Mr Dutton — I have sent (today) 58A
Ms Yuille a copy to Dr Jenkins
hopefully he will agree

NOTE OF THE 1ST MEETING OF THE RECONVENED ADVISORY GROUP ON TESTING FOR THE PRESENCE OF HEPATITIS B SURFACE ANTIGEN AND ITS ANTIBODY. HELD ON 7TH DECEMBER 1978 AT THE DHSS, HANNIBAL HOUSE.

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PRESENT:

Dr W J Jenkins (Chairman)
Dr C M Patricia Bradstreet
Dr C J Burrell
Dr J D Cash
Dr D S Dane
Dr T H Flewett
Dr R S Lane
Professor Dame Sheila Sherlock
Dr Elise M Vandervelde
Professor A J Zuckerman

SHHD
Dr A E Bell

DHSS
Mr T E Dutton)
Dr Sheila L Waiter) joint secretaries

Mr D A Kennedy
Dr Phyllis M Furnell
Mrs S C Yuille

APOLOGIES: Were received from Dr G W G Bird and Dr G H Tovey.

Dr Burrell explained that he would be leaving for Australia in March, but is willing to serve until then.

BACKGROUND:

The Advisory Group first met during 1970-71 and the first report, Revised Report of the Advisory Group on Testing for the Presence of Australia (Hepatitis Associated) Antigen and its Antibody was issued in 1972. Subsequently as information on all aspects of hepatitis B antigen accumulated some of the advice issued in the 1972 report became outdated. The Advisory Group was therefore reconvened and met five times during 1972-75 and based on their recommendations the Second Report of The Advisory Group on Testing for the Presence of Hepatitis B Surface Antigen and its Antibody was published in 1975. It has since become evident that further review is necessary and the Advisory Group has been reconvened to advise the DHSS on updating the Report.

MEMBERSHIP:

Four members of the current Advisory Group served on the previously reconvened Advisory Group: Dr C M Patricia Bradstreet, Dr D S Dane, Dr T H Flewett and Professor A J Zuckerman, and amongst these the latter three were members of the original panel from the outset. A list of members of the present group has been circulated.

TERMS OF REFERENCE:

Draft Terms of Reference were tabled. The following were agreed:

The six questions outlined in AGHB(78)P.1. to be considered and in the light of progress in the field of viral hepatitis

(1) To revise the Second Report of the Advisory Group on Testing for the Presence of Hepatitis B Surface Antigen and its Antibody.

(2) To advise the Department on measures which should be introduced to offer greater safety to recipients of blood and blood products and to protect the interests of blood donors.

(3) To consider other relevant matters which may be raised.

It was also agreed that the primary concern of this committee was with donors and not with the care of patients in hospital.

The Chairman recommended and obtained agreement on the following points:

(1) That there would be consultation with appropriate persons or professional groups as necessary. Experts could be co-opted.

(2) A member could nominate a deputy to attend in his/her place.

(3) When considered appropriate working groups would be set up to consider special subjects.

FAMILIES OF PATIENTS SUFFERING FROM HAEMOPHILIA AND RELATED DISEASES AS BLOOD DONORS: AGHB(78)P1.2

To exclude families of patients suffering from haemophilia from being blood donors was considered inappropriate as there is no good evidence that these constitute a risk group themselves and such action would necessitate consideration of exclusion of other groups, for example, families of patients on haemodialysis, immunosuppressive therapy, steroids etc. Further, as this group is to review more sensitive methods for testing for hepatitis antigen and antibody it can be expected to arrive at more meaningful criteria on which exclusion of potential donors would be based and these would cover the question at issue. Dr Flewett, Professor Zuckerman and Dame Sheila Sherlock were averse to the exclusion of the families of haemophiliacs from the blood donor panel.

The Department will convey this view to Regional Transfusion Directors who had raised the question.

"STOP GAP" PROVISION FOR PLASMA FRACTIONATION AT BPL, ELSTREE: AGHB(78)P1.3

Dr Lane stated that BPL is aiming for considerably increased production of factor VIII and that the system of sending 5 litre packs of pooled plasma from Regional Transfusion Centres is disadvantageous both to the processing and the yield of factor VIII. Plasma from which factor VIII is derived is tested by RIA at BPL. and it is desirable that single pack collections should be individually tested in future by RIA.

