Meeting on the Utilization and Supply of Human Blood and Blood Products

Organized by the World Health Organization and the League of Red Cross Societies Berne, Switzerland, December 9–13, 1975

1. Introduction

The meeting was held at the Central Laboratory of the Transfusion Service of the Swiss Red Cross, Berne. It was attended by 15 participants, 3 observers and members of the World Health Organization (WHO) and League of Red Cross Societies (LRCS) Secretariat. Both the International Society of Blood Transfusion and the Council of Europe were represented (see Annex I).

Prof. A. Hässig was elected Chairman, Dr. A. Kellner and Prof. S. Hollan Vice-Chairmen, and Drs. d'A Maycock, J. Morris and R. Perrault were appointed Rapporteurs. The draft agenda was adopted.

On behalf of the WHO, Dr. F. Lothe explained that the main purpose of the meeting was to discuss how the WHO and the LRCS might implement the resolution of the World Health Assembly on the Utilization and Supply of Human Blood and Blood Products (WHA 28.72), the operative paragraphs of which read as follows:

(1) thanks the Director-General for the actions taken to study the problems related to commercial plasmapheresis in developing countries;

(2) urges Member States (a) to promote the development of national blood services based on voluntary non-remunerated donation of blood; (b) to enact effective legislation governing the operation of blood services and to take other actions necessary to protect and promote the health of blood donors and of recipients of blood and blood products;

(3) requests the Director-General (a) to increase assistance to Member States in the development of national blood services based on voluntary donation, when appropriate in collaboration with the LRCS; (b) to assist in establishing co-operation between countries to secure adequate supply of blood and blood products on voluntary donations; (c) to further study the practice of commercial, plasmapheresis including the health hazards and ethical implications, particularly in developing countries; (d) to take steps to develop good manufacturing practices specifically for blood and blood components in order to protect the health of both donors and recipients, and (e) to report to the World Health Assembly on developments in these matters.

On behalf of the LRCS, Dr. Z. S. Hantchev briefly explained the activities of the LRCS in the area of blood transfusion and stressed the similarity of its aims and those of WHO.

2. Present and Future Needs for Blood and Blood Components

It was considered whether a transfusion service, dependent upon voluntary unpaid donors can provide the means for adequate component therapy and sufficient plasma for the preparation of albumin and coagulation factors, so that plasmapheresis has to be used only to collect plasma with special components (e.g. specific antibodies).

The experience in Switzerland might be used
as an example of what could be achieved. In this country, as in other industrial countries, about 50,000 donations per year per 1 million population are necessary to meet the needs for red cells.

The need for albumin, which is high in Switzerland, is about 28,000 units per 1 million population, each unit containing 10 g of albumin. If 80% of the donations required to meet the demand for erythrocytes are included in a component programme, 85% of these albumin needs could be covered by the plasma thus obtained.

The need for antihaemophilic globulin, mainly provided as a freeze-dried small pool cryoprecipitate, could comfortably be met from a 80% component programme. If a concentrate of this globulin were to be used more extensively for treatment of haemophiliacs (including home treatment), more plasma would be needed and Factor VIII might then displace albumin as the governing factor for the amount of plasma needed.

It has been shown by pilot trials carried out in Berne and in Baden-Württemberg, that the use of this high proportion of red cell concentrates is feasible; even so, such a programme would provide only about 85% of the estimated need for albumin. The deficit could be overcome by the judicious use of plasma substitutes such as gelatin or dextran, preferably the former. At the same time, it would be essential to ensure that albumin is used only when there is a definite medical indication, e.g. to repair a blood volume deficit in specific circumstances, provide transport protein in the presence of severe jaundice in haemolytic disease of newborn, and to treat interstitial pulmonary oedema and certain cases of ileus. Whereas albumin is indicated for the treatment of certain cases of hypoproteinaemia, it should not be used as a nutrient by the intravenous route.

If such a programme is to be developed in another country the national background cannot be ignored, as the availability of trained staff and finance are critical factors.

In Finland, a pilot study is now in progress to determine whether plasmapheresis of voluntary unpaid donors could serve as a supplementary source for meeting the national need for plasma. If the reasons for this procedure are fully explained to them, it seems that they can be recruited without undue difficulty. In the United Kingdom such donors have been obtained without much difficulty but they have been recruited only in small numbers for special purposes, e.g. as donors of specific antibody plasma.

The practice of screening donors to obtain plasma containing certain antibodies has shown that 3% of donors in France have 8 international units per millilitre of tetanus antitoxin and that in certain parts of the United Kingdom 5% of donors have 5 or more units. This might meet the needs for anti-tetanus immunoglobulins. Screening for other antibodies, e.g. anti-vaccinia and anti-varicella is also being undertaken.

