Long-term immunogenicity and efficacy of a recombinant hepatitis B vaccine in Egyptian children

I.H. El-Sawy 1 and O.N. Mohamed 2

Abstract in English

In 1992, Egypt adopted a hepatitis B vaccine schedule at 2, 4 and 6 months of age. We evaluated the long-term immunogenicity and efficacy of vaccination using this schedule in 180 children whose time lapse since last vaccination varied between 1 month and 5 years. None of the participants had clinical hepatitis. HbsAg was not detected in any participant and all but one had negative results for anti-HBc test. Although a high seroprotection rate (93.3%) was elicited 1 month after vaccination, there were low initial anti-HBs concentrations and both declined rapidly over time. Thus, the short interval (2 months) between the second and third doses of vaccine is less desirable in the long term. We recommend booster inoculations for all previously vaccinated children and a new vaccination schedule at 1, 2 and 9 months.

Abstract in French

L’immunogénicité à long terme et l’efficacité du vaccin recombiné contre l’hépatite B chez des enfants égyptiens

RÉSUMÉ En 1992, l’Egypte a adopté un calendrier de vaccination contre l’hépatite B à l’âge de 2, 4 et 6 mois. Nous avons évalué l’immunogénicité à long terme et l’efficacité de la vaccination avec ce schéma vaccinal chez 180 enfants pour lesquels l’intervalle depuis la dernière vaccination variait entre 1 mois et 5 ans. Aucun des sujets n’avait une hépatite clinique, l’AgHbs n’a été détecté chez aucun d’entre eux et tous sauf un avaient des résultats négatifs au test de détection des anticorps anti-HBc. Bien qu’un taux de séroprotection élevé (93,3%) ait été obtenu 1 mois après la vaccination, les concentrations initiales d’anticorps anti-HBs étaient faibles et les deux ont diminué rapidement avec le temps. Le court intervalle (2 mois) entre la deuxième et la troisième dose de vaccin est donc moins souhaitable à long terme. Nous recommandons un rappel de vaccination pour tous les enfants déjà vaccinés et un nouveau calendrier de vaccination à 1, 2 et 9 mois.

1Department of Paediatrics, Faculty of Medicine, University of Alexandria, Alexandria, Egypt.
2Department of Microbiology, High Institute of Public Health, University of Alexandria, Alexandria, Egypt.

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Introduction

Infection of infants and young children with the hepatitis B virus (HBV) represents an important health hazard, since the younger the age at which the infection is acquired, the greater the predisposition to the carrier state, chronic liver disease and subsequent development of cirrhosis and hepatocellular carcinoma [1,2]. The World Health Organization (WHO) has targeted hepatitis B as one of eight infectious diseases that should be controlled by vaccination [3]. In most developing countries, HBV infection is endemic, and attempts to prevent infection must be made very early during childhood [2,4,5]. Accordingly, in 1992, Egypt started a programme of universal immunization in infancy. The schedule adopted by the Egyptian Ministry of Health was three doses of a yeast-recombinant HB vaccine administered to all infants at 2, 4 and 6 months of age to coincide with other compulsory vaccines [diphtheria, tetanus, pertussis and oral polio (DTP-OPV)].

Although advantageous for practical reasons to incorporate HB vaccination into the schedule of the routine childhood immunization programme, many authors have shown that short intervals of 1 or 2 months between the second and third doses of HB vaccine are accompanied by significantly lower levels of antibodies to HB surface antigen (anti-HBs) when compared to longer intervals of 4 months or more [1,5–10]. In addition, antibody levels to HBsAg decline over time and the duration of protection correlates strongly with the peak level achieved following the basic immunization series [8,11].

To the best of our knowledge, there have been no national studies on the long-term immune response to the HB vaccine for Egyptian infants. Also the duration of immunity and the possible need for booster inoculations has not been determined. This study was undertaken to evaluate the long-term immunogenicity and efficacy of the recombinant HB vaccine as administered to infants according to the Egyptian vaccination schedule.

Subjects and methods

Study population

This cross-sectional study was conducted between October 1997 and January 1999 on 180 children aged between 7 months and 5.5 years. All the children had been given three doses of a recombinant HB vaccine (Engerix B, Smith Kline Beecham) at 2, 4 and 6 months of age; at the same time as other compulsory routine DTP-OPV. Each paediatric dose (0.5 mL = 10 μg) had been administered intramuscularly in the anterolateral region of the middle third of the right thigh. All the participants had been vaccinated at official vaccination centres in health offices in Alexandria city and nearby districts. The study population comprised six equal groups (30 children in each group, 15 boys and 15 girls) at different post-vaccination intervals following the completion of the third dose of HB vaccine: 1 month (group 1), 1 year (group 2), 2 years (group 3), 3 years (group 4), 4 years (group 5), and 5 years (group 6).

