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Immunisation against hepatitis B viral infection — a study of South African anaesthesiologists

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Introduction. The practice of anaesthesia involves exposure to blood or bloodstained secretions which may be contaminated with transmissible pathogens including the hepatitis B virus (HBV). This study was undertaken to assess the impact of freely available hepatitis B vaccine and applications of universal precautions against blood exposure on the uptake of immunisation and prevalence of HBV markers in South Africa anaesthesiologists.

Methods. Anaesthesiologists from the Department of Anaesthesia of the University of Natal and those attending a continuing medical education course in Cape Town in March 1993 participated in the study. Each participant completed a questionnaire giving details of previous exposure to HBV, immunisation status and details of immunisation. Blood samples were obtained on a voluntary basis for determination of HBV serology.

Results. One hundred and twenty-one anaesthesiologists participated in the study; 36 were unimmunised, of whom 18 (50%) were seropositive for HBV markers. More experienced anaesthesiologists (> 10 years) tended both not to be immunised and to be seropositive, indicating previous exposure to HBV. Eighty-five participants were immunised. Intradermal immunisation caused significantly less seroconversion than the intramuscular route (35% v. 81%; $P < 0,05$). Of 7 non-responders to intradermal immunisation, 5 responded to a single intramuscular booster injection.

Discussion. Exposure to HBV is common in anaesthetic practice, as evinced by the 50% seropositivity in unimmunised anaesthesiologists, which means that routine serological testing before immunisation is warranted. Intramuscular immunisation provides the best protection against HBV.

Post-immunisation serological testing should be performed to demonstrate an adequate antibody response. The intradermal route may save cost with similar efficacy if combined with post-immunisation testing and a single intramuscular booster injection for non-responders.

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Health care workers, particularly those whose clinical duties regularly involve contact with patients' blood or blood-stained secretions, are at definite risk of infection by blood-borne viral pathogens including HIV and hepatitis B virus (HBV).[1,2] Protection against both these pathogens is provided by application of the blood and body fluid precautions (universal precautions) prescribed by the Centers for Disease Control (CDC) in the USA.[3] However, although HBV is transmitted at least 10 times more readily than HIV,[1] protection against HBV can be obtained via immunisation with hepatitis B surface antigen (HBsAg).[4] HBsAg may be derived from the serum of chronic carriers (serum-derived) or from brewer's yeast into which the gene for HBsAg has been inserted by recombinant technology. Both vaccines are expensive and recommendations for their optimal use remain controversial. Only one previous study, conducted in Bloemfontein in 1986, investigated the prevalence of HBV markers in South African anaesthesiologists.[5] In 1986 the universal precautions had not yet been published and only serum-derived vaccine was available; recombinant vaccine was still in the process of being released.[4] This study was therefore undertaken to determine the HBV serological status of a broader group of South African anaesthesiologists, and aimed to assess the impact of universal precautions and vaccine availability and define appropriate recommendations for immunisation.

Methods

The study comprised two parts. The first part involved the circulation of a questionnaire which requested demographic information on years spent in medical practice, including time in anaesthesia and any of the surgical disciplines. In addition, information on previous episodes of clinical jaundice or suspected hepatitis was sought, including source of infection, type of infection and length of time since infection. Immunisation status was assessed by questions on type of vaccine received, number of doses and boosters, route of administration and post-immunisation serological status if known. The questionnaire was completed by two groups of anaesthesiologists. The first group was drawn from the staff of the Department of Anaesthesia of the University of Natal, while the second group was drawn from anaesthesiologists throughout South Africa who were attending a SASA CME course in March 1993.

The second section of the study involved venous blood sampling from participants on a voluntary basis. Samples were separated within 8 hours and serum was stored at –4°C. Serological tests were performed on all specimens in a single run using standard radio-immunoassay kits (Abbott Laboratories, Chicago, Illinois). The level of antibody to HBsAg (anti-HBs) was quantitated by calibration against a standard; a protective level was taken to be greater than 50 milli-international units/ml. Results were analysed with the χ^2-test; a P-value less than 0,05 was considered significant.

Results

The first group studied comprised 69 anaesthesiologists from the University of Natal and the second 52 from the CME course. These groups differed only in that those

attending the CME course were more experienced; only 6 (11,5%) of the CME group had less than 5 years' anaesthetic experience, compared with 34 (49%) of the Natal group. There were no other differences, so the groups were combined to make a total study population of 121 (Table I); blood was obtained from 110. Thirty-six respondents (30%) had not been immunised before. Their serological results are shown in Table I. Only 4 seropositive patients were aware of a previous HBV infection, and only 1 of these had resulted from percutaneous exposure to the blood of a HBV carrier in an occupational setting. There were no anaesthesiologists who were either HBsAg- or HBeAg-positive, neither were there any anti-HBs-negative respondents who were anti-HBc-positive.