Although placenta were a source of immunoglobulin and albumin, their collection and testing for the presence of hepatitis B antigen presents major problems. As a consequence the use of this source appears to be declining. After a long discussion, the following principles were agreed upon:

A non-profit blood transfusion service relying upon unpaid blood donors and collecting enough blood to satisfy the need for erythrocytes can provide sufficient plasma for the preparation of albumin, coagulation factors and immunoglobulin. The consistent use of component therapy, a sound logistic organization and the judicious supplementary use of plasma substitutes and electrolyte solutions are essential for this purpose.

The small deficit of plasma needed for preparing albumin and perhaps Factor VIII concentrate that may be encountered in a components programme, and the collection of certain specific antibody plasma (haemagglutinins or anti-bacterial or antiviral antibodies) are indications for plasmapheresis. Voluntary unpaid donors should be recruited for this.

Specific antibody plasma can be obtained to a significant extent by screening normal blood donations.

The use of human plasma or serum for reference purposes or quality control should whenever possible be replaced by the use of animal sera.

Although generally agreeing with the views expressed above, the observers felt that these ideas, if strictly followed, were not realistic, as voluntary agencies could not provide for the full needs of the world at the present time; whilst irresponsible commercialism is recognized and condemned by the responsible sector of the industry, the world needs the participation of private enterprise be-
cause their products are still very much required today. Finally it was recognized that although it is not feasible to alter the present system from one day to another, it should be, nevertheless, the aim to change it as soon as possible.

3. Physiology of Replacement of Plasma Constituents After Plasmapheresis

4. Health Hazards of Plasma Plasmapheresis


5. Blood Transfusion and Plasmapheresis in Developing Countries

The general situation of blood transfusion and plasmapheresis in developing areas of the world was reviewed.

Blood transfusion services in Latin America have mainly been developed and are run by individual hospitals, private persons, communities and local Red Cross organizations rather than by the national health authorities. Frequently blood is obtained from relatives of the patients and often from paid donors, but the number of voluntary unpaid donors is increasing due to the efforts of National Red Cross Societies and Latin American Associations of Voluntary Donors. Large national blood programmes are only now being developed as an increasing number of nations recognize the need for controlled technical standards, for centralized administration and organization and for laws regulating the utilization and supply of blood and blood products. Component therapy is used in some of the larger centres but fractionation of the plasma is only done in three countries. Commercial plasmapheresis is still performed but the tendency has been for governments to stop such activities except where fractionation plants exist.

In the Maghreb countries, the blood transfusion services are restricted to providing whole blood and no plasmapheresis or fractionation is practised. The services are under the control of the health authorities and exist either as national blood transfusion services or as independent blood transfusion services for individual hospitals. The blood donors are unpaid and their recruitment is difficult for social, religious and cultural reasons. The National Red Crescent Societies assist in the recruitment of donors. Most frequently, blood donors are relatives of the patients.

Anti-A, anti-B and anti-A-B blood group sera are produced, but in insufficient amounts for the needs, and anti-D is only produced in one centre from women immunized through pregnancy.

The transfusion services in the Asian Pacific area are well developed in Japan, Australia, New Zealand and Singapore. Japan has converted to voluntary donations since 1966. Provision of whole blood is now entirely voluntary, whereas the production of plasma fractions is still in commercial hands. Australia has one government-operated fractionation plant.

The requirements of the Pacific Islands are small and simple, and are based on individual hospitals in larger towns. They will not grow quickly.

In other Asian countries there is a wide variation in the standard of services but most need help, particularly in the recruitment of donors, training of staff and provision of equipment. Some services have limited funds and therefore functions only intermittently and without good supervision.

The Australian Red Cross runs regular group training courses under the Colombo Plan for blood bank physicians and technologists and gives individual training on request. An important problem is the fact that the courses are restricted to people speaking English. People with only a knowledge of a local language have an additional difficulty regarding access to scientific literature. A further problem is that professional workers in many countries have private practices in addition to their work in blood banks and so are reluctant to leave home for training as this results in loss of income.

Blood transfusion in the Pacific is now entering a stage of rapid development and will need a considerable and growing amount of help and support over the next decade. After this review there was general agreement that:

(1) National health authorities should have the responsibility of blood transfusion services in all
countries; such services should be completely independent of any control by commercial interest. The participation of National Societies which are members of the LRCS should be encouraged; their role and activities should be determined in consultation with national health authorities. Blood donation would be a suitable priority field for their contribution, starting with donor recruitment.

(2) Although in certain parts of the world it may still be necessary to enlist the co-operation of commercial firms to produce plasma fractions, priority should be given to establishing fractionation plants as part of national transfusion services or on an intercountry basis. In either case they could carry out fractionation for several countries. The establishment of such a plant in a national service acts as an incentive to improve the service because it has control of its plasma and is able to prepare those fractions that are needed.