The participants were recruited from infants and children who were receiving health care at the Alexandria University Children’s Hospital, Alexandria, Egypt. The study was approved by the Researches Committee, Faculty of Medicine, University of Alexandria. The date and dose intervals of HB vaccine were confirmed by checking the vaccination record written on the birth certificate of each child. Children with a history of medical conditions that might compromise their immune systems
(e.g. those with a history of premature birth, low birth weight or severe protein-energy malnutrition during the first year of life) were not included in the study. The purpose of the study was carefully explained to the child’s parents or guardians and informed consent to participate in the study was obtained before blood sampling. Parents were informed of their child’s serological results and HB vaccine booster inoculation was offered to those with non-protective titres (serum anti-HBs < 10 mIU/mL).

Clinical assessment
Before blood sampling, a detailed history was obtained and the following data recorded: child’s code number, age, sex, date of birth, residence, name of their vaccination centre, date and dose intervals of HB, DTP-OPV, history of increased exposure risk to HBV infection (e.g. previous blood transfusion, blood products injection, contaminated syringe use, renal dialysis, HBsAg-positive mother or contact with other carriers). Any history of symptoms suggesting clinical hepatitis in the children or their family members and any history of an illness suggesting immune deficiency in the participants was verified. In addition, a full clinical examination was completed for each child.

Blood sampling and serological tests
About 5 mL of venous blood were collected from each child. The sera were rapidly removed from the cells after clotting and centrifugation. Serum samples of 250–500 μL were aliquoted into four labelled sterile Ependorff tubes to avoid repeated freezing and thawing. Serum samples for testing for HBV markers were stored frozen at −20 °C before being analysed in batches, while those for the determination of alanine aminotransferase (ALT) levels were immediately transported to the laboratory for assay. All the serum samples had code numbers and were tested blind.

Serum samples for each participant were tested for the qualitative and quantitative determination of the antibody to hepatitis B surface antigen (anti-HBs), qualitative determination of the antibody to hepatitis B core antigen (anti-HBc) and qualitative determination of hepatitis B surface antigen (HBsAg) using microparticle enzyme immunoassay (MEIA) technology. Commercially available MEIA kits, AUS-AB, CORE and HBsAg (Abbott Laboratory, Illinois, USA) were used for the testing of anti-HBs, anti-HBc and HBsAg respectively, via the fully automated IMx analyser (Abbott) in accordance with the manufacturer’s instructions. Levels of anti-HBs were expressed in milli-international units per millilitre (mIU/mL). Serum ALT levels were measured by the fully automated analyser (Hitachi 911, Boehringer Mannheim, Germany) using commercially available kits (ALT, Boehringer Mannheim, Germany) at 37 °C, with values below 41 U/L considered normal.

Definitions
The initial vaccine-induced antibody response was taken to be the anti-HBs level at 1 month following the third vaccine dose. Children with non-measurable (0.0) anti-HBs titres were considered seronegative (non-responders) and those with anti-HBs levels < 10 mIU/mL were considered to have an inadequate response. These last two groups were not seroprotected. Those with anti-HBs levels ≥ 10 mIU/mL were considered to be seroprotected. The seroprotection rate was defined as the percentage of participants with anti-HBs ≥ 10
mIU/mL. Those with anti-HBs levels between 10 mIU/mL and 100 mIU/mL were rated as having a low immune response and those with anti-HBs levels > 100 mIU/mL were rated as having a good immune response to the HB vaccine. HBV infections were diagnosed when tests for HBsAg and/or anti-HBc showed positive results. The aforementioned definitions and cut-offs have also been used by other investigators in similar studies [1,4,11–13].

Statistical analysis
Data were analysed using SPSS (version 6). The arithmetic mean of both the absolute values and the logarithms (log) of values of anti-HBs levels were calculated. In addition, the geometric mean titre (GMT) of anti-HBs was determined as it is more useful and representative than the arithmetic mean when describing a series of fractional values such as serum antibody titres. Statistical significance was analysed using the Mann–Whitney U test, the ANOVA test for variables measured on a logarithmic scale and the Scheffe test for comparing different groups. The Kruskal–Wallis test, chi-squared test ($\chi^2$) and Mantel–Haenszel test for linear association were also used. A $P$-value less than 0.05 was considered significant.