Table I. Serological status and uptake of immunisation related to time spent in medical practice

	Years in practice		
	0 - 5	6 - 10	> 10
Seropositive	1	2	15
Seronegative	5	5	5
Immunised	20	24	41
Not immunised	6	9	21

No serology available — 3 unimmunised participants; 8 immunised participants.

Eighty-five participants had received some form of immunisation; this gave an uptake rate of 70%. Differences in uptake with increasing experience are shown in Table I.

Of the 85 immunised respondents, post-immunisation serological data were available for 83 (Table II). Three of the seronegative respondents had previously been seropositive and another 4 had been immunised more than 7 years previously without post-immunisation serology.

Table II. Anti-HBs level related to route of immunisation and time since last immunisation

	Anti-HBs level			
	0	< 50 mIU/ml	> 50 mIU/ml	Unknown
Route of immunisation*				
Intradermal	15	2	6	0
Intramuscular	10	10	32	2
Time since immunisation (yrs)†				
< 1	0	2	4	1
1 - 3	11	6	17	3
4 - 6	5	2	10	2
> 6	4	3	6	1

* Route unknown: 8.
† Time unknown: 4.
Non-responders: 4.

Five respondents were previously seropositive and 1 seronegative on post-immunisation serology prior to this study. These 6, together with a further 2 immunised respondents, declined serological testing in this study. There was a significantly better seroconversion rate via the intramuscular route, 81% v. 35% ($P < 0,05$) (Table II). There was no clear relationship between time since last dose of vaccine and antibody level (Table II). Only 36 (42%) of the immunised respondents knew the type of vaccine administered to them and only 25 (29%) had received less than the recommended three doses. Response to booster injections of participants who failed to respond to initial attempts at immunisation is shown in Table III.

Table III. Response of initial non-responders to booster injections

Route of initial immunisation	No.	Booster	Response to booster: Sero-positive	Response to booster: Sero-negative
Intradermal (ID) 3 doses	7	IM 1 dose	5	2
Intradermal (ID) 2 doses	1	ID 2 doses	1	0
Intramuscular (IM) 3 doses	3	IM 1 dose	1	1
		IM 3 doses	0	1

Discussion

Hepatitis B poses a significant threat to health care workers, with an estimated 8 700 cases occurring annually in health care workers in the USA as a result of exposure to contaminated blood or body fluids. Up to 440 of these require hospitalisation, 200 of whom die from acute or chronic complications such as chronic active hepatitis, cirrhosis or hepatic carcinoma.[6] The situation is exacerbated in South Africa as hepatitis carrier rates approach 10% in certain rural areas, especially in Natal.[7] Urban prevalences are similar to the 0,5 - 1,5% quoted for the USA[8] and the UK.[2]

In this study, 50% of unimmunised anaesthesiologists were shown to have had a previous subclinical episode of hepatitis B, evinced by the presence of anti-HBs antibodies. This is in contrast to studies from the UK[9] and USA,[10] and a previous study from Bloemfontein in 1987[3] shown in Table IV. The most significant feature of this study is that no recent infections were identified.

Table IV. Comparison of HBV markers in unimmunised anaesthesiologists (%)

	Bloemfontein 1987	Durban & SASA 1993	Oxford 1987	Multicenter USA 1985
Seronegative	64	42	97	87
Seropositive (recent infection)	32	0	0	10
Anti-HBs-positive	4	50	3	3

The CDC published their universal precautions in 1987.[3] Since then these guidelines have been widely popularised, sharply reducing exposure of health care workers to both HIV and HBV. The people with recent acute infections observed in the Bloemfontein study would now probably only be anti-HBs-positive, as seen in the low or absent incidence of recent infection in our study, although progression of some of the cases from 1986 to a carrier state cannot be excluded.

The implication of a high level of previous exposure to HBV in an unimmunised population is that pre-immunisation serological testing may be warranted.[11] The cost of the serological test for anti-HBs is R40 (Scale of Benefits) while the cost of three intramuscular injections of recombinant vaccine is R153,03. Therefore, if more than 27% of an unimmunised population were anti-HBs-positive, the unneeded vaccine saved would outweigh the cost of the tests for the whole group. This would not seem to be justified in the UK or the USA, with low levels of previous exposure. However, both this study and the previous Bloemfontein study[5] seem to indicate that pre-immunisation

testing of South African anaesthesiologists would be cost-effective, especially for those with more than 10 years' experience.

