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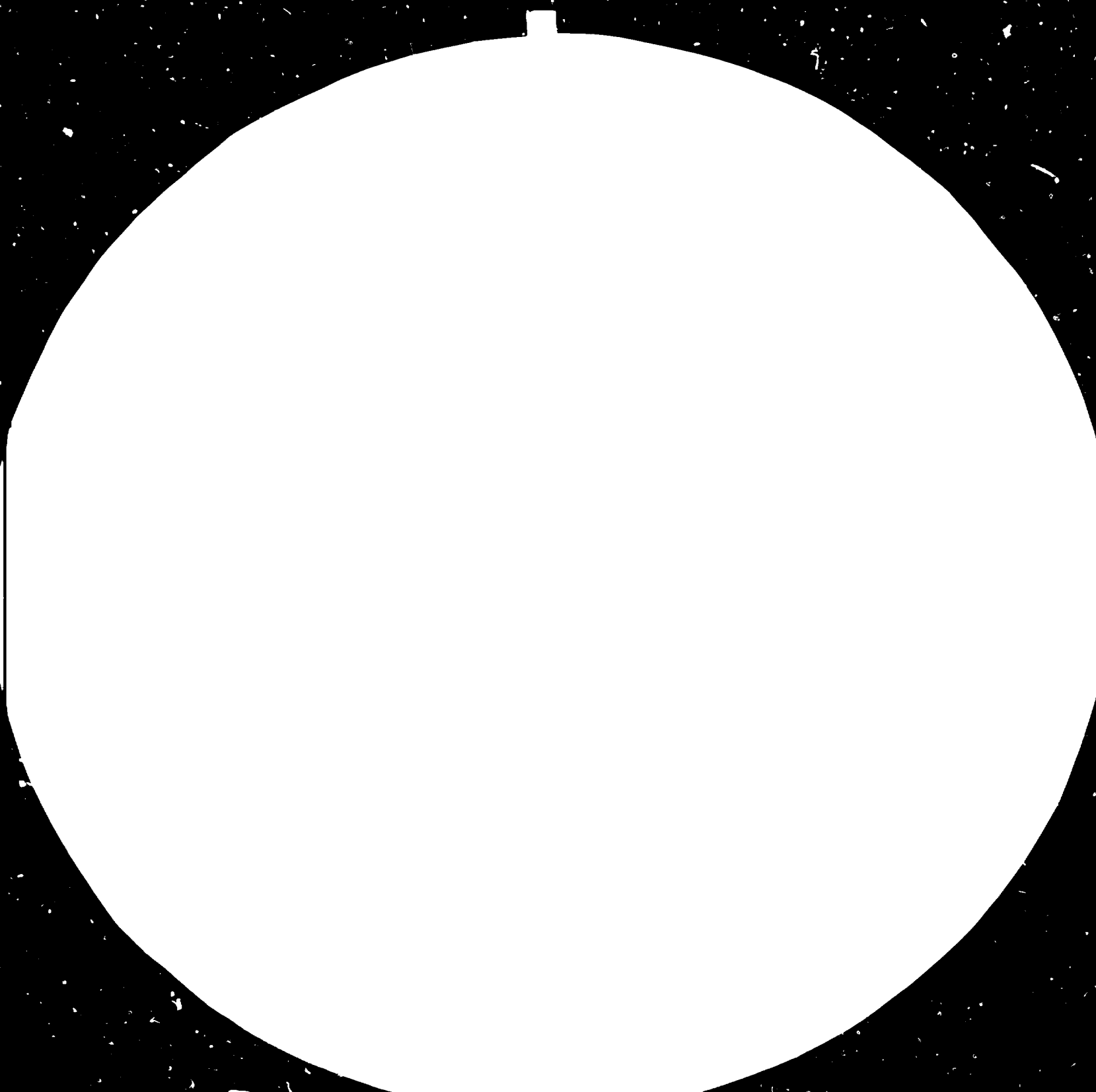