Results
None of the participants had a documented history or clinical evidence of symptomatic HBV infection. Most had no history of increased exposure risk to HBV infection except for five children who had a history of blood transfusion (single or repeated) due to acute haemolytic anaemia (famism). No family history of HBV infection was recorded for any of the participants.

Serological markers of HBV infection
HBsAg was not detected in any of the children and all but one had negative results for the anti-HBc test. This was a 1.5-year-old boy and his serological profile was: anti-HBs = 213.1 mIU/mL, negative HBsAg test, positive anti-HBc test and normal serum ALT level (23 U/L). In addition, this child had no history or clinical evidence of symptomatic hepatitis.

Seroconversion rate
As shown in Table 1, the seroconversion rates for groups 1–6 were 93.3%, 73.3%, 66.7%, 66.7%, 53.3% and 53.3% respectively. The seroconversion rate was highest in the group 1 (1 month post-vaccination) and lowest in groups 5 and 6 (4 and 5 years post-vaccination). The differences in seroconversion rates were highly significant ($P = 0.0097$) and there was a significant association between the time lapse since the last vaccine dose and the seroconversion rate ($P = 0.00028$), whereby the longer the time lapse after vaccination, the lower the seroconversion rate.

Mean anti-HBs levels
As shown in Table 1, the anti-HBs GMT was highest (196.2 mIU/mL) in group 1 and lowest (28.1 mIU/mL) in group 6. The differences between mean absolute values of anti-HBs in the different groups were significant (Kruskal–Wallis test $\chi^2 = 33.13$, $P = 0.000$). The same pattern was observed when absolute anti-HBs values were transformed into logarithmic values ($F = 6.73$, $P = 0.0000$). The Scheffe test showed that the differences between groups 1 and 4, 1 and 5, and 1 and 6 were significant at the 5% level. As shown in Figure 1, the mean anti-HBs level was highest 1 month post-vaccination (group 1) and had declined rapidly by 1 year post-vaccination (group 2) with a
Table 1 Seroprotection rates, mean anti-HBs levels and geometric mean titres (GMTs)

<table>
<thead>
<tr>
<th>Group (n = 30) (time lapse)</th>
<th>Seroprotection rate (%)</th>
<th>Anti-HBs (mIU/mL) Mean ± s</th>
<th>Anti-HBs (log values) Mean ± s</th>
<th>GMT</th>
</tr>
</thead>
<tbody>
<tr>
<td>Group 1 (1 month)</td>
<td>93.3%</td>
<td>371.3 ± 357.1</td>
<td>2.29 ± 0.61</td>
<td>196.2</td>
</tr>
<tr>
<td>Group 2 (1 year)</td>
<td>73.3%</td>
<td>201.8 ± 261.5</td>
<td>1.99 ± 0.69</td>
<td>99.9</td>
</tr>
<tr>
<td>Group 3 (2 years)</td>
<td>66.7%</td>
<td>118.0 ± 159.0</td>
<td>1.83 ± 0.64</td>
<td>67.5</td>
</tr>
<tr>
<td>Group 4 (3 years)</td>
<td>66.7%</td>
<td>99.6 ± 181.7</td>
<td>1.70 ± 0.62</td>
<td>48.7</td>
</tr>
<tr>
<td>Group 5 (4 years)</td>
<td>53.3%</td>
<td>49.7 ± 69.8</td>
<td>1.52 ± 0.59</td>
<td>33.4</td>
</tr>
<tr>
<td>Group 6 (5 years)</td>
<td>53.3%</td>
<td>36.6 ± 36.4</td>
<td>1.45 ± 0.55</td>
<td>28.1</td>
</tr>
</tbody>
</table>

*a2 = 15.161, P = 0.0097 and Mantel-Haenzel test for linear association = 13.191, P = 0.00028

*Kruskal-Wallis test *2 = 33.131, P = 0.000

ANOVA (F) test (between means of logarithmic values of anti-HBs) = 6.7339, P = 0.000

Mean log values and GMT were used only for positive values, i.e. cases who were seronegative (anti-HBs < 0.0) were not included.

s = standard deviation

Figure 1 Mean anti-HBs titre from 1 month up to 5 years post-vaccination

more gradual decline following over the subsequent years.

