Letter

Human leucocyte antigens (HLA) in neonates with an inadequate response to hepatitis B vaccination

Inadequate responses to hepatitis B vaccine occur in approximately 5–15% of neonates. Factors that influence the response to vaccination include the immunogenetic state of the vaccine recipient: carriers of the human leucocyte antigen (HLA)-B8, DR3 do not develop adequate responses to hepatitis B vaccine[1]. To determine the importance of the immunogenetic factor for the outcome of hepatitis B vaccination in neonates, we investigated the HLA type of infants with an inadequate response to hepatitis B vaccination and analysed the subgroups non-infected low responders and infected non-responders for differences in the specific HLA type.

Between 1982 and 1991, 705 healthy newborns from HBsAg-positive mothers received HBIg at birth and were vaccinated within the first year with plasma or recombinant-DNA vaccine according to a three- or four-dose vaccination schedule[2]. During the first year blood was assayed for HBsAg and anti-HBs (IU/l) at 3, 6, 11 and 12 months of age. Sixteen of the 705 newborns (2.3%) with anti-HBs titres <10 IU/l were identified; eight infants with an anti-HBs level below 10 IU/l and negative tests for HBsAg (non-infected low responders) and another eight infants who became anti-HBs negative but HBsAg-positive (infected non-responders).

HLA typing for class I and II antigens was performed, using standard microcytotoxicity test on peripheral blood mononuclear cells.

Table 1 shows the HLA phenotypes of the eight non-infected low responders and the eight infected non-responders to hepatitis B vaccine. HLA-DR3 was present in four of the eight (50%; 95% CI: 15–85%) non-infected low responders and in none of the eight (0%) infected non-responders. Two non-infected low responders were probably homozygous for HLA-DR3.

This study confirms that the HLA-DR3 haplotype plays a role in the low responsiveness to hepatitis B vaccination in non-infected neonates. In our study with only a small number of ethnically heterozygous individuals, all four DR3-positive children were non-infected low responders and two of them were probably homozygous for DR3. These low responders were not absolute non-responders, since all of them developed protective anti-HBs levels after hepatitis B revaccination in their second year of life[3]. The two children homozygous for HLA-DR3 produced anti-HBs in the lowest range (45 and 55 IU/l, respectively) after revaccination in comparison to the other six revaccinated low responders (median 171, range 49–3497 IU/l). The observation that none of the eight non-responders, who became infected with hepatitis B virus, was DR3-positive suggests that HLA-associated low responsiveness is *not* causally related to this type of failure of hepatitis B vaccination.

Table 1 HLA type for eight non-infected low responders and eight infected non-responders to hepatitis B vaccine

Group	Ethnic background[a]	HLA type B		DR	
Non-infected low responders					
1	Medit.	7	**8**	**3**	–
2	Neth.	62	18	**3**	–
3	Medit.	13	35	1	**3**
4	Neth.	**8**	56	1	**3**
5	Medit.	18	35	4	–
6	Medit.	35	53	–	11
7	Cap. V.	58	–	13	11
8	Medit.	60	72	13	15
Infected non-responders					
1[b]	Medit.	18	48	4	14
2[b]	Medit.	18	48	4	14
3	Medit.	49	35	7	–
4	Medit.	35	37	11	–
5	Medit.	35	–	11	8
6	Asia	58	–	15	13
7	Medit.	52	63	15	7
8	Asia	55	61	11	13

–, Possibly homozygous

[a]Ethnic background: Mediterranean, The Netherlands, Cape Verde Islands, Asia. A rough estimate of expected DR3 homozygotes in this ethnic group is 1–2%

[b]Infected non-responders 1 and 2 are brother and sister

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