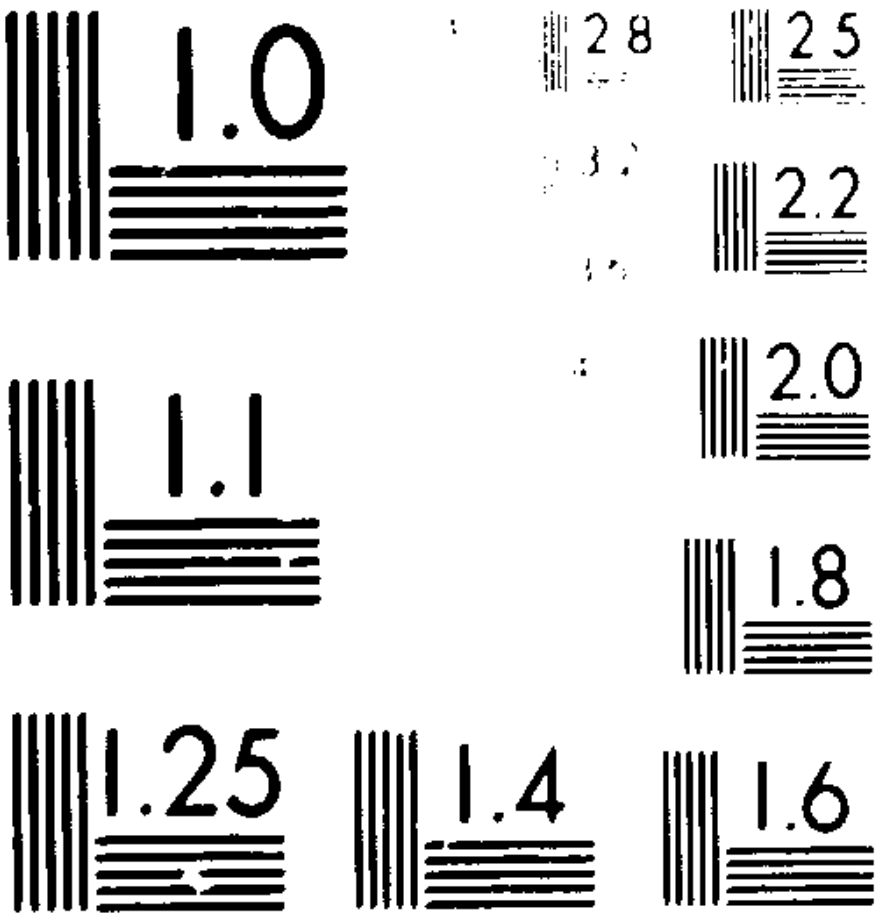

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UNITED NATIONS
INDUSTRIAL DEVELOPMENT ORGANIZATION

Seminar on National Self-Reliance
in Blood and Blood Fractions for
Developing Countries

Stockholm, Sweden, 27 September - 1 October 1982

REPORT * (Seminar on
blood and blood fractions).

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INTRODUCTION

The utilization of blood components in recent years has enabled the clinicians to treat patients with the specific component which they lacked. This also facilitated the most economic use of blood so that a single donation can be used to treat patients suffering from a variety of conditions. The component therapy also yields excess blood plasma which can be fractionated into still more therapeutic prophylactic, diagnostic and quality control material. Blood and blood fractions, therefore, form essential components in the health care programme of any country. In the absence of blood products, obstructed labour and post partum haemorrage are likely to be fatal and people with severe haemophilia rarely live more than three years. There is a constant need for human albumin in revival, nephrology and treatment of toxic syndromes. Most of the developing countries, however, depend entirely on imports of these essential products.

