously normal in GPT after the therapy. While, out of 74 patients treated Ara-A, 22 patients (29.7%) are continuously normal in GPT. And concerning the continuous negative rate of eAg, it is 35.1% by CWT and 20.3% by Ara-A. Patient with normal liver function test at least more than 6 months after the treatment, which are called "clinical cure", accounted for 56.8% in CWT. But out of 74 patients treated with Ara-A with 16g-32g, only 14.9% became continuously negative to eAg, and only 29.7% showed "clinical cure". In the CWT, as well as the treatment interferon and Ara-A more satisfactory result can be obtained if the treatment is given to patients who have high level of transaminases and low level of HBV markers such as DNA-P and eAg.