There were 85 anaesthesiologists in this sample who had elected to be immunised, giving an uptake of 70%, which is much higher than the 2% in Bloemfontein and also higher than in the UK,[12] where only 49% of doctors in a 1991 study were shown to be immunised. The good uptake rate shown in our study could be explained by awareness of higher carrier rates of HBV in our population and a general increase in awareness of blood-borne viral infections.

Implementation of mandatory immunisation programmes should increase uptake rates to levels close to 100%. However, this study has shown that up to 30% of those immunised may remain seronegative and therefore continue to be at some risk of HBV infection. Confirmation of seroconversion by post-immunisation serological tests adds further costs to an already expensive process, but is justified in the light of this significant non-response rate. Previous studies in the general population quote seroconversion rates of 90 - 95%[8] and post-immunisation serology is not recommended for community vaccination programmes. Post-immunisation serological testing which shows an adequate initial level of anti-HBs also indicates adequate priming of the immune system. Should antibody levels subsequently decline, memory B cells would persist and would be able to mount an adequate response on re-exposure to the HBV, preventing the chronic and acute sequelae that cause morbidity and mortality.[4,8]

Seroconversion following vaccination is dependent on a number of factors, including route of administration of vaccine, dose of vaccine, type of vaccine and number of doses of vaccine. Vaccine manufacturers recommend that 10 µg of serum derived or 20 µg of recombinant HBsAg in 1 ml of carrier solution be injected into the deltoid as an initial dose; this is repeated at 1- and 6-monthly intervals for a total of 3 doses.

The cost of hepatitis B vaccine has led to strategies to reduce the amount required while maintaining efficacy. This led to the development of immunisation by intradermal injection, a method that requires one-tenth of the intramuscular dose. Adequate seroconversion rates of 80 - 90% were reported initially[8] but a subsequent report has failed to confirm this,[13] with response rates of less than 50% found in three groups immunised intradermally. Our results showed that the seroconversion rate was only 35% among participants immunised by the intradermal route. This is probably due to decreased efficacy caused by inadvertent subcutaneous administration of the vaccine.[14] Some priming of the immune system must have occurred, as shown by the seroconversion of 5 of the 7 respondents who were initially seronegative after receiving a full course of intradermal vaccine after a single intramuscular booster. However, the 2 respondents who failed to respond to this regimen may require a full intramuscular course of immunisation.

The intramuscular route, however, is not foolproof. The response rate in this study was at least 81% but could be higher, as a further 4 participants (8%) had been immunised more than 7 years before and their initial response may have faded, as occurs in 30 - 50% of cases.[3] Intramuscular immunisation may have been given into the gluteus or been deposited subcutaneously, both of which would have reduced efficacy.[8] The two participants who failed to respond to two courses of intramuscular immunisation may benefit from a full course of intradermal immunisation or a further course of intramuscular immunisation with an increased dose. Apart from this indication the intradermal route would therefore seem to be a non-viable alternative despite its reduced cost. However, if the need for post-immunisation serological assessment is accepted, non-responders would be identified. This study suggests that 70% of these non-responders should respond to a single intramuscular booster, although the numbers are small (5 of 7) and may not extrapolate. The extra cost of a single intramuscular booster plus a further serological test would still be less than a full course of intramuscular vaccine. This study can, however, find no good reason to contradict the manufacturers' recommendations as outlined above.

Our recommendations based upon the findings in this study are that: (*i*) protection against HBV infection in anaesthesiologists be maximised by increasing the uptake of immunisation to levels approaching 100% as infection may have significant early and delayed consequences and, even with 100% uptake, protection is not assured, as shown by the four non-responders to two courses of immunisation in this study; (*ii*) unnecessary immunisation be minimised by pre-immunisation serological tests, which should be performed in all cases but especially on unimmunised staff with more than 10 years' experience; and (*iii*) seroconversion be confirmed, particularly when the intradermal route is chosen. Adequate levels of anti-HBs demonstrated post-immunisation may also preclude the need for further booster injections.

All these measures will not provide full protection for all anaesthetic staff against HBV, and provide no protection against HIV exposure. Only rigorous application of universal precautions will reduce exposure to both HBV and HIV and thus reduce the likelihood of infection. These precautions are the basis of any campaign to reduce the incidence of HBV in anaesthetic staff and, combined with immunisation, should make HBV infection among anaesthetic staff extremely rare.

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