With few exceptions, blood and blood products are produced only in the developed countries. Some awareness of the importance of Blood Banks has been created, primarily through the promotion by the Red Cross and WHO. But this has not progressed much beyond this. Consequently, the developing countries are not able to meet even a fraction of the demand for blood and blood fractions. This can be guaged from the fact that the average consumption of albumin in some developing countries in North Africa is about 9 kg. per one million inhabitants as compared to a corresponding figure of 203 kg. in Europe and 296 kg. in the U.S.A. It is also a fact that the supplies of blood and blood fractions available to the developing countries are not adequate to cope with the needs of even 40 percent of the population of cities and the situation in the rural areas is even worse.

Thus most of the developing countries have been depending on imports of blood and blood fractions. The cost of the imported product is often beyond the reach of many in these countries. Such imports would also mean the depletion of scarce foreign exchange resources available to them. Of late the governments of developed countries tended to limit the production of these items to the resources available in their respective countries and restrict the importation of blood for further processing. These measures, no doubt prevent the depletion of scarce resources of blood from developing countries. However they will adversely affect the availability of blood and blood fractions on the international market and boost their prices due to limited availability. In view of this, a local supply, even a limited one produced by 'Technology' suitable to their environment could be of great value to the poor in these countries. Blood products are among the WHO model list of essential drugs. These are also included in the 26 essential drugs selected by UNIDO out of the WHO list for the purpose of production in the developing countries.

In the light of above, it is important that governments of developing countries give due consideration to the production of these items since the raw material is available in these countries. In this connection the developing countries should be acquainted with the most appropriate methods available for blood collection, processing, storage, and usage of the products in order to secure the availability of these essential products for their people. The collection and fractionation of blood requires organizational and technological skills. The technology for the processing of blood into blood fractions is rather sophisticated and is available mainly in a few developed countries.

The Lima Declaration and Plan of Action for Economic Co-operation and Development calls for the share of developing countries in total world industrial production to increase to at least 25 per - cent by the year 2000. From the foregoing it is obvious that there exists a very wide gap between the present level of production capability relating to blood and blood derivatives in the develop - ing countries and the target envisaged by the Lima Declaration. In view of this UNIDO and the Committee for International Co-operation on Pharmaceuticals of the Swedish Ministry of Health and Social Affairs have organized the above Seminar on blood and blood derivatives with a view to acquaint the representatives of developing countries with the various facets of this industry. More specifically UNIDO is endeavouring to assist developing countries in this special industry by providing information through consultations and technical co - operation amongst developing countries.

ORGANIZATION OF THE MEETING

The Seminar, which was held in Stockholm, Sweden from September 27 to 1 October 1982, was inaugurated by Her Majesty, the Queen of Sweden. Mr. Aman, President of the Swedish State Company Group, welcomed the delegates and requested Her Majesty the Queen of Sweden to inaugurate the Seminar. The Queen of Sweden while inaugurating the Seminar expressed her concern regarding the non-availability of these important products in developing countries and wished the Seminar every success. Ms. Karin Söder, Minister of Social Affairs, welcomed the participants and highlighted the importance of blood and blood fractions in health care programmes. Dr. A. Tcheknavorian, Chief of Pharmaceutical Industries Unit - UNIDO, conveyed the greetings of the Executive Director of UNIDO to the gathering and briefly out - lined the mandate of UNIDO and the importance of the Seminar in this

context. She expressed her gratitude to the Swedish Government and the Swedish Pharmaceutical Industry for their co-operation with UNIDO which was beneficial to the developing countries. She hoped that the Seminar would lead to formulation of a plan of action involving the combined efforts of the Governments of developing countries, United Nations and industries for the benefit of developing countries. Dr. B. Sankaran, Director WHO, while conveying the greetings of the Director General WHO spoke of the generous contribution from the Swedish Government and SIDA to the WHO programmes in health care.

ADOPTION OF THE AGENDA

The agenda was adopted without any changes being made. In general, it was agreed that the length of the presentation of papers and the duration of the ensuing discussions be kept flexible according to the interest shown.

PRECIS OF THE SEMINAR

Eighteen international experts presented papers covering various facts of blood and blood fractions ranging from collection, storage and fractionation to usage. After the presentation of papers, detailed discussions ensued. The summaries of papers are given below together with some important comments which are relevant to the subject and which supplement the papers.

