Public Health England

The national dried blood spot testing service for infants of hepatitis B positive mothers

Rationale for not requiring high anti-HBs levels in infants born to HBsAg positive mothers

Dr Mary Ramsay
Consultant Epidemiologist and Head of Immunisation, Hepatitis and Blood Safety Department

About Public Health England

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Public Health England
133-155 Waterloo Road
Wellington House
London SE1 8UG
Tel: 020 7654 8000
http://www.gov.uk/phe
Twitter: @PHE_uk

Prepared by: Matthew Olley
For queries relating to this document, please contact: phe.enquiries@phe.gov.uk

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Evidence of response to vaccine in infants

In the initial studies of hepatitis B vaccine and HBIG in the UK, of 49 babies immunised and successfully followed up, six (12%), all born to anti-HBe negative women, became infected. The remaining 43 (88%) (of whom 15 were anti-HBe negative) became immune, suggesting that response to vaccine in infants vaccinated under trial conditions was close to 100% (28/28 born to anti-HBe positive and 15/15 born to HBeAg positive women).[1] An extensive review of field evaluations of infant vaccination conducted in 2000 identified only 13 studies, comparable to the current UK situation, where serological results were reported (table). In some of these studies the results are not confined to fully immunised infants and in many, resolved infection was not specifically excluded. Overall, however, 1.3% became chronically infected and around 87% acquired active immunity. Many studies used 100iu/l as the putative protective level; and should therefore represent the minimum proportion of children protected under the current UK recommendations. For example, in the large study from East London[2] only 3/217 (1.3%) children had levels below 10iu/l.

[1] Wheeley SM, Boxall EH, Tarlow MJ, Gatrad AR, Anderson J, Bissenden J, Chin KC, Mayne A. Hepatitis B vaccine in the prevention of perinatally transmitted hepatitis B virus infection: final report on a West Midlands pilot study.J Med Virol. 1990 Feb;30(2):113-6.

[2] Larcher VF, Bourne J, Aitken C, Jeffries D, Hodes D. Overcoming barriers to hepatitis B immunisation by a dedicated hepatitis B immunisation service. Arch Dis Child. 2001 Feb;84(2):114-9.

A more recent large evaluation in the UK summarised the follow-up of infants born to anti-HBe negative women in the UK—all of the babies were eligible to receive HBIG and vaccine.[3] A blood test was taken from 555/906 (61%) at of after one year of age. Of the children tested, 15 samples were insufficient for testing, leaving a total of 540 results for analysis. Twenty-six children were HBsAg positive suggesting an overall rate of chronic infection of 4.9%; a further 34 (6.3%) were found to have evidence of resolved infection. Of the remaining 480, 460 children without known infection were tested for anti-HBs and 443 (96%) were reported to be immune (anti-HBs levels greater than 10 iu/l). Of the 267 with quantitative anti-HBs results available, 222 (83%) had levels above 100iu/l and 45 (17%) between 10 and 100 iu/l. Amongst the 17 children who had not developed active immunity, eight had no documented test for infection and so may have had chronic or resolved infection. Of those on the 0, 1, 2 and 12 months schedule, 288/295 (98%) were reported to be immune compared to 155/165 (94%) on the 0, 1, and 6 months schedule. Therefore, this large study suggests that, under the current UK recommendations, amongst infants who escape infection a maximum of 2% of will not make any immune response.

[3] Sloan D, Ramsay M, Prasad L, Gelb D, Teo G. Prevention of perinatal transmission of hepatitis B to babies at high risk: an evaluation. Vaccine. 2005 Dec 1;23(48-49):5500-8.

Practical issues

Based on this experience, the risk of chronic infection in high-risk infants (born to anti-HBe negative women) is significantly higher than the risk of non-response. To inform management of the infant, it is therefore important to test for HBsAg. As drop out rates increase with the number of visits[3], it is recommended that the blood sample is obtained at the same time as the fourth dose to maximise compliance with testing. As the major risk of transmission is at the time of birth, and because the response rate is high in those who escape infection, the need to document immunity for prospective management is therefore negligible. Many children will also be boosted by the vaccine given at the same time as the test is taken.

