MEDICAL RESEARCH COUNCIL

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HAHG. 64/6.

Working Party on Human Anti-Haemophilic Globulin

Minutes of the seventh meeting, held at 20, Park Crescent, London, W. 1. at 2.15 p.m. on Monday, 16th March, 1964.

PRESENT: Professor P.L. Mollison (Chairman), Dr. Rosemary Biggs, Professor G.V.R. Born, Professor J.V. Dacie, Dr. R.M. Hardisty, Dr. R.A. Kekwick, Dr. R.G. Macfarlane, Dr. W. d'A. Maycock, Mr. L. Vallet (Secretary).

Dr. P. Barkhan and Dr. J. McI. Matthews were present by invitation. Dr. M. Gorrill (Headquarters Staff) also attended the meeting.

1. The Chairman informed members that Professor Armitage had indicated his wish to resign as he felt that the clinical trial of human anti-haemophilic globulin had reached a stage where he could no longer usefully contribute.

2. Minutes: The Minutes of the last meeting (HAHG 63/8) were confirmed and signed as a correct record.

3. Matters arising from the Minutes.

The Chairman reported that the proposed analysis of the incidence of post-operative bleeding after treatment with 2 ml/kg. and 4 ml/kg. of human AHG had been abandoned because the data from cases was not adequate.

4. The Clinical Trial.

The report (HAHG 64/1) on the use of human AHG at Oxford was discussed. In most categories a sufficient number of patients had been studied to reach definite conclusions about treatment, but more data were needed on the use of human AHG, followed by fresh plasma, for severely affected adults having extractions of 2 or 3 teeth.

In children, the transfusion of fresh frozen plasma would often be sufficient to control bleeding but the variable AHF content of the plasma was in practice a serious disadvantage. Because some batches of fresh frozen plasma had an AHF level which was very much lower than that of absolutely fresh plasma it was impossible to be sure whether a good

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therapeutic effect would be produced from a given amount. By contrast the AHF content of human AHG was known in advance (for any particular batch) so that its therapeutic effect could be predicted. Human AHG had, of course, other advantages compared with plasma. Thus, cross-matching was unnecessary; the risk of overloading the circulation was virtually eliminated and the transfusion time greatly reduced; in children these advantages could be obtained with the expenditure of relatively small amounts of human AHG.

Dr. Biggs informed the Working Party that a monograph was being prepared, setting out the experience gained at Oxford. Members of the Working Party felt that in order to make the information generally available it was most desirable that a report should also be published in a medical journal; they considered that this should have the Oxford workers as sole authors but that the paper should be described as a report to the Working Party. A statement on the present shortage of materials would have to appear with the paper.

The Chairman thanked Dr. Biggs for preparing her detailed and valuable report.

5. Supplies of Human AHG.

The paper (HAHG 64/2) was discussed. Members agreed that the estimated need of human AHG from 35,000 blood donations a year was about right. While less than one fifth of known haemophiliacs might need treatment for major episodes, the number having minor episodes might exceed two fifths, especially if all paediatric cases were treated, though many could be given fresh frozen plasma.

Of the alternative schemes for preparation, a central laboratory was favoured although it was recognised that continuity of production was less secure when concentrated in one laboratory and that there was much to be said for preparing human AHG at one or possibly two of the proposed major treatment centres. The freezing of plasma after separation from cells was a necessary stage to dissociate the preparation of AHG from the collection of the blood. It was preferable to send frozen plasma to a central laboratory for complete fractionation than to prepare human AHG at regional laboratories and to send "supernatants" which contained solvents. Decentralization to hospital pathology laboratories, the third alternative, was not favoured.

It was believed that ethanol fractionation would give a product similar to that obtained with ether.

It was agreed that a trial should be made using bags of the Fenwal type to collect blood and allow of an aseptic separation of plasma, which would be frozen and sent to the Blood Products Laboratory where it would be thawed, assayed and used for AHG preparation. It was also agreed to recommend to the Council to send the paper HAHG 64/2, together with

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the comments of the meeting, to the Ministry of Health.

6. Treatment Centres.

The position arising from the considerable advance in the treatment of haemophiliacs was discussed. The Chairman pointed out that an anomalous situation had arisen. The M.R.C. Blood Coagulation Research Unit had gained recognition through the country as the centre to which every really grave problem of bleeding in a haemophiliac should be referred. Evidently this situation could not continue indefinitely as although it might be the function of certain M.R.C. units to introduce advances in treatment, it was not their function to remain responsible for applying them. It seemed clear that the National Health Service should now take over the responsibility for the work by making appropriate senior medical appointments and providing beds and necessary laboratory space and facilities.

It was considered that the best arrangement would be to have two centres, one at Oxford for the South of England and one at a place to be decided for the North. The two centres were intended only for the treatment of major episodes in haemophilia such as planned surgical operations or road accidents.

For the treatment of minor episodes small centres in all regions were needed so that patients would not normally have to travel for more than 50 miles. Possibly one or two centres in a hospital region would suffice. A major factor in determining the locality of a centre would be the presence of a haematologist with a declared interest in haemophilia. In establishing the centres some assistance with laboratory facilities and staffing might be necessary.

The establishment of centres could not precede the increase in supplies of human AHG without which they could not operate effectively.

7. Fresh Frozen Plasma.

Dr. Hardisty described the preparation of fresh frozen plasma from blood taken in Fenwal bags. The plasma was transferred aseptically into a second bag which was then frozen in dry ice and acetone and stored in dry ice. When thawed, an average of 95% of AHF activity was recovered. Some plasma was lost because bags cracked while frozen.

8. Hepatitis in Patients infused with Human AHG.

A review of hepatitis survey reports (HAHG 64/4), collected as part of the clinical trial, was given by Dr. Maycock. The summary of patients at the beginning of the paper was amended as follows:

In 4 patients not traced.....5 episodes.

In 63 patients traced.....70 episodes.

Patients in whom jaundice reported..... 2

/One case

One case was of short incubation period, typical of infectious hepatitis, and the second had an exceptionally long incubation. As the HAHG concentrate prepared from plasma pools of up to 30-40 litres in volume apparently carried a risk of transmitting serum hepatitis, it was considered inadvisable, when planning increased production, to increase the plasma pool volume much above this size, unless further observations indicated that the risk was smaller than the present series of cases suggested.

There being no other business, the meeting was adjourned.