The Directors of the Blood Transfusion Service are opposed to the idea of a "double standard" using RIA testing for the protection of recipients of plasma components and RPHA testing for recipients of cell components. A collaborative project between Dr Dane and his staff at the Middlesex Hospital, Dr Lane and his staff at BPL, and Dr Cleghorn and his staff at Edgware, has developed an RIA system of considerable sensitivity and low cost. It is intended to offer the test system to the Regional Transfusion Directors to introduce into the Regional Blood Transfusion Service, after this Advisory Group has approved of the test and its suitability.

Dr Jenkins said that Dr Lane carries the responsibility for deciding the test required for plasma before fractionation in BPL and if he felt RIA test on single packs is requisite, then there would be pressure for Regional Transfusion Centres to commence testing for HB_sAg by RIA.

The possibility of commercialising the RIA test system formulated by the project team referred to earlier was considered and opinion was divided on the idea.

It was agreed that it is desirable for Regional Centres to move to a test more sensitive than RPH.

It was also agreed that other tests besides RIA, including ELISA, merit careful consideration, before any decisions on RIA (including the Dane/Lane/Cleghorn test) are made.

Assessment was also needed on consideration of capital costs, short life of reagents, machine breakdowns, before choosing RIA over non-radioisotope techniques, Dr Burrell also stressed other factors needed examination, such as ease of recording, ease of reading, sensitivity of the test and false positive rate.

Dr Waiter focussed attention on the questions of alternative arrangements should Drs Lane, Dane or Cleghorn not want to continue production of their RIA test system at the required scale; whether a patent should be considered and what quality control of the test could be exercised. She also reminded members of the reasons given when the Advisory Group advised previously against using RIA for HB_sAg testing throughout the BTS.

With regard to single packs, Dr Cash stated that the Scottish Fractionation Unit does NOT want single pack collections.

There was agreement in principle that tests should continue to be done on a two tier system (by RPH in the majority of Regional Transfusion Centres and by RIA at the central processing laboratories) until further decisions on this are taken. Double standards, however, would not be permanently acceptable.

It was decided to establish a working group to assess the various sensitive tests available (including the Dane/Lane/Cleghorn test) and to discuss the Standardisation and Quality Control of the reagents.

Professor Sherlock and Professor Zuckerman felt strongly that if test reagents were available for a realistically large number of tests using the Dane/Lane/Cleghorn RIA test then application for a Patent and Commercialising gains must be looked into.

Ways of maintaining production of the reagents were considered. One possibility is production by the PHLS at Porton, on a contract basis for the Department.

Dr Flewett was willing to raise this question with the PHLS.

Mr Kennedy undertook to report on obtaining a Patent and Commercialisation of the Test.

It was agreed that a working group would be formed (Chairman Dr Dane) with Dr Lane, Dr Cleghorn, who would be invited to join the main committee and Mr Kennedy, DHSS to examine the details of the RIA test, and report back.

Commercialisation of the Test.

Dr Lane observed that the test is orientated to the interests of the Blood Transfusion Service; he was not in favour of involving the PHLS/Porton. The Blood Products Laboratory can produce a package of any kind and experts can be involved in the Quality Control and Standardisation of the test and reagents.

The working group with Dr Dane, Dr Lane, Dr Cleghorn and Departmental representation (v.s.) will also consider available commercial and the Dane/Lane/Cleghorn RIA tests.

COMPARATIVE STUDY OF A NUMBER OF TESTS FOR HEPATITIS B SURFACE ANTIGEN AND AN EVALUATION OF THE 'HEPANOSTIKA' (MICROELISA) TEST: AGHB(78)P1.4

Dr Flewett spoke to this. The study showed RIA to be more sensitive than ELISA. Professor Zuckerman pointed out that nevertheless ELISA could be the test to introduce because it is possible to test other antigens and antibodies related to blood transfusion with this test system. The stability of reagents, length of shelf life of the test, ease of use, lack of carcinogenicity of reagents, ease of reading, dependance on counters or photometers and their capital cost, will all need evaluation for any test being considered. Mr Kennedy referred to testing by the method of fluoroassay which is a possible test in the future.

Dr Burrell stated that radiation risks have been shown to be practically nil where testing with RIA is done. He will send a supporting paper 'Evaluation of Tests (RIA and ELISA)' by Barr et al to Dr Waiter for circulation to members.

The Chairman put to the vote a decision on acceptance of RIA for all blood transfusion work but members agreed that it was too early to decide this point, and the decision was then deferred.