**Degree of immune response**

As shown in Table 2 and Figure 2, 63.3% of the children in group 1 had a good immune response (anti-HBs > 100 mIU/mL), in groups 2 and 3 this had dropped to 43.3%, to 23.3% in group 4, 6.7% in group 5 and in group 6 (5 years post-vaccination) none of the children had a good immune response (0.0%). However, the percentage of participants who were seronegative was 3.3% in group 1, 13.3% in group 2, 16.7% in group 3, 20.0% in group 4 and 23.3% in the groups 5 and 6. The difference between the study groups was statistically significant (*2 = 45.6, P = 0.00006). Also, there was a significant association between the time lapse since the last vaccination dose and the degree of immune response (P = 0.000), i.e. the longer the time lapse, the weaker the immune response.

**Sex and anti-HBs levels**

Table 3 shows that both boys and girls had similar mean anti-HBs levels in all the study groups (all P-values > 0.05).

**Discussion**

Although there have been many previous controlled studies which have shown that HB vaccines are well tolerated, immuno-
Table 2 Comparison between groups according to the degree of immune response

<table>
<thead>
<tr>
<th>Anti-HBs titre (mIU/mL)</th>
<th>Group 1 (1 month)</th>
<th>Group 2 (1 year)</th>
<th>Group 3 (2 years)</th>
<th>Group 4 (3 years)</th>
<th>Group 5 (4 years)</th>
<th>Group 6 (5 years)</th>
</tr>
</thead>
<tbody>
<tr>
<td>No response (0.0)</td>
<td>1 3.3</td>
<td>4 13.3</td>
<td>5 16.7</td>
<td>6 20.0</td>
<td>7 22.2</td>
<td>7 22.2</td>
</tr>
<tr>
<td>Inadequate response (&lt; 10)</td>
<td>1 3.3</td>
<td>4 13.3</td>
<td>5 16.7</td>
<td>4 13.3</td>
<td>7 23.3</td>
<td>7 23.3</td>
</tr>
<tr>
<td>Low response (10-100)</td>
<td>9 30.0</td>
<td>9 30.0</td>
<td>7 23.3</td>
<td>13 43.3</td>
<td>14 46.7</td>
<td>16 53.3</td>
</tr>
<tr>
<td>Good response (&gt; 100)</td>
<td>19 63.3</td>
<td>13 43.3</td>
<td>13 43.3</td>
<td>7 23.3</td>
<td>2 6.7</td>
<td>0.0 0.0</td>
</tr>
<tr>
<td>Total</td>
<td>30 100</td>
<td>30 100</td>
<td>30 100</td>
<td>30 100</td>
<td>30 100</td>
<td>30 100</td>
</tr>
</tbody>
</table>

\[ \chi^2 = 45.596, P = 0.00006 \]
Mantel–Haenszel test for linear association = 27.677, \( P = 0.000 \)

![Graph showing distribution of participants according to the degree of immune response and time lapse since the last vaccination](image)

Figure 2 Distribution of participants according to the degree of immune response and time lapse since the last vaccination

Genic and effective in preventing HBV infection [4,5,7,10,12,14,15], those evaluating the long-term immunogenicity and the duration of protection afforded by these vaccines are limited and inconclusive [9,11,13]. In addition, these studies have not clearly established the need for booster inoculations. Both host and immunization factors affect the immune response to the HB vaccine and, consequently, can influence the duration of immunity [8]. Host factors include age, weight, the immuno-
Table 3  Mean anti-HBs levels for males and females

<table>
<thead>
<tr>
<th>Group * (time lapse)</th>
<th>Mean anti-HBs (mIU/mL) ± s</th>
<th>P-value b</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Males</td>
<td>Females</td>
</tr>
<tr>
<td>Group 1 (1 month)</td>
<td>330.2 ± 346.8</td>
<td>412.4 ± 374.5</td>
</tr>
<tr>
<td>Group 2 (1 year)</td>
<td>210.5 ± 298.9</td>
<td>193.1 ± 228.4</td>
</tr>
<tr>
<td>Group 3 (2 years)</td>
<td>114.0 ± 138.9</td>
<td>123.9 ± 181.8</td>
</tr>
<tr>
<td>Group 4 (3 years)</td>
<td>105.5 ± 178.9</td>
<td>93.7 ± 190.4</td>
</tr>
<tr>
<td>Group 5 (4 years)</td>
<td>37.3 ± 54.2</td>
<td>62.0 ± 82.6</td>
</tr>
<tr>
<td>Group 6 (5 years)</td>
<td>37.4 ± 33.9</td>
<td>35.7 ± 39.9</td>
</tr>
</tbody>
</table>