I A COUNTRY-WIDE WHOLE BLOOD TRANSFUSION

(a) National Organizations

H. Nevanlinna

The main issue discussed in the organization of the national blood transfusion services was the advantages of centralization versus decentralization.

The second issue was that of partial or complete blood and national blood transfusion services. This latter issue referred mainly to the inclusion or not of fractionation as part of the total services.

Other points of significance referred were : general constraints affected the decision on centralization versus de - centralization. The second point was the statement that any established format was not likely to be changed once in place.

One of the advantages of centralization is rapidity of decision making and better co-ordination of research. In the end the tax payers of each country are responsible for the total expenditure.

At the request of Dr. A. Tcheknavorian of UNIDO, it was felt to be important to gather data on the blood banking services of participating countries. In support of this, the Chairman suggested that a questionnaire be designed immediately for participating countries to assist in assessing the state of blood banks and needs in various countries.

Dr. Peretz of IFPMA stated that no country to his knowledge was depending on voluntary services and that industry had a clear role. Similarly no country was totally dependent on private enterprise in this field.

Dr. Högman stated that decentralization of services could work well for certain aspects of blood transfusion but de - centralized services might work better when it came to plasma fractionation, provided that there was a central will in given countries to unite efforts in that direction.

The Singapore representative stated that her country was attempting self-sufficiency in whole blood but foresaw difficulty in producing sufficient plasma.

Professor Nevanlinna then commented that the basic steps should always be the procurement of sufficient blood supported by sufficient safety measures for donors and patients and then if adequate financial resources were left, the final step to plasma self-sufficiency should be taken.

(b) Recruitment and Selection of Blood Donors

B. Gullbring

The recruitment of blood donors worldwide and particularly in developing countries often comes in circumstances of increasing debts and different levels of malnutrition and illiteracy. This sets the stage for various constraints in donor recruitment. Therefore, it is important to have a good analysis of the social situation to under - stand the global aspects of blood donor recruitment where there is a long tradition of paid donors, this is sometimes difficult to change.

(c) Organization and Operation of Blood Banks

C. G. Lopez

A clear impression was gained that Malaysia has achieved its goal to develop a strong national blood transfusion services. Many steps were taken such as the definition of objectives, the structuring of donor recruitment and the standardization of techniques and paper work in all the blood banks in the country. Difficulties were commonly encountered with equipment maintenance due to poor servicing by large companies. The developments made by the Malaysian services in the past 15 years were reviewed, the most notable of which were :

a) Remarkable improvement in haemophilia care.

b) Extensive red cell antibody investigation facilities.

c) The joint operation of Blood Transfusion and hematology services in a number of areas.

d) Careful study of incidence of Hepatitis B in blood donors and hemodialysis patients.

In general discussions, Mr. Curling, raised the issue of whether self-sufficiency and self-reliance should be applied to blood and blood products alone or should it include plasma and plasma products as well. In the discussion that followed it was felt that self-sufficiency should be applied to both. In support of this view Professor Nevanlinna stated that the integration of plasma fractionation inside national blood transfusion services provided valuable technical feedback which might not occur otherwise.

With regards to the paper presented by Dr. Lopez, Dr. Hollan wanted to know why such a high priority was given to the treatment of haemophilia in Malaysia. She was particularly concerned about this in a country where the incidences of hepatitis was already

high. Dr. Lopez replied that the treatment was straightforward and it yielded faster results than with some complex diseases such as thalassemia.

In further discussion, Dr. B.K. Verma, stated India's three main goals :

1. The motivation of blood donors
2. Collection and testing of blood
3. Blood group research and plasma fractionation

On the issue of plasma fractionation in smaller countries, both Dr. Hollan and Dr. Nevanlinna suggested this approach, although in itself it might prove not to be economic. On the other hand the advantages of such a technique have other benefits that could be developed by a country seeking self-sufficiency.

