AG HB(73)N1

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NOTE OF THE FIRST MEETING OF THE RECONVENED ADVISORY GROUP ON TESTING FOR THE PRESENCE OF AUSTRALIA (HEPATITIS ASSOCIATED) ANTIGEN AND ITS ANTIBODY (KNOWN IN THIS REPORT AS HB Ag AND HB Ab) HELD ON 6TH DECEMBER 1973 AT THE DEPARTMENT OF HEALTH AND SOCIAL SECURITY, EUSTON TOWER.

MEMBERS OF THE ADVISORY GROUP

Dr W d'A Maycock (Chairman)
Dr C C Bowley
Dr C M Patricia Bradstreet
Mr C H Collins
Dr Yvonne Cossart
Dr D S Dane
Dr T H Flewett
Dr F O MacCallum
* Professor B P Marmion
* Dr F Stratton
Dr J Wallace
Professor A J Zuckerman

14/823/944

Representing DHSS

Mr D U Jackson
Dr Sheila L Waiter (Secretary)

Representing SHHD

* Dr A E Bell

* Not present

BACKGROUND

Since the first report of the Advisory Group was issued in 1972 much has been learnt about Australia antigen (HB Ag) and its antibody (HB Ab). Information on all aspects of HB Ag has accumulated : more sensitive tests have been developed for the detection of HB Ag and HB Ab and the merits and disadvantages of these tests have been extensively discussed. Attitudes are changing to the significance of the presence of HB Ab without HB Ag. Some of the advice issued in the 1972 report, as anticipated at that time (see paragraph 6 of that report), is now out of date. The need to provide reference preparations for HB Ag and HB Ab is pressing: variations in the incidence of HB Ag and HB Ab reported by different regional transfusion centres where all donations of blood and plasma had been tested for HB Ag since 1972 may be due to differences in techniques of testing, or in potency and specificity of the reagents used, or to a combination of these factors.

It was therefore decided that this is an opportune time to reconvene the Advisory Group which met during 1970-71, and which published in 1972 the revised report "Testing for the presence of Australia (Hepatitis Associated) Antigen and its Antibody" under cover of HM(72)33.

The first meeting of the reconvened Group was held on 6th December 1973. Members were asked to advise the Department on some of the problems which have arisen since it last met, and to undertake the revision of the 1972 report, in the light of this advice.

MEMBERSHIP

The membership of the reconvened Advisory Group comprises the members of the earlier Group under the Chairmanship of Dr Maycock, with the addition of Dr Bradstreet. Apologies were received from Professor Marmion and Dr Stratton, who were unable to attend this meeting.

TERMS OF REFERENCE

The following terms of reference were agreed:

"To reconsider the report issued in 1972, and in particular to advise on the following:

1. The use to be made, in routine testing, of the more sensitive methods of detecting HB Ag and HB Ab.

2. The provision of reference preparations of HB Ag and HB Ab.

3. The position of the HB Ab positive individual."

METHODS OF DETECTING HB Ag AND HB Ab.

There are now many serological methods and reagents available for the detection of HB Ag and HB Ab. These are of varying sensitivity, specificity, simplicity and cost. It is agreed that if the more sensitive screening tests are used by regional transfusion centres (RTCs), an increasing number of HB Ag positive donations will be found. It has also been demonstrated that these low-titre HB Ag positive donations, undetected by the less sensitive method of immuno-electro-osmophoresis (IEOP) which is the routine screening test in RTCs at present, can be icterogenic, or can produce sero-conversion. The Advisory Group agreed that it was desirable to recommend that RTCs should use a more sensitive test than IEOP to test donations routinely for HB Ag and that advice concerning suitable more sensitive techniques should be given.

The Advisory Group considered papers AG HB(73)P1.1 by Dr Dane, AG HB(73)P1.2 by Professor Zuckerman, and AG HB(73)P1.3 by Dr Wallace, who had been invited to put forward their views on the more sensitive methods now available for the detection of HB Ag, and their merits as screening tests for blood donations.

The report of a WHO Scientific Group (1973) states that the method used for the detection of HB Ag in blood donors should be simple, rapid, sensitive and specific. In addition, one could add that the numbers of positives found by any sensitive test and requiring verification should be manageable and the numbers of false-positives should be minimal.

Radioimmunoassay (RIA)

Radioimmunoassay (RIA), typified by the Ausria-125 test supplied in kit form by Abbott Laboratories, is probably as sensitive a method as is currently available, but there are difficulties in its use: it is expensive both for capital equipment (for example, a scintillation counter is necessary) and for reagents; the test is tedious to perform on the large scale and unpopular with technicians; it is dependent upon sophisticated equipment which may be subject to variable performance or to actual breakdown. Although numbers of false positive results are now fewer than when Ausria kits were first introduced, it is generally accepted that significant numbers still need to be submitted for verification tests.

Reversed passive haemagglutination (rHA)

An alternative sensitive method is reversed passive haemagglutination (rHA) using, for example, the Hepanosticon reagent prepared by Organon Laboratories. It is expected that a number of other tests will be developed using a similar technique. There are significant advantages to using rHA: there is little capital outlay and the method could be adopted with minimal disturbance or expense in regional transfusion centres. The test is simpler to perform than IEOP. Results are more rapidly available than by RIA. Reagents are less expensive than RIA reagents and should become considerably cheaper: in addition they are stable over long periods. False screening test positives can occur, but simple verification tests are available.