* Each group included 15 males and 15 females.

b Mann–Whitney U test
s = standard deviation

competence of the host, smoking habits and genetics. The dose of vaccine administered, site of immunization and vaccine schedule are among the immunization-related factors. All the participants in our study were of the same ethnic group, the same age and healthy at the time of vaccination. They were administered the same doses of the same brand of the vaccine, at the same body site and according to the same schedule. So, both host- and immunization-related factors that might affect our results were similar for all participants and the only variable was the time lapse from the completion of the vaccination schedule to the date of blood sampling. The immune response (mean anti-HBs levels) was similar for both boys and girls at all different post-vaccination times. An absence of gender-related differences has also been reported by other authors [8].

The rationales behind the vaccination schedule adopted in Egypt are; first, the immune response to a combination of HBsAg and DTP-OPV given simultaneously has been found to be similar to that observed after administration of these vaccines separately [5,15,16]. Secondly, the simultaneous administration of multiple antigens in infancy can markedly reduce the number of physician visits for immunization, thus improving the cost–benefit ratio to the community and enhancing parental compliance [5]. Thirdly, another advantage of an early start and short spacing is rapidly attained seroprotection to guard against early HBV infection and to minimize the carrier state due to perinatal HDV transmission which represents the most important risk factor for the acquisition of infection in children [1,2,8]. Many authors have agreed that the first two doses of HB vaccine should be at least 1 month apart, but increasing the interval beyond 1 month adds no immunogenic advantage. On the other hand, the second and third doses should be separated by a minimum of 2 months and an interval of 4 months or more is optimal [1,5–7]. In addition, some authors have shown that a schedule of three doses 1–2 months apart requires a later fourth booster dose after the primary vaccinations as means of improving the antibody levels [4,7]. As yet a fourth booster dose has not been included in the routine Egyptian immunization programme for infancy and childhood.
In our study, none of the children had clinical evidence of symptomatic hepatitis, HBsAg was not detected and all but one had negative results for the anti-HBc test. This child was asymptomatic with no identifiable risk factors and he might have been infected perinatally (vertical transmission) from an asymptomatic HbsAg-positive mother or postnatally (transverse transmission) from an asymptomatic carrier in his family.

The prevalence rate of HBV infection in our study population was 0.56% (one out of 180 participants) and the HBsAg carrier rate was nil. Because vaccination has been obligatory since 1992, there could be no control group (non-vaccinated children) to assess the protective efficacy rate of the vaccine. However, in a previous national study in 1985, El-Marsafy reported seropositivity to HBsAg of 7.5% among normal, non-vaccinated Egyptian children [17]. So, in comparison to this figure, the protection afforded by the HB vaccine for our study population appears to be good. Also, our results were similar to those of the studies conducted by Goh et al. [11] and Wainwright et al. [13] who were using a schedule of 0, 1 and 6 months. Goh et al. found that all the participants remained asymptomatic and free from HBV infection during a 4-year follow-up and Wainwright et al. found that out of 1630 individuals, 4 developed antiHBc and none had HBsAg or clinical hepatitis in a 5-year follow-up. So the hepatitis B vaccine, even with a 2-month interval between the second and third doses, seems to be equally effective at preventing the clinical disease, the development of carriers and the transmission of HBV to susceptible children for at least 5 years following vaccination. However, the low exposure risk of most of our study participants should be taken into consideration before making firm conclusions.

The initial immune response to the HB vaccine following the basic immunization programme is an important determinant of the duration of immunity [8]. Obviously, the progressive decline of anti-HBs to undetectable levels will occur more rapidly if the specific antibody concentration obtained after vaccination is low [8,18]. Potency measurements for groups of vaccinated children must include both the seroprotection rate (percentage of children with anti-HBs ≥ 10 mIU/mL) and the geometric mean anti-HBs concentrations [8]. The most appropriate time for determining these values is 1–3 months after the final inoculation in a basic immunization series [5,7,8,11].

