Mr Berkage

NATIONAL BLOOD TRANSFUSION SERVICE
NORTH LONDON BLOOD TRANSFUSION CENTRE
COLINDALE AVENUE
LONDON
NW9 5BG
Telephone: 081-200 7777
Fax: 081-200 3994

Dr. M CONTRERAS
Director

Dr Harold Gunson, CBE, MD
Medical Director
National Blood Authority
Gateway House
Piccadilly South
Manchester M60 7LP

MC/ajc/gunson

18 October 1993

Dear Harold

Anti-HBc testing of blood donations

Thank you for your letter of 8 October 1993 regarding the above.

I was dismayed that the DH Advisory Committee on MSBT has decided not to introduce routine testing of all blood donations for anti-HBc. I have had a long discussion with Dr David Dane and John Barbara and we have concluded that some of the reasons that the Committee has given are very difficult to defend:

(i) It is true that ELISAs for anti-HBc give false positive results, but so do ELISAs for anti-HCV yet the DH had no problems in introducing universal donor testing for anti-HCV. Furthermore, reducing agents appeared to enhance specificity of certain anti-HBc assays very strikingly and several of the kits without reducing agent produce a remarkably *lower* level of false-positive reactions than the ten-fold rate you quote in your letter.

(ii) The primary object of donor testing is to provide safe blood. Naturally you want to give the donor accurate information about his/her condition, but you can only do your best. A true 'anti-HBc only' donor has had an icteric or an anicteric HBV infection in the past, has recovered and is not going to suffer from any long term illness as a result even if there is a risk of residual infectivity 'by the pint'. It is fairly easy to say to the donor that you cannot be quite certain about the HBV infection having taken place, (ie the result may be a false positive one), and so there is nothing to worry about anyway. In any case, are we able to provide definitive health information for donors found positive or, even more problematically, indeterminate for HCV antibodies? In contrast, we can be very reassuring to anti-HBc-positive donors and would have few problems, in practice, when counselling them. Furthermore, the management of anti-HBc false positive donors is now easier since we now have an official mechanism for their readmission.

Please copy to
Dr J Metters
Mr J Canavan

Mrs Sandilands
To see & for file pl Bcos
TBC14 Berkage 3/11

From: DR. Rejman 20/10/93

DHSC0004709_151_0001

(iii) Does the Committee mean that we do not have an anti-HBs standard above which we consider that a donation which tests positive for anti-HBc can be considered to be safe? I do not think that this is a major problem, especially when we can quantitate anti-HBs in international units and allow for kit epitope-detection variations by applying a more conservative cut-off. We would have thought that the accepted level for post-vaccination immunity would have provided a safe enough cut-off level.

(iv) We know for a fact that many cases (up to 80%) of HBV infections are sub-clinical, but that does not mean that the chronic effects of such an infection will be sub-clinical as the asymptomatic cases are the ones that are more likely to develop the carrier state. A significant proportion - perhaps 10% - of the subclinical cases will become long-term carriers. In Dr Dane's experience the carrier state may develop after a sub-clinical attack, but not after an icteric infection. Only carriers are liable to suffer from severe complications such as cirrhosis and hepatoma. I personally would prefer to suffer from a clinical HCV infection than a sub-clinical, or any, HBV infection. Nobody has been able to show that the chronic effects of post-transfusion hepatitis C are worse than the controls even after 18 years follow-up. Furthermore, when HBV is symptomatic, it can be very serious indeed (as several hepatitis experts have often pointed out). It is clear from presently available evidence that the overall risk from an HBV infection is greater than from an HCV infection even though the majority of HBV infections are inapparent and have no sequelae. More strikingly, HBV is <u>far</u> more readily transmitted from mother to child or to sexual partners than is HCV.

(v) Since when has the Department been concerned about the cost of blood derivatives? Were they concerned about this when testing for HCV was introduced? I for one am acutely aware of costs, but believe in spending the money when it is needed. Even though the number of hepatitis infections prevented by HCV testing may be greater than those prevented by anti-HBc testing, the net benefit from anti-HBc testing could well be greater. Have we any definite information on this?

(vi) Nobody would dream of withdrawing units with anti-HBc and moderate to high levels of anti-HBs from the plasma pool destined for fractionation.

If anti-HBc testing has been shown <u>not</u> to be cost effective then I hope that patients who get PTHB will have no valid claim. But has this been shown?

I would be grateful if you could ask MSBT whether the DH will cover the costs of law suits, a few of which I believe are currently in progress, emanating from patients who acquire PTHB from "anti-HBc only" blood. The cost of law suits might be higher than the projected £3 000 000 per year for anti-HBc testing. In any case, reagent costs for anti-HBc may well be reduced in "package deals" with manufacturers.

Of course, I agree that the recommended policy should be implemented uniformly, provided that the option for performing large scale trials to corroborate the data from

Liverpool is left open. Such trials will be vital to get more hard data on cost-effectiveness of screening. Certainly, we have not shown that anti-HBc is *not* cost-effective. However, this does not mean that I agree with the policy. I trust that the continuing MSBT review will take comments from the Centres into account.

Several other points are worth stating:

1. Isolations of HBV mutants that are HBsAg negative in sensitive monoclonal ELISAs, but anti-HBc positive, are a reality. At least one has already been reported in the literature and we know of one recently that has a Hepatest titre of 1 in 1,600, but is flat negative on a front-line ELISA. Such isolates are likely to be detected with increasing frequency and strengthen the value of anti-HBc as a back-up for HBsAg testing.

2. The lack of accurate figures relating to residual PTHB does not mean it does not occur and is a reflection of our own lack of central collation. Under-reporting (even of obvious cases) is another reality. For example, one of our own Mediterranean anti-HBc positive "tail-end" carriers was identified in a PTH enquiry and we discovered that the recipient of his previous donation had suffered icteric PTHB misdiagnosed due to inadequate testing and therefore was not reported to us.

3. Why were not alternative strategies such as new-donor testing at least considered before such an important decision was made when at one point the potential risks even from anti-HBs positive donors were raised as an issue of safety?

With best wishes.

Yours sincerely

Marcela Contreras MD MRCPath FRCP(Edin)
Chief Executive - Medical Director

Copy to: Mr J.F. Adey
Dr A. Rejman
Dr F. Ala
Prof. J.D. Cash
Dr J.A. Barbara