II PREPARATIONS FOR HEMOTHERAPY

Dr. B. Sankaran, WHO, chairing the morning session gave an overview of health care in developing countries and emphasized that so far the production of blood and blood components for therapeutical use had not received first priority among health services in most countries. However, when the standard and degree of complexity of medical care increased, the need of such products became obvious and stressed the importance of making attempts to get further development in the field.

(a) Whole Blood and Blood Components

C. Högman

The importance of sufficient aseptic techniques and sterile equipments, were emphasized since blood was a good substrate for microorganisms and contamination might lead to serious or fatal complications for the recipients of the products. Blood which is anticoagulated with acid citrate-glucose solutions is a useful product in itself but also forms the source material for other products. It was emphasized that a well functioning organization producing whole blood should be the first step providing products for hemotherapy, followed by blood component production. Of the blood components red cells and plasma should be given first priority, other cell products and some plasma products, such as cryoprecipitate, may be following more or less closely in the time tale. Since the use of collapsible plastic bags makes the preparation of blood components much easier and safer than the use of glass bottles, some emphasis should be put on the proper supply with appropriate anticoagulant / preservation container systems. Some new developments concerning technology and composition of anticoagulant/preservative solutions were described in the lecture and at the practical demonstrations. The need of red cell products may be covered by about 50,000 blood donation per million inhabitants per year but this may not be sufficient to cover the need of coagulation factors.

(b) Coagulation Factors

R. Perrault

The need of coagulation factor preparations for the treatment of congenital and acquired deficiencies was reviewed. The definition of requirements, the procurement policies, and the socio-economic

aspects of both the requirements and the production policies were reviewed. In many industrially developed countries special emphasis has been given to the proper treatment of hemophilia A. Quoting a recent conference arranged by the International Society of Blood Transfusion (Budapest 1982) Dr. Perrault concluded that 10,000 IU of Factor VIII per patient per year was not enough and that more than 60,000 IU per patient per year was virtually impossible to produce with current technology. For reasonably effective therapy at least 20,000 - 30,000 IU should be achieved. Since Factor VIII is easily decomposed during storage and handling, care must be taken to get a sufficient yield out of the source plasma. Less than 200 IU per liter of starting material was considered unsatisfactory by the quoted conference. Further it was emphasized that 400 - 500 IU can be achieved with good techniques of producing cryoprecipitate which is a Factor VIII preparation relatively simple to produce by a well equipped blood center. In many countries the need of albumin is well covered within the volume of plasma needed for coagulation factors. Several questions concerning the most appropriate ways of meeting the requirements was discussed, notably either by overcollection and discarding the red cells or by plasmapheresis, if unsufficient plasma was made available within the frame of a blood component programme.

(c) Electrolyte Solutions and Plasma Substitutes

T. Mellstrand

The patho-physiology of body fluids and the need of replacement fluids useful for intravenous therapy were reviewed. Also the possibility of replacing the water-maintaining function of the circulating blood with plasma substitutes, such as dextran

solutions, was reviewed. Such solutions have different capacity in the mentioned respects, the dextran solutions being among the most efficient. However, all plasma substitutes may have more or less serious side effects. The new possibility of avoiding most of the anaphylactoid reactions by using a very low molecular weight ("hapten") dextran was mentioned. The great importance of a programme to supply a country with solutions for intravenous use was emphasized. However, the production of parenteral products is complicated and includes a number of steps which demands high professional skill and sophisticated equipment. The solutes, such as glucose, sodium chloride, dextran etc., must meet with very high standards concerning chemical and microbiological purity. The final laboratory control of the products includes identification and quantitative analysis of the content, microbiological test for sterility, pyrogen testing etc. The materials of the containers, stoppers etc. are also a matter of concern.

From the discussion that followed the introductory presentations it was apparent that the stage of development of blood transfusion services and plasma fractionation varied considerably among the participating countries, some of them having efficient blood programmes in rapid evolution. Sharing views and ideas will hopefully be of value to the participants in their attempts at improving the hemotherapy programmes in their respective countries.