(3) The particular attention of Governments should be drawn to the importance of transfusion services. This might be done through the inclusion of this subject on the agenda of WHO regional meetings.

(4) It is a moral obligation of the most advanced countries to help others in the field of blood transfusion and thus enable them to resist incentives offered by commercial firms in return for permission to set up plasmapheresis centres and use paid donors.

The optimum form of aid has to be adjusted to individual countries. The general technical training is still the greatest need, but assistance might also be required in the organization of donor panels, management of blood transfusion services and provision of certain equipment and reagents. Prolonged support, even up to ten years or more, might be necessary to ensure a firmly established blood transfusion service.

Finally, there was general agreement that bilateral or multilateral aid be given to assist countries when needed in the establishment or further development of national transfusion services; the decision concerning the form in which the aid is delivered (bilateral or multilateral), is left to the donor nation and the technical co-ordination might be provided by WHO in close co-operation with the LRCS. An outline of a suitable programme is presented in Annex II.

6. Legal and Ethical Problems

The therapeutic use of human blood and its derivatives has become of enormous importance in medicine during the last few years and has given rise to considerable commercial involvement in the collection of human blood and plasma as well as in the production of their derivatives.

This situation, created by the commercialization of human blood, raises ethical and legal problems, besides the health aspects, and has already been discussed by the World Health Assembly and the LRCS.

Rules and legislation are urgently needed in most countries to govern the whole field of utilization and supply of human blood and blood derivatives, and should include good manufacturing practices as strongly recommended by the Twenty-eighth World Health Assembly. Importation and exportation of human blood and its derivatives should be carefully considered in any legislation. WHO has prepared a draft report on Good Manufacturing Practices and this document is now being circulated to experts for their views and comments. It is expected at a later stage that it will be distributed to health authorities to assist them in the preparation of their national legislation.

The collection of blood and the preparation of its components and derivatives should be under the control of medically directed establishments, on a non-profit basis. The voluntary non-remunerated donation of plasma as well as blood was considered to be the only acceptable basis for a sound development in this field.

7. International Co-Operation between National Non-Profit Blood Transfusion Services for the Exchange of Blood and Blood Products

The basis of international exchange of blood and blood products is the avoidance of wastage and therefore any surplus components or derivatives should be sent to where they are needed. An example of this was given where surplus red blood cell concentrates were sent from one country to another; however, such a transfer requires good organization and the risk of transmitting disease should be considered. Countries should aim at
self-sufficiency and should avoid bleeding more than the required amount for their own needs. Their own plasma could be processed abroad when necessary and their derivatives returned.

The movement of blood and blood products across national boundaries would naturally be subject to the approval of health authorities.

8. Future Role of the WHO and the LRCS in the Field of Blood Transfusion

The level of assistance to Member States in the field of blood transfusion depends on the availability of funds and therefore it was suggested that WHO should look for extra-budgetary funds to support the development of such activities. This also applies to the LRCS.

Although standard techniques and practices should be established on a global basis, plans must be drawn separately for each national programme as there are considerable differences in the socio-economic development of Member-States. Therefore, some activities might be established on a regional or intercountry basis, such as the facilities for fractionation and training of personnel. For this purpose regional meetings are strongly recommended.

New transfusion services need to go through various stages of development. A basic whole blood programme must operate before component therapy is introduced.

Plasmapheresis should be restricted to those countries where substantial amounts of component therapy are used.

In brief, the main role of the WHO and LRCS in the field of blood transfusion, is to promote the development of national services and coordinate activities carried out on an international basis. Within the limits of their budget they should also provide advice and technical assistance to Member Countries.

9. Final Recommendations

The participants unanimously adopted the following recommendations:

Recommendation 1. A non-profit national blood transfusion service should rely upon voluntary unpaid donors and relate its activities to the country's need, particularly for erythrocytes. In so doing it could provide most if not all of the plasma needed to prepare albumin, coagulation factors and immunoglobulins. The use of component therapy consistent with the stage of development of the health services in the country, a sound logistic organization and the judicious supplementary use of plasma substitutes and electrolyte solutions are essential.

Plasmapheresis should only be a part of a national blood transfusion programme and used to cover any deficit of plasma needed for the preparation of clinically useful derivatives. As in the case of whole blood donation, only voluntary unpaid donors should be recruited for plasmapheresis. Routine screening of blood for the procurement of specific antibodies should be employed to the greatest possible extent to minimize the need for active immunization of donors. The use of animal plasma and artificial substrates should be encouraged whenever possible for the preparation of reference materials and quality control and other diagnostic reagents.

Recommendation 2. Because the plasma protein which is most slowly regenerated after plasma withdrawal appears to be albumin, the interval between plasmapheresis should be long enough to allow the total body content of albumin to return to normal well before the next donation. The donation of plasma by a healthy individual should therefore not exceed 600 ml on each occasion with a maximum of 15 litres per annum. The interval between two consecutive plasmaphereses should in general not be less than 2 weeks.

