)TE OF THE THIRD MEETING OF THE RECONVENED ADVISORY GROUP ON TESTING FOR THE PRESENCE OF HEPATITIS B SURFACE ANTIGEN AND ITS ANTIBODY

Held on 1 November 1979 at Hannibal House, DHSS

Present: Dr W J Jenkins (Chairman)
Dr T E Cleghorn
Dr J Craske
Dr D S Dane
Dr E A C Follett
Dr T H Flewett
Dr G H Tovey
Dr E M Vandervelde
Professor A J Zuckerman
Dr H Thomas for Professor Dame Sheila Sherlock
Mrs Margaret Supran on an interim basis
Professor Gardiner replacing Dr Bradstreet

SHHD Dr A E Bell

DHSS Mr D A Kennedy
Mrs S Yuille
Mr T E Dutton) Joint Secretaries
Dr Phyllis M Furnell)

1. Apologies for Absence and Wellcome

Apologies were received from Professor Dame Sheila Sherlock, Dr Lane, Dr Bird and Dr Cash.

The Chairman welcomed Professor P S Gardiner who has replaced Dr Bradstreet as Director of Microbiological Research and Quality Control, PHLS Colindale and as a member of this Advisory Group.

2. Minutes of the Second Meeting AGHB(79)N2

The minutes were agreed subject to the following matters:

i. Item 3(v) last sentence: the record should state that Mr Dutton said that although it was understandable that medical scientists may not themselves wish to get involved with the machinery for patenting inventions, there were specific requirements within the NHS for ensuring that benefits from work which was patentable were not lost.

Mr Kennedy explained that the non-association with commercialisation referred to in the sentence meant that reagents should not be sold to commercial companies. Regarding patenting and commercialisation, there was very little chance that the former would infringe any rights but doubtful that the BPL test was patentable itself. On consideration of whether the state should sell rights of the complete test to a British or other firm he suggested that this should be deferred until the test was well established.

The Chairman said this question should be looked at in the light of action of other groups within similar situations and what was effected by them.

ii. Page 3, observations in the fifth paragraph, which had been attributed to Dr Vandervelde and Mrs Supran had in fact been made by Professor Zuckerman.

iii. Item 3(vi) should have read "Professor Zuckerman asked for a correction in line 5 item 7: delete 'carcinogenicity' substitute 'radioactivity'".

iv. Professor Zuckerman said references to anti-hepatitis B immunoglobulin should correctly read hepatitis B immunoglobulin (HBIG).

v. Reference Standards: It was agreed that reference should be made to "units" not "nanograms", though use of 'Abbott's nanograms' was accepted in a proper context.

3. Matters Arising Not Otherwise on the Agenda

a. Non-A, Non-B Hepatitis

Professor Zuckerman reported that the Medical Research Council Working Party on Non-A, non-B Hepatitis was working on three projects and a fourth was in hand. Chimpanzee work was going well and challenge work was in progress. Professor Zuckerman said that it was important to recognise the problem and to arrange for sera from possible non-A, non-B cases to be made available for testing. The Chairman informed the members that Regional Transfusion Directors had been asked to assist in this and he would check at their next meeting whether they had been able to make appropriat arrangements to do so.

It was agreed that Professor Zuckerman in consultation with Dr Dane and Professor Dame Sheila Sherlock should write to the medical press (eg the Lancet), to draw attention to the possibility of non-A, non-B hepatitis and to ask clinicians to provide serum samples to Blood Transfusion Directors with details of cases of hepatitis occuring after the administration of blood and blood products including Factor VIII, and which had been shown to be HBsAg negative. This would facilitate a) studies into the extent of the problem, and b) provide material for research.

Dr Craske pointed out that the Medical Research Council was reconvening the Group concerned with Blood Transfusion work and post-transfusion cases of hepatitis which were HBsAg negative would be examined and a paper would be presented to the Advisory Group, in due course. He said that it was worth noting that NHS Factor VIII was associated with a low incidence of hepatitis.

It was decided that for the present material from icteric cases only would be studied as documented cases of infection would be desirable for studies directed at finding a detectable agent, and covert cases could be considered later.

It was agreed that all cases would be notified to the PHLS as well, and that the letter would include reference to jaundice in haemophiliacs.

b. Reference Standards - Progress Towards a British Standard AGHB(79)3.1

The Chairman reported that together with Professor Zuckerman and Dr Dane he had attended a meeting at NIBSC, Chaired by Dr Smith, to discuss the production of a British Standard for HBs antigen. Burroughs-Wellcome and Glaxo had declined invitations to become involved in the work on development of a standard because of concern about ampouling 'dangerous materials'. Satisfactory arrangements had now been made which would enable NIBSC to proceed with the work. Dr Schild would make the standard under study available and NIBSC would organise the distribution of the test material.

Dr Dane and Dr Lane will supply NIBSC with a list of those laboratories willing to collaborate, and Professor Zuckerman and Dr Dane will continue to advance this project.

c. Enzyme-Immunoassay

It was reported that Dr Lane has all the required reagents and materials at the BPL for developing an enzyme-immunoassay technique, and if results were satisfactory the system could be made available. Progress reports would be given at future meetings.

d. Antigen-Testing of Staff

Dr Furnell reported that the matter was under consideration within the Department and it was agreed that the Advisory Group did not wish to make recommendations to the Department, and would await Departmental guidance on the matter.