The Advisory Group concluded that:

1. There is a need for a more sensitive screening test for HB Ag which can be applied to all donations, and which would replace IEOP which is the technique currently used.

2. An rHA method is favoured on grounds of simplicity, sensitivity, and potentially low cost.

3. RIA may eventually be the method of choice as a routine test, but for the present should be used by reference laboratories who would be concerned with verification.

4. Facilities for RIA to which the RTC can have access should be available in each Region. PHLS reference centres could be used, but consideration should also be given to other laboratories.

Further information should be obtained before firm plans can be made. It is desirable to know the probable numbers of tests which will be referred to Reference Centres, and also the future sources of reagents. Supply Division of the DHSS should be asked to obtain information regarding which commercial firms are interested in the production of reagents for RIA and rHA: it was noted that Lepettit have approached one member already and expressed an interest. Others who might be approached include the Radiochemical Centre, Amersham; Burroughs Wellcome; Organon.

Other methods for detection of HB Ag will be kept under review by members of the Advisory Group, for example, micro-RIA and other developments in RIA methods.

THE PROVISION OF REFERENCE PREPARATIONS OF HB Ag AND HB Ab

Since testing for HB Ag of all blood donations was introduced in the UK, a variation in the apparent regional incidence has been noticable. For example, reported incidence in new donors ranged from 1 in 520 to 1 in 3059 during the period October 1972 - April 1973. This variation cannot be explained satisfactorily on variations of population or geography, and therefore it is probably due to differences of sensitivity of reagents, or of techniques used to detect the antigen. At present RTCs collect their own working reagents. They were advised by this group in their 1972 report, but no exact procedures for performing the screening tests were laid down. It was intended at that time to provide a reference serum, but so far it has been possible to provide only a limited service, and only a few RTCs have submitted antigen preparations and antisera for examination.

Dr Bradstreet, referring to her paper AG HB(73)P1.6, expressed the opinion that it is now feasible for the Standards Laboratory to provide a standard reference preparation to RTCs. The recommendations made in this paper were endorsed by the Advisory Group, with the added comment that in all probability rHA would supersede IEOP as the routine screening test for HB Ag in RTCs. A panel of HB Ag of a range of potencies and different sub-types could be supplied at approximately six month intervals to RTCs for use in routine testing and in quality control tests. This supply would depend on the cooperation of the 20 RTCs in the UK who are to be asked to send donations from strong HB Ag positive donors detected by IEOP to the Standards Laboratory. Dr Dane can supply weaker antigens. Samples will also be obtained from the 13 PHLS reference laboratories.

Professor Zuckerman reminded members that there will be an International Standard in due course and that it is desirable to have a UK standard meanwhile.

Dr Bradstreet will continue to examine reagents submitted by RTCs until the intended scheme is underway.

THE POSITION OF THE HB Ab POSITIVE INDIVIDUAL

Papers AG HB(73)P1.4, P1.5, P1.7, P1.8 and P1.9 were discussed.

At present following the advice offered in the 1972 report of this Advisory Group, HB Ag positive donors are excluded from giving blood intended for clinical use. Any donation they may have made should be used only for the preparation of reagents.

Although there has been no definitive statement on the significance of the presence of HB Ab alone in an individual, at present an HB Ab positive donor is treated in a similar way, as it has been demonstrated that further testing by more sensitive methods for HB Ag among HB Ab positive individuals will detect a significant number with HB Ag not detected by less sensitive routine tests, for example, by IEOP.

The Advisory Group is of the opinion that the advice given in Chapter 9 of the 1972 report should now be revised in view of recent developments of more sensitive tests for HB Ag.

HB Ab occurs in about 1 in 700 new donors tested by IEOP; there is no evidence to associate it with post-transfusion hepatitis. There is a firm statement to support this in the WHO Technical Report on Viral Hepatitis No. 512(1973). Not only would the exclusion of HB Ab donors detected by sensitive techniques result in a significant loss of blood donations, but there may also be a diminution in acquired passive immunity among recipients. This protection could be particularly useful to those who require multiple transfusions. There will still be a need to identify HB Ab positive individuals from whom blood can be obtained for production of reagents or specific HB immunoglobulin. Most RTCs have a panel of known high-titre HB Ab positive donors who can be called upon for these purposes.

The Advisory Group therefore recommend:

1. Blood from HB Ab positive donors should not be excluded from clinical use providing that:

   a. there is no history of hepatitis

   b. the blood has been tested for HB Ag by a sensitive method and found to be negative. RIA is recommended as this is a good method for detecting HB Ag in the presence of HB Ab.

2. For the present, screening of all donations for HB Ab should continue in RTCs.

DATE OF NEXT MEETING

The Advisory Group agreed to meet on Thursday 28 February 1974.

Meanwhile officers of DHSS together with the Consultant Adviser for Blood Transfusion will undertake a preliminary revision of the 1972 report in the light of advice given by the Advisory Group at this meeting.

Dr Sheila L Waiter
19 February 1974