THE COLLECTION, FRACTIONATION, QUALITY CONTROL, AND USES OF BLOOD AND BLOOD PRODUCTS

World Health Organization
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The World Health Organization is a specialized agency of the United Nations with primary responsibility for international health matters and public health. Through this organization, which was created in 1948, the health professions of more than 150 countries exchange their knowledge and experience with the aim of making possible the attainment by all citizens of the world by the year 2000 of a level of health that will permit them to lead a socially and economically productive life.

By means of direct technical cooperation with its Member States, and by stimulating such cooperation among them, WHO promotes the development of comprehensive health services, the prevention and control of diseases, the improvement of environmental conditions, the development of health manpower, the coordination and development of biomedical and health services research, and the planning and implementation of health programmes.

These broad fields of endeavour encompass a wide variety of activities, such as developing systems of primary health care that reach the whole population of Member countries; promoting the health of mothers and children; combating malnutrition; controlling malaria and other communicable diseases including tuberculosis and leprosy; having achieved the eradication of smallpox, promoting mass immunization campaigns against a number of other preventable diseases; improving mental health; providing safe water supplies; and training health personnel of all categories.

Progress towards better health throughout the world also demands international cooperation in such matters as establishing international standards for biological substances, pesticides and pharmaceuticals; formulating environmental health criteria; recommending international nonproprietary names for drugs; administering the International Health Regulations; revising the International Classification of Diseases, Injuries, and Causes of Death; and collecting and disseminating health statistical information.

Further information on many aspects of WHO's work is presented in the Organization's publications.

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THE COLLECTION, FRACTIONATION, QUALITY CONTROL, AND USES OF BLOOD AND BLOOD PRODUCTS

RESOLUTION WHA28.72, ADOPTED BY THE TWENTY-EIGHTH WORLD HEALTH ASSEMBLY, MAY 1975

Utilization and Supply of Human Blood Products

The Twenty-eighth World Health Assembly,

Conscious of the increasing use of blood and blood products;

Having considered the information provided by the Director-General on the utilization and supply of human blood and blood products;

Bearing in mind resolution XVIII of the XXII International Conference of the Red Cross;

Noting the extensive and increasing activities of private firms in trying to establish commercial blood collection and plasmapheresis projects in developing countries;

Expressing serious concern that such activities may interfere with efforts to establish efficient national blood transfusion services based on voluntary non-remunerated donations;

Being aware of the higher risk of transmitting diseases when blood products have been obtained from paid rather than from voluntary donors, and of the harmful consequences to the health of donors of too frequent blood donations (one of the causes being remuneration),

1. THANKS the Director-General for the actions taken to study the problems related to commercial plasmapheresis in developing countries;

2. URGES Member States:

   (1) to promote the development of national blood services based on voluntary nonremunerated donation of blood;

   (2) 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:

   (1) to increase assistance to Member States in the development of national blood services based on voluntary donations, when appropriate in collaboration with the League of Red Cross Societies;

   (2) to assist in establishing cooperation between countries to secure adequate supply of blood products based on voluntary donations;

   (3) to further study the practice of commercial plasmapheresis including the health hazards and ethical implications, particularly in developing countries;

   (4) 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

   (5) to report to the World Health Assembly on developments in these matters.

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INDICATIONS AND CONTRAINDICATIONS FOR THE USE OF NORMAL AND SPECIFIC IMMUNOGLOBULINS

Preface

In 1975, the Twenty-eighth World Health Assembly adopted an important resolution (resolution WHA28.72) on the utilization and supply of human blood products that is reproduced at the front of this book. In it the Director-General was requested, inter alia:

— *to further study the practice of commercial plasmapheresis including the health hazards and ethical implications, particularly in developing countries, and*
— *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.*

In the implementation of these requests, the Requirements for the Collection, Processing and Quality Control of Human Blood and Blood Products were formulated and published in 1978. (For the convenience of the reader, these requirements are reproduced in Annex 1.) A number of problems were identified by the WHO Expert Committee that considered those requirements, and it became evident that more detailed advice on some procedures in the collection and use of plasma and plasma fractions would be useful, particularly to health authorities contemplating the collection of blood and blood component therapy on a national scale. Accordingly, four further groups of experts (see Annex 2) met in Geneva to formulate more specific advice on:

1. *plasmapheresis and the immunization of donors;*
2. *the indications and contraindications for the use of albumin solutions;*
3. *the indications and contraindications for the use of coagulation factor concentrates; and*
4. *the indications and contraindications for the use of normal and specific immunoglobulins.*

Their recommendations and the requirements mentioned above have been assembled in order that all the relevant material should be available in a single volume.

Plasmapheresis and the immunization of donors

Introduction

Plasmapheresis in human beings is an ethical and medically safe procedure, provided that adequate measures are taken to protect the health of donors. There are valid medical needs for plasma derivatives that may be met by plasma collected in this way, it being understood that no operation should take place without the knowledge of the government, which is responsible for the health of the nation.