Recommendation 3. As the long-term effects of repeated plasmapheresis and hyperimmunization on the health of the donor are not well known, both retrospective and prospective controlled studies should be undertaken to identify and evaluate the health hazards that may be inherent in these procedures, and to serve as a basis for future regulations and operating practices. Plasmapheresis should not be performed if there is any reason to suspect that latent disease or malnutrition might be present.
Recommendation 4. International aid programmes should be established to assist countries to set up or improve national blood transfusion services; this aid might be given through WHO in collaboration with the LRCS at least coordinated by these organizations. Suitable guidelines concerning such assistance are contained in Annex II.

Recommendation 5. National blood services which have a surplus of blood, blood components or derivatives should be encouraged to offer them on a non-profit basis to other national non-profit voluntary blood services in need of them with due recognition of the possible hazards which may be involved.

Recommendation 6. National health authorities should have the responsibility of blood transfusion services in all countries. The participation of National Societies which are members of the LRCS should be encouraged; their role and activities should be determined in consultation with national health authorities.

Recommendation 7. Effective legislation should be enacted in all countries regulating blood donation (including the collection of plasma by plasmapheresis), processing, distribution, export and import of blood and blood products. Such legislation should take into account the medical and ethical problems involved, and protect donors and recipients against commercial exploitation.

Annex I

List of Participants: Prof. A. André; Dr. J. Asvall; Prof. M. Benabadi; Prof. P. Cazal; Dr. C. Ehrieh; Prof. A. Hässig (Chairman); Prof. S. Hollan (Vice-Chairman); Dr. A. Kellner (Vice-Chairman); Prof. J. J. van Loghem; Prof. P. Lundgaard-Hansen; Dr. W. d’A Maycock (Rapporteur); Dr. J. P. Morris (Rapporteur); Prof. H. Nevanlinna; Dr. R. Perrault (Rapporteur); Prof. F. Weilbauer.

Observers. Dr. J. Ashworth; Prof. W. Hennesen; Dr. H. Zaugg.

Secretariat. Dr. L. Greenberg; Dr. Z. Hantchev; Dr. F. Lothe.

Annex II

Development of a National Blood Transfusion Service in a Developing Country and the Organization of a Training Course in that Field

General Proposals for a Project

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Objectives of the Project

It is the intention in the first year of this project to assist the development or improvement of a national blood transfusion service based on voluntary unpaid donations of blood. Following upon such an improvement of the service, it is intended in the second year to run a training course to improve the knowledge of senior staff of countries in the area in the organization, administration and operation of a blood transfusion service. It is visualized that this project will form part of a future WHO programme in the development of blood transfusion services.

Action Proposed

In order to achieve these objectives, assistance will be needed to improve the work already being done and to introduce new methodologies where needed. Provision of a moderate amount of equipment and reagents will be necessary and it is possible that certain internal modification in the blood transfusion centre may be required.

The target country of this project would have to be decided through consultations between the donor country, WHO, LRCS and prospective recipient countries.

Personnel

One consultant, who will make a preliminary visit of 2 weeks (this consultant who will be accompanied by a WHO staff member will make the final selection of the country for this assistance as well as assess the local needs during these 2 weeks), will later be required for approximately 2 months to help staff of the selected blood transfusion service to improve the performance in basic aspects of their work. Such assistance would include the handling and storage of blood, grouping and cross-matching, preparation of giving and
taking sets, anti-coagulant solutions, grouping sera and other reagents, cleaning and sterilization of bottles, recruitment of donors and organization of bleeding sessions, as well as all administrative matters involved.

In order to help with the implementation of the recommendations of the consultant, a medical or technical officer experienced in the field of blood transfusion would be needed for a longer period, for example, 6–12 months. It is envisaged that the consultant and medical or technical officer will be supplied by the donor nation whenever possible.

Equipment and Reagents

It is expected that some equipment will already be available. However, there may be inadequate facilities for refrigeration, centrifugation, and deionization and distillation of water that would have to be supplemented, as well as minor equipment such as bottles, tubes, needles and syringes. The reagents that might be needed would include blood grouping sera, bovine albumin and anti-human globulin. It is likely that certain internal structural alterations will have to be made in the premises of the blood transfusion service such as the provision of extra benches, electric points, taps and wash basins in view of the extra workload and to improve the facilities for training.

Training Course

In the second year of the project, it is proposed to run in the improved blood transfusion centre, a 6-week training course in basic essentials for the organization and operation of a blood transfusion service for 15 participants from countries with a similar social and environmental background. One consultant for 2 months and one for 1 month would be needed as well as extra equipment and reagents, allowances and travel costs for the participants and allowances for national teaching staff.