CORE ANTIBODIES AND THEIR SIGNIFICANCE: REFER TO AGHB(78)01.1 para (2)

Professor Zuckerman raised the question of the need to introduce a test for total core antibody. It is purported by German workers to pick up the "window" which occurs when using other available tests. Members agreed that there is no evidence to support this view.

DR VANDERVELDE TABLED A PAPER ON THE PREVALENCE OF ANTI-HBC (SUBSEQUENTLY NUMBERED AGHB(78)P1.5)

THE SIGNIFICANCE OF ELEVATED TRANSAMINASE LEVELS: REFER TO AGHB(78)P1.1para (3)

It was agreed that the matter required consideration but that too stringent a ruling to exclude donors on the basis of a single raised transaminase, which is a non-specific indicator of liver dysfunction, might lead to the rejection of an unacceptably high number of donors. It was reported that Dr Cleghorn (RTD, Edgware) had been measuring transaminase levels in a series of blood donors. The results would be of interest to this committee. At this time the Advisory Group are opposed to the routine determination of transaminase levels. It was thought advisable to set up a Working Group to study the question raised in AGHB(78)P1.1 on Transaminases in the context of blood transfusion and to co-opt Dr Cleghorn to it. Meanwhile the chairman decided to defer further discussions on this matter to the next meeting when it was anticipated Dr Cleghorn would be present.

NON-A, NON-B HEPATITIS: AGHB(78)P1.1 para (4)

The report of a trial published in the Journal of Hygiene volume 73, pps 173-188 (1974) was referred to. The Advisory Group after discussion, made a strong recommendation to the Department that research in 2 areas be undertaken -

(1) a retrospective study of chronic hepatitis and

(2) a trial on the lines of that described in the Journal of Hygiene

It was felt that this research is appropriate for the MRC and the Department agreed to pass on the committee's recommendations to the office of the Chief Scientist.

THE POSITION OF DONORS WITH A HISTORY OF HEPATITIS: AGHB(78)P1.1(5)

It was agreed to consider whether they should be re-examined with a view to re-admission to the donor panel, when the appropriate section of the Report was being revised.

THE RESPONSIBILITY TO ANTIGEN POSITIVE CARRIERS SEEKING DENTAL TREATMENT

The Department undertook to circulate copies of the Report of the Expert Group on Hepatitis in Dentistry chaired by Sir Robert Williams. It was expected to be available about mid-January.

ANY OTHER BUSINESS:

1. Professor Zuckerman raised the question of Arrangements for the supply of Hepatitis B Immunoglobulin. It was thought that the distribution of immunoglobulin, which is presently through the PHLS, could go through to the Blood Transfusion Service, which also produces it.

Dr Waiter will write to the PHLS about present distribution arrangements. Dr Waiter will also check within the Department what means are available to promulgate advice on the use of anti-hepatitis B immunoglobulin. It was agreed that a sub-group comprising Dr Lane (chairman), Dr Dane and Professor Zuckerman should consider the arrangements for distribution and use of the specific immunoglobulin. Dr Waiter would be associated with this sub-group and it was thought advisable to co-opt a pharmacist onto the group. Dr Cash undertook to let the sub-group have details of the arrangements adopted in scotland.

2. QUALITY CONTROL FOR TESTING METHODS FOR DETECTING ANTI-HBs was discussed. Regional Transfusion Centre, Edgware and Dr Dane's department at the Middlesex Hospital are willing to provide training.. Dr Bradstreet agreed to set up a Working Group on Quality Control. Dr Dane will let Dr Bradstreet have an outline of what he would need in respect of this.

3. Dr Flewett sought the Advisory Group's views on the need of the Blood Transfusion Service for PHLS Reference Laboratory confirmation of positive RIA test results. It was agreed that a second independent opinion is required. It was questioned whether all these Reference Laboratories needed to be under PHLS auspices.

4. REFERENCE STANDARDS:
The following was noted and agreed: WHO is establishing standard reference preparations in terms of nanograms. Steps should be taken to evaluate national standards and attempt to match established National Standards to the International Reference Preparations. This is the responsibility of the National Institute for Biological Standards and Control (NIBSC). Dr Waiter agreed to discuss this with Dr Smith, (Director of NIBSC).
ANTIGEN TESTING OF STAFF: This will be put on the Agenda for the second meeting.

DATE OF NEXT MEETING:
The second meeting will be held on Thursday, 22 February 1979, starting at 14.00 hours. NB: not on 15 February which was agreed at the first meeting. Further details to follow.

Sheila L Waiter)
T E Dutton) Joint Secretaries

January 1979