

## BLOOD TRANSFUSION RESEARCH COMMITTEE

### Review of activities since 1967

The Council's Blood Transfusion Research Committee was reconstituted in 1967 with the same terms of reference as previously, namely "to advise the Council on matters relating to the research aspects of blood transfusion". The Committee has taken the view that its function has been mainly to advise on problems referred to it although it has occasionally taken the initiative in promoting work, as in the following examples:

(a) Examples of initiatives taken by the Committee:

(1) Encouragement of investigations into the formation of particulate matter in stored blood.

Dr. G. Wright of Keel University was invited to a meeting of the Committee in 1975 to discuss his work on the effects of the formation of particulate matter in blood during storage. The Committee were impressed with the importance of the work and made representations to Council which resulted in the award of a special project grant to Dr. Wright.

(2) Stimulation of the use of frozen red cells in clinical practice.

At a meeting in 1969, after hearing evidence from people working in this country and from Dr. A.W. Krijnen, a specially invited Dutch visitor, the Committee made informal recommendations to the then Ministry of Health and to the Scottish Home and Health Department. As a result special funds were made available for work at one Blood Transfusion Centre in England and at one in Scotland. Following the successful development of the work banks of frozen red cells were set up at many other transfusion centres and the use of red cells recovered from frozen blood was introduced into routine clinical practice.

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(3) Pressure on the DHSS to produce plasma protein fraction.

Just before the Committee was reconstituted, the previous Committee had recommended that small-pool plasma should be replaced by plasma protein fraction. This advice was passed by Council to the DHSS who acted upon it. In retrospect it seems that this too was an important initiative taken by the Committee and that without it the change from plasma to plasma protein fraction might have been considerably delayed.

(4) Dose-trials of anti-D in the suppression of Rh immunization.

In 1967 the Chairman of the Committee represented to Council that there was scope for properly conducted clinical trials in assessing the value of passively-administered anti-Rh in the suppression of Rh immunization. As a result Council agreed to set up a Working Party which, during the following five years, successfully completed the only dose-trial ever conducted or ever likely to be conducted in this field. The Report of the Working Party has had a very substantial influence in other countries and has, for example, recently led to a reduction in the dose used routinely in Australia.

b) Examples of advice which the Committee has given:

- 1) At its first meeting in 1967 / <sup>the Committee</sup> was asked to consider both the possible occurrence of malignant cells in blood from apparently healthy donors and the consequences which would arise from the transfusion of such blood. The Committee prepared a memorandum which Council used in replying to enquiries which had been made.
- 2) The Committee was asked by the Consultant Advisor on Blood Transfusion to the DHSS to consider the use of plasma protein fraction as a replacement fluid in plasma exchange carried out as a therapeutic measure and to discuss the related priorities. At a meeting held in 1976 the problem was discussed with various co-opted physicians

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and appropriate recommendations were made.

c) Working Parties:

The Committee has set up the following Working Parties.

1) Working Party on Cryoprecipitate.

This was established in 1967 with 3 objectives: a) to determine the incidence of hepatitis in haemophiliacs treated with plasma or plasma products;

b) to determine the incidence of Factor VIII-inhibitors; and c) to produce a standard preparation of Factor VIII. In fact, the third objective was the one of the most direct interest to the Committee and the studies initiated by the Cryoprecipitate Working Party have eventually led to general agreement that concentrates of Factor VIII prepared centrally are more satisfactory than cryoprecipitates prepared by individual users;

2) Working Party on Post-Transfusion Hepatitis

This was set up in 1967 to consider the feasibility of carrying out a survey of the incidence of post-transfusion hepatitis, and to arrange for any such survey.

The objects of the survey were:

- 1) To obtain information about the incidence of icteric and anicteric post-transfusion hepatitis.
- 2) To establish the frequency of hepatitis B surface antigen (HBsAg) and the corresponding antibody (anti-HBs) in blood donors and patients, and to try to correlate their presence with transfusion therapy and its complications.
- 3) To determine the frequency of transmission of Epstein-Barr virus (EBV) and cytomegalovirus (CMV) by transfusion and their role in causing post-transfusion liver damage.

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The results of a two-year prospective study of 778 recipients of whole blood in a London hospital were published (J. Hyg., Camb., 1974, 73, 173-188). There had been no significant change in the incidence of icteric hepatitis since an earlier study (Ministry of Health, 1954, Lancet, i, 1328-1329), but the new survey established for the first time the incidence of post-transfusion anicteric hepatitis. This information will be particularly valuable if subsequent studies are made on (a) the effect of screening donations for the presence of HBsAg by modern sensitive methods on the incidence of icteric and anicteric post-transfusion hepatitis and (b) the importance of 'non-B' hepatitis in the United Kingdom.