4. Working Party on the Distribution and the Use of Hepatitis B Immunoglobulin AGHB(79)P3.3

It was decided that as there was difficulty concerning the availability to members of this Working Party of the MRC Report on the subject, (presently in a draft form) it would not be possible to give consideration to it.

Paper 3.3 included Enclosure 1, a Note of the 1st Meeting of the Dr Lane's Working Group Convened by the AGHB and held on 11 June 1979, and Enclosure 2 which presented "Recommendations for Use of Human Hepatitis B Immunoglobulin" were considered.

In Dr Lane's absence Professor Zuckerman spoke to these papers. Professor Zuckerman stated that the two points of importance were:

i. Holding and distribution arrangements as discussed before have been agreed with the Director of the Public Health Laboratory Service Board and stocks from BPL could be obtained by direct application made by Regional Transfusion Centres and Specialist High Risk Centres.

ii. Recommendations for use of HBIG. Members were asked to comment on the paper and advised that it was the intention to supply printed information presenting these as "interim recommendations" with ampoules of immunoglobulin Members attention was directed to Item 6 in Enclosure 1. This reads:

"It was noted that a need for a regular review of the recommendations for use exists and that the recommendations should be made available to holders of stocks. It was considered that this was a matter for the Department, and that this Working Group would recommend to the Department via the Advisory Group on Testing for the Presence of Hepatitis B Surface Antigen and its Antibody, that a body, perhaps entitled "Review Committee on Recommendations for the use of Hepatitis B immunoglobulin in Prophylaxis, including the use of vaccines" should be convened. This could be a sub-group of a Hepatitis Advisory Group which is presently under discussion within the Department.

Dr Vandervelde said she could agree the modifications in the main, but questio the soundness of the recommendation relating to post-exposure prophylaxis. It was important first to clarify that immunoglobulin should not be issued when a doubtful situation prevails without preliminary enquiries, as to the nature of the inoculation accident and the antigen status of the patient; and secondly to realise that if administration of the immunoglobulin within 48 hours of an incident were considered essential then a 24 hours laboratory antigen testing service would be required. If all involved in such accidents were to be given immunoglobulin regardless of whether the blood involved were HBsAg positive or not, this would result in uneconomical use of immunoglobulin, ~~might be seen to be unethical~~, as 90% of the doses might be unnecessarily administered.

Professor Zuckerman stated that in his opinion it would be ~~unethical~~ wrong to delay administration until test results were available, and that it was essential to administer the immunoglobulin within 48 hours, and further cited the experience of Dr Cash that administration without testing did not lead to excessive use.

Dr Jenkins suggested that testing should be done prior to administration of immunoglobulin for accidents which occurred during the working day. For those which occurred outside laboratory hours HBIG could be administered without prior testing of the inoculum for HBsAg.

Dr Thomas and Dr Flewett suggested that clinicians should use discretion in deciding which cases present high risk situations.

Dr Vandervelde expressed concern that use of immunoglobulin for minor incidents could mean that stocks would be exhausted. Professor Zuckerman believed Dr Lane had indicated adequate stocks were available to meet demands. Dr Dane said that the new recommendations would require a repeat dose which amounted to double the demand based on present use. Dr Jenkins pointed out that this Advisory Group had obtained levels of demand from the PHLS based on a single dose routine, and it would appear that administration of HBIG without antigen testing and with a double dose regime could result in a large increase over the single dose regime. It was doubtful whether Dr Lane had taken this into consideration at the time of his estimates. Mr Dutton pointed out that Dr Lane had recently indicated that BPL was unable to take on production of another immunoglobulin unless extra money was forthcoming and if these recommendations had resource implications they could prove an embarrassment to the Department.

Members considered it could be economical to indicate the time beyond which it would not be useful to give HBIG, and that clear guidelines relating to those for whom the HBIG was not indicated would assist PHLS Directors because otherwise these recommendations could possibly have certain legal implications. Dr Vandervelde also stated that indications for use of HBIG in mentally sub-normal institutes could not be based on the recommendations as they stand because of the occurence of frequent incidents in these places.

The Chairman had suggested that Enclosure 2 should be re-considered by the Working Party in respect of the recommendation of 48 hours for the first dose, and with regard to whether doubtful cases could be managed on results of tests available in 12 hours and this could further depend on the availability of a 24 hours laboratory service.

Dr Flewett said the recommendations required expansion to be helpful to all responsible for the use and administration of HBIG.

Dr Craske noted that 20% of likely inocula were not readily available for testing.

Professor Zuckerman considered that in his opinion there was no need to reconsider the recommendations, but that if high risk groups were defined eg the police, and if decisions to administer HBIG are based on clinical judgement then no testing should be required. retrospect judgement of tests of value.

Members considered the suggestion that the recommendations might be sent out in their present form and their operation in practice observed.