For example, human immunoglobulins are more effective than animal immunoglobulins; the former remain in the circulation longer and do not carry the risk of hypersensitization to animal proteins. It is for the national health authority to decide on the type and source of immunoglobulins used in its health care services — i.e., whether animals should be immunized to provide hyperimmune globulins for human use, whether normal blood from donors should be fractionated, or whether donors should be immunized to provide human immunoglobulins. In any case, laboratory services are needed for the selection of source materials and quality control of the final product.

Plasmapheresis has been practised for many years, and there is no evidence from the developed countries that it poses unacceptable health hazards when carried out correctly (see Annex 1). However, each country must decide how plasmapheresis may be carried out, having regard to the health of the donor, the frequency of the procedure, the volume of plasma removed, and national demand for plasma derivatives. The guidelines given below may prove useful to countries wishing to establish plasmapheresis programmes.

It is important that all centres and procedures involved in plasmapheresis should be registered by the national health authority. The health of donors should be protected and the safety and quality of plasma and plasma derivatives should be ensured.

The immunization of donors for the provision of specific immunoglobulins calls for special attention. Only vaccines that comply with the appropriate WHO requirements for the production and control of vaccines or experimental vaccines approved by the appropriate authority should be used. Where erythrocytes or other immunogens such as blood group substances are used, additional conditions need to be taken into consideration.[1]

These guidelines record present knowledge on the immediate and long-term effects of plasmapheresis and hyperimmunization. In some countries, more information is needed on safeguards for the conduct of plasmapheresis. This information will help countries to decide whether or not to establish their own blood services.

Plasmapheresis

1. Definition

Plasmapheresis is a procedure by which whole blood is withdrawn from a donor, prevented from coagulating immediately upon withdrawal, and separated into its components by either continuous or discontinuous methods. As part of the procedure, the separated erythrocytes are returned to the donors by intravenous infusion. Each plasmapheresis procedure must be carefully supervised by a physician, and no donor may be subjected to such a procedure unless he has been previously informed in detail about the possible hazards involved and his consent in writing has been obtained prior to donation.

The frequency and volume of the plasma withdrawn from a donor in a given period will determine the number, types, and frequency of examinations that must be performed on that donor.

Plasma obtained by plasmapheresis may be used either for transfusion or for the manufacture of therapeutic, prophylactic, or diagnostic substances.

2. Donations by plasmapheresis

Plasmapheresis may be performed at three levels of intensity.

At the *first level*, a donor participates in a plasmapheresis programme once or twice a year.

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[1] WHO Technical Report Series, No. 468, 1971.

At the *second level*, a donor participates in a plasmapheresis programme in which the quantity of plasma and the frequency of sessions are planned in such a way as to allow both the serum levels and the synthesis rates of the serum proteins to return to normal before any subsequent collection.

The *third level* of plasmapheresis, as permitted by some countries, allows the removal of 1000–1200 ml of plasma per week and 50–60 litres per year from each donor. Several studies in donors subjected to this plasmapheresis schedule have revealed that, although their plasma protein levels change from the initial values, they may remain within accepted normal ranges. However, physiological studies have indicated that, under these conditions of plasmapheresis, the rates of plasma protein synthesis may not have returned to normal before any subsequent collection.

In the USA, studies in small groups of healthy, well-nourished donors undergoing third-level plasmapheresis have shown no overt clinical diseases. However, caution should be exercised in extrapolating these clinical findings to other donor populations, which may have a different health status.

Epidemiological studies as well as studies of serum constituents such as lipoproteins and antithrombin III are needed to characterize further the safety of third-level plasmapheresis.

3. Effects of plasmapheresis on plasma constituents

Albumin

Normally the synthesis of albumin balances catabolism, which is at the rate of 0.2 g per kg of body weight per day, i.e., about 10% of the intravascular albumin per day. A maximal threefold increase of synthesis may occur, but a more usual rate following a 20-g albumin (500-ml plasma) donation is 0.3 g/kg/day. Thus a 500-ml plasma donation requires 3 days for the replacement of the protein by synthesis and, in the event of weekly donations of 1000 ml of plasma, synthesis required for replacement approaches the maximum rate for albumin. Such synthesis rates are dependent on an adequate dietary intake of protein.

Long-term studies of donations at the rate of 1 litre of plasma per week invariably show a fall in serum albumin from initial values, but levels usually remain within the accepted normal range. Normal serum albumin levels may conceal a depleted total albumin pool. Since this albumin pool is responsible for intravascular replenishment, problems of hypovolaemia may occur between 6 hours and 2 days after plasma donation. This is unusual, however, if the serum albumin level is normal at the beginning of plasmapheresis.