In view of the small volume of blood routinely available, anti-HBs testing should only be performed if there is sufficient blood and/or if required to help clarify the child's infection status. As PHE Colindale has identified four infants who are HBV DNA positive in the presence of anti-HBs levels above 100iu/l, anti-HBs should never be used as a substitute for HBsAg testing.

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Author	Relevant intervention group	Tested	HBsAg positive		Protective Anti-HBs	
Polakoff[4]	HBIG + vaccine	102	4	3.9%	83	81%
Evans[5]	HBIG + vaccine	29	0	0.0%	23	79%
Jonas[6]	HBIG + vaccine	64	1	1.6%	60	94%
Okun[7]	HBIG + vaccine	67	0	0.0%	66	99%
Chernesky[8]	HBIG + vaccine	31	0	0.0%	27	87%
Smith[9]	HBIG + vaccine	3	1	33.3%	1	33%
Niu[10]	Completed vaccination	26	0	0.0%	24	92%
Marion[11]	HBIG + vaccine	703	6	0.9%	630	90%
Sangfelt[12]	Various vaccine schedules	212	2	0.9%	110	52%
Kohn.[13]	Completed vaccination	130	2	1.5%	140	108%
Hale[14]	Vaccine (+/- HBIG)	367	6	1.6%	345	94%
Larcher[2]	Vaccine (+/- HBIG)	217	2	0.9%	181	83%
Wallis[15]	Vaccine (+/- HBIG)	21	2	9.5%	17	81%
Total		1972	26	1.3%	1707	87%

[4] Polakoff S, et al. Immunisation of neonates at high risk of hepatitis B in England and Wales: national surveillance. BMJ. 1988 Jul 23;297(6643):249-53.
[5] Evans JE et al. Compliance with hepatitis B immunoprophyllaxis in the neonatal period. J Paediatr Child Health. 1990; 26(2): 108-9

[6] Jonas MM et al. Hepatitis B infection in a large municipal obstetrical population: characterization and prevention of perinatal transmission. Am J Gastroenterol. 1990;85(3):277-80.
[7] Okun NB et al. Success of a program of routine prenatal screening for hepatitis B surface antigen: the first 2 years. CMAJ. 1990 Dec 15;143(12):1317-21.
[8] Chernesky MA, et al.Analysis of a pregnancy-screening and neonatal-immunization program for hepatitis B in Hamilton, Ontario, Canada, 1977-1988. J Med Virol. 1991 Sep;35(1):50-4.
[9] Smith CP, Parle M, Morris DJ. Implementation of government recommendations for immunising infants at risk of hepatitis B. BMJ 1994;309:1339
[10] Niu MT et al. Prevention of perinatal transmission of the hepatitis B virus. Outcome of infants in a community prevention program. Am J Dis Child. 1992 Jul;146(7):793-6.

[11] Marion SA et al. Long-term follow-up of hepatitis B vaccine in infants of carrier mothers. Am J Epidemiol. 1994 Oct 15;140(8):734-46.

[12] Sangfelt P et al. Prevention of hepatitis B by immunization of the newborn infant--a long-term follow-up study in Stockholm, Sweden. Scand J Infect Dis. 1995;27(1):3-7.
[13] Kohn MA et al. The need for more aggressive follow-up of children born to hepatitis B surface antigen-positive mothers: lessons from the Louisiana Perinatal Hepatitis B Immunization Program. Pediatr Infect Dis J. 1996 Jun;15(6):535-40.

[14] Hale J. Personal communication. Audit of hepatitis B programme in Lambeth, Soutwark and Lewsisham
[15] Wallis DE et al. Immunisation of infants at risk of perinatal transmission of hepatitis B: retrospective audit of vaccine uptake. BMJ. 1999 Apr 24;318(7191):1112-3.

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