Regarding Neonatal Prophylaxis, Dr Flewett stressed that infants of mothers who were eAg carriers should not continue to receive HBIG indefinately though prolonged follow up is required. Professor Zuckerman said this was a valuable suggestion which should be noted.

Members were informed that Dr Lane wanted to send these recommendations under the AGHB approval, with every ampoule of HBIG.

Mr Dutton informed members that present Departmental Policy did not favour further dissemination of information and alternative methods worth considering were via the media to the field eg Prescriber's Journal, the Lancet and BMJ.

Dr Furnell pointed out that any action should be deferred until the appropriate Division of the Department which was responsible for Policy on Vaccination and Immunisation had considered the recommendations, as it would not be appropriate for the Advisory Group to act independantly especially if there should be a conflict with other departmental advice and if there should be consequences and implications for pathology services which had not been fully considered.

It was decided that Mr Dutton would establish the position relating to resource implications.

The Advisory Group considered possible ways by which the recommendations could be made known, eg via journals, and to Directors of Blood Transfusion Centres and Public Health Laboratories. This could be effected via Dr Tovey and Sir Robert Willia and in addition by a joint communication from Dr Lane and Dr Tovey to the editors of various medical journals.

Suggestions

Finally, it was noted that Professor Zuckerman would make certain amendments to the recommendations before they were sent out.

5. Working Party on Quality Control for test methods for detecting low-titre HBsAg
AGHB(79)P3.4

Dr Supran explained that at the last meeting of the Advisory Group it had been decided that a panel of negative and very low-titre HBsAg should be set up and held at the Standards Laboratory at Colindale. It was felt that laboratories performing RIA, ELISA and sensitive HAI tests should have available to them a range of low-titred sera which had been evaluated by a number of expert laboratories. Results so far had been summarised in the Report, and the table of results would be sent with every Panel to participating laboratories. The Panel would enable workers to check the performance of the tests in their laboratories. Thirty-two panels were still available. The Chairman agreed that Regional Transfusion Directors and the PHLS should be informed of the availability of these panels. Members agreed that they would wish to see the results obtained by using the panels. Dr Craske and Dr Thomas registered their willingness to receive sets. Dr Tovey and Dr Craske undertook to inform the BTS and PHLS of this service.

6. Working Party to Evaluate New Test Procedures for Hepatitis BsAg and anti-HBs in the NBTS

Dr Dane, who was reporting on behalf of Dr Lane said that over the past seven years half a million tests had been undertaken at the BPL, other laboratories and at Regional Transfusion Centres. Oxford Regional Transfusion Centre had been using the BPL test for about two months and the results had been satisfactory. South Western. West Midlands and North East Thames Regional Transfusion Centres would shortly also be using the tests. A package containing a washer and a sixteen-well counter could be loaned from the Blood Products Laboratory, and Centres which wished to continue using the tests would be able to buy their own equipment. At [illegible] West Thames Regional Transfusion Centre where the BPL test had been used, [illegible] positive screen tests had been reduced to less than 1:10,000 with experience, [illegible] were no repeat false positives in the 20,000 donations so far tested. Of the [illegible]y thousand tested at the Centre, sixteen thousand were new donors. Of these, thi[illegible]ive were found to be positive by the Hepatest, thirty-seven were positive by the modified Hepatest, and the same thirty-seven were positive by the BPL test. It has been calculated that the cost per screen test would be three pence for the reagents, but technician's time had not been costed. It was thought that the cost of two million tests a year (national service) would be about £60,000 which was the same as the annual cost of the Abbott RIA test in one Centre.

The Chairman referred to an earlier approach from Dr Sheila L Waiter to Supply Division and asked whether the Department had considered funding two packages which could be circulated to Regional Transfusion Centres, to enable comparative studies with Ausria II to be done. Mr Kennedy explained that Evaluation Funds were being sought and this had received Supply Division and Medical (Med SM4) support.

7. Correspondence from Dr Darnborough and Dr Tovey

i. The Chairman reported that Dr Darnborough had written to him expressing concern about the HBsAg tests which involved use of human reagents from paid commercial donors. The Chairman had replied assuring Dr Darnborough that the test which the Advisory Group was advocating did not involve reagents from paid donors.

ii. Dr L A D Tovey brought to the attention of the Chairman the case of an elderly lady who died from liver failure and who was shown to be antigen positive. This result was missed by the Hepatest and picked up on RIA testing. It was doubtful that her antigen status contributed to her demise, but the case highlights problems of not adopting the use of the most sensitive tests available.

8. Comparative Assessment of the Ausria II and Connaught Laboratories RIA Test for Hepatitis B Surface Antigen AGHB(79)P3.2

Dr Flewett noted that results of both tests were comparable. He also asked for the paper reporting a comparative study between the BPL and Hepa-Tab-G(RIA) (which was previously submitted to Dr Waiter) to be distributed to members.

9. Any Other Business

Ausria

It was agreed that Dr Craske's paper on "Factor VIII and IX associated transfusion hepatitis in the UK" which was tabled should be considered at the next meeting.

10. Date of next meeting

6 March 1980

DHSS
NOVEMBER 1979