In our study, 93.3% of participants investigated 1 month following completion of the vaccination series had anti-HBs titre ≥ 10 mIU/mL. This high seroprotection rate was close to the figures (95%-100%) published by other investigators whether they used shorter (1–2 months) or longer (4 months or more) intervals between the second and third doses of HB vaccine [5,6,10,11]. On the other hand, the initial anti-HBs GMT (196.2 mIU/mL) of the same participants in our study was low when compared to the initial GMTs reported by other investigators who used longer intervals between the second and third dose of vaccine. Keyserling et al. (using schedules of 2, 4 and of either 12 or 15 months) found that the peak GMTs a month after vaccination were 1558 mIU/mL and 3424 mIU/mL respectively [7]. Giammanco et al. found significantly higher anti-HBs GMT (3777.8 mIU/mL) in a group of infants where 6 months was allowed between the second and third dose of vaccine, compared with two other groups where only 1 and 2 month intervals were allowed (GMTs = 327.9 and 1301.9 mIU/mL respectively) [5]. In addition, a more than 10-fold in-
crease in GMTs was observed in both last groups following a fourth booster dose of HB vaccine given 6 months after the third dose. These data seem to suggest either a longer interval between the second and third vaccinations or the addition of a fourth, later vaccination after the basic immunization series are a means of achieving high antibody levels. Such an approach may be beneficial in combating the endemicy of HBV infection in developing countries.

Our results showed that the drop in anti-HBs titre over time was significant, as was the decrease in the percentage of children with protective titres. The decline in both the seroprotection rate and anti-HBs GMT was rapid over the first year following the last vaccination, with a more gradual decline over subsequent years. At the fifth year post-vaccination the GMT (28.1 mIU/mL) and the seroprotection rate (53.3%) were markedly low when compared to other long-term follow-up studies where there was a longer interval between the second and third doses of vaccine (e.g. a schedule of 0, 1 and 6 months) [9,11,18]. Tsega et al. [9] and Lin et al. [18] found that the seroprotection rates were 89% and 75% at 5 years and 6 years following the last vaccination respectively. Also, Goh et al. found that the seroprotection rate and GMT declined from peak values of 100% and 1699.5 mIU/mL 3 months after completion of the third dose to 87% and 118 mIU/mL at 4 years post-vaccination [11]. They also found that the persistence of anti-HBs is related to the peak level achieved after completion of the vaccine schedule.

The marked drop in seroprotection rate and anti-HBs GMT in the participants of our study when compared to these aforementioned trials could be explained by the lower initial (peak) anti-HBs levels due to the shorter interval (2 months) between the second and third vaccine doses. In accordance with our explanation, many authors have shown that antibody levels to HBsAg gradually decline over time and the duration of maintained protective levels correlates strongly with the peak level achieved [8,11,15]. However, it is noteworthy that the relation between the persistence of anti-HBs and the duration of protection against HBV infection is still unclear. Low or undetectable levels of circulating anti-HBs may not necessarily indicate loss of protection. In high-risk adults, protection persists even when humoral antibody is no longer detectable [19]. Moreover, when a booster dose was administered to healthy adults with undetectable anti-HBs 5–7 years after vaccination, an anamnestic response was elicited, implying that immunological memory persists [20]. Thus, once an immune response has been induced by vaccination, it can be stimulated by exposure to the wild virus, with an active increase in anti-HBs during the early phase of the incubation period of the disease, thereby protecting against clinical illness or the development of the carrier state. In an endemic setting, repeated exposures to hepatitis B carriers could sustain or even boost the anti-HBs response without any serological evidence of infection [21].

Conclusions and recommendations

Although a high initial seroprotection rate was elicited by the current HB vaccination schedule adopted in Egypt, the low initial anti-HBs antibody concentrations and the rapid decline of these levels, coupled with the rapid drop in the seroprotection rates over time, may make the short interval (2
months) between the second and third dos-
es of the vaccine less desirable in the long-
term. Based on the findings of our study and
other relevant trials, we recommend a
fourth inoculation of HB vaccine to all pre-
viously vaccinated Egyptian children one
or more years after completion of their ba-
sic immunization series to boost their
present immune protection. In addition, we
also suggest a new HB vaccine schedule at
1, 2 and 9 months of age, for future children
to obtain a more potent and longer lasting
immune response and to minimize the need
for an early booster dose. The advantages
of this schedule are the early start (to guard
against early HBV infection), and a longer
duration between the second and third dos-
es of vaccine (for a better immune re-
response). It also coincides with other routine
vaccinations, namely BCG during the first
month, DTP-OPV at the second month and
measles at the ninth month of life. For firm-
er recommendations a controlled prospec-
tive study, including the two vaccine
schedules, over a larger population is sug-
gested.

References


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