There was serological evidence of the transmission of CMV or EBV in 42 recipients (5.4 per cent). Nearly all of these infections were symptomless, but the outcome might have been different in recipients exhibiting immunosuppression. The risk of infection with these viruses was greater with fresh blood, but contrary to earlier observations it was shown that infection can be transmitted by blood stored for several days. This aspect of the survey raises an important practical implication for transfusion services which now provide intensive therapy for immunosuppressed patients. Is it advisable to maintain a special panel of donors who are safe in respect of the transmission of CMV and EBV?

Although this Working Party has not met for two or three years, one of its members, Professor A.J. Zuckerman, has recently been pressing for the Working Party to be reconvened to consider the entire problem of virus infections transmitted by the transfusion of blood and blood products. He has pointed out that there are no data from the UK or Europe on the importance of so-called non-A, non-B viruses and that their importance is taken so seriously in the USA that a survey has recently been set up at the cost of some eight million dollars to be spent over a five-year period. It is considered likely that a screening test for non-A, non-B hepatitis will be developed in the USA within the next two years and there may well be pressure on clinicians to use only blood which has been screened. When a test becomes available, it will be difficult to decide on policy in the UK unless the size of the problem is known.

Professor Zuckerman also points out that there is a need to investigate the incidence of Hepatitis B in the offspring of immigrants and other potentially high-risk groups.

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3) Working Party  
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This Working Party was set up in 1973 because increased supplies of Factor IX concentrate had led to sporadic use in patients suffering from liver disease as a rapid reversal of anticoagulant therapy and in infants with coagulation defects. There had been reports from outside the UK that some Factor IX concentrates could be harmful, particularly in patients with liver disease, and it was felt desirable to maintain close supervision over the use of the

The Medical Research Council obtained licences for two clinical trials which began during October - November 1976:

- I. Clinical Trial on Rapid Anticoagulant Reversal with Prothrombin Complex Concentrates vs. Whole Plasma.
- II. Controlled Trial of Factor IX-Prothrombin concentrates for Patients prior to Liver Biopsy.

It was decided to defer action on the question of the treatment of neonatal coagulation defects pending the outcome of a study by Drs. Cash and Turner of Edinburgh on the early detection and correction of haemostatic defects in selected high risk neonates. This study recently concluded that efforts to maintain normal haemostasis in these patients were without demonstrable benefit.

Meetings of the local co-ordinators of the two trials were held in June and October 1977 respectively. The rate of patient entry into both trials was slower than anticipated. Some participants in the trial of concentrates for patients requiring liver biopsy expressed the opinion that a factor VII concentrate was required in addition to a concentrate of factors II, IX and X for satisfactory correction of the prothrombin time ratio in some patients. A meeting of the Working Party is being arranged early in 1978 to decide whether the Committee on Safety of Medicines should be asked to agree to this extension of the scope of the trial.

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4) Working Party on the optimal content of anticomplement in antiglobulin reagents.

This Working Party was set up in 1976 to examine the controversial and extremely important question of which anticomplement components should be present in antiglobulin reagents for clinical use. The setting up of the Working Party at that time was particularly opportune since Dr. Hugh Chaplin of St. Louis, U.S.A., who had done a great deal of work on the subject, was spending a sabbatical year with the Council's Experimental Haematology Unit and he attended the first meeting of the Working Party. The Working Party has already issued a brief preliminary report (BT 77/3).

d) The possible role of the Committee in the future

In the past the Committee has acted in effect as a Research Committee for the National Blood Transfusion Service. That Service is not manned, equipped or housed to conduct research, although individual Centres have overcome these problems and have produced work of very substantial value. Nevertheless, it seems clear that there is a function for a strong scientific committee to look at the problems which arise in blood transfusion and to advise on work to be undertaken. It still seems to be true that Council is the one body which can succeed in bringing together those scientists who are most likely to contribute to their solution. Although such scientists could obviously be invited to join a future Committee set up within the Transfusion Service itself, it is possibly true that they would be less likely to attend such meetings if they were not sponsored by Council.

The majority of the members of the present Committee have come to the conclusion that the Committee has fulfilled an important role in the past and that it should continue in some form under the aegis of Council. If the Committee were to continue it would certainly need to be reconstituted since of the fifteen members appointed in 1967 (and apart from the representatives of the

... of the Services), three have resigned,  
... has died, one has recently retired and at least five more will be retiring  
within the next 2 years.

The Committee would like to suggest that if a new Committee is appointed it  
should report to the Systems Research Board at regular intervals. It is felt  
that in this way the Committee's recommendations could more readily be put into  
effect.