The afternoon session was devoted to a visit to Upsala, where demonstrations and discussions at the blood bank of the University Hospital and Fortia - Pharmacia took place. Some details of organization, blood donation, blood component preparation, plasmapheresis and the use of the products were demonstrated to the participants.

III The Use of Human Blood and Blood Substitutes

As regards clinical application of transfusion therapy, the lectures and discussions covered anaemia (red cell concentrates), shock (plasma, albumen and plasma substitutes), bleeding disorders (Factor VIII and IX concentrates) and infection (immunoglobulins). Special attention was paid to the misuse of blood and its compouents.

(a) Blood and Blood Components in Treatment of Anaemia

J. Waldenström

A revue of different forms of anaemia where iron deficiency was the most common etiological factor at least in the developed countries was made. As the anaemia can be effectively treated with iron administration, there is seldom reason to administer blood. On the contrary, uncritical use of blood can cause sever overloading complications. The same holds true with other deficiency anaemias. In far advanced cases blood, which always should be given as red cell concentrates, might be used if the patient is bleeding, pregnant near the term, is in need of major surgery or suffers from a severe infection.

(b) Blood and Blood Components in Treatment of Shock and Surgical Bleeding

L. Thorén

The haemodynamics of bleeding shock was described in detail and a therapeutical scheme was based on losses caused by perspiration, exudation of plasma to wounds or burn injuries and bleeding. Much blood can be saved by allowing the haematocrit to fall around 30% and by using crystalloid solutions, plasma

substitutes instead of whole blood. In profuse bleedings whole blood transfusion still has a position although modern - and expensive - technology can cover the patients needs with platelet concentrates and fresh frozen plasma.

(c) Use and Abuse of Blood and Blood Components with Special Reference to Complications

S. Hollán

Different means to achieve optimal use of blood were outlined. The importance to use other fluids than those of human origin, crystalloids and plasma substitutes was stressed. Different hazards of transfusion which are depending on the effectiveness of blood bank technology and the geographical location were described at length. A revue of the prospects to use "artificial blood", haemoglobin solution or fluoro carbons was also given. At the present time they have not reached a stage of practical application in the clinical work.

(d) Plasma and Plasma Derivatives in Treatment of Coagulation Disorders

I-M Nilsson

The present situation of the treatment of Swedish haemophiliacs and von Willebrand patients was described. In order to reach a sufficient level of the deficient coagulation factor, different concentrates must be used. Sweden was the first country to introduce such a concentrate, namely the factor 0-1 Blombäck and Blömback. The selection of an appropriate concentrate is mainly a question of economics specially if it can be used in home therapy. The good results reached in Sweden depended on concentration of the patients in two

centers (Stockholm and Malmö), minute follow-up and the application of home or prophylactic therapy.

(e) Immunoglobulins and Infection

J . Leikola

A critical revue of the use of normal and hyperimmnune immunoglobulins was made. The abuse of normal gammaglobulin in different viral and specially bacterial infections was criticized. In certain parts of the world measles might still form an indication for the use of gammaglobulin whereas in the rest of the world hepatitis A prophylaxis is the only relevant indication. Special immunoglobulins (anti-D, anti-zoster, anti-HBsAg, anti-vaccinia, etc.) have their special indications.

IV BLOOD PLASMA FRACTIONATION

(a) Importance of Blood as Basic Material for Local Production of Blood Derivatives Essential for the Health Care Programmes of Developing Countries.

A. Tcheknavorian

C. Chari

Dr. Tcheknavorian while introducing the above UNIDO paper highlighted the importance of local production of blood derivatives in developing countries. Human blood and placenta are the raw materials for this industry and technologies are available for processing these two materials separately. However, lack of infrastructure and production facilities, paucity of skilled personnel, non-availability of suitable technology and lack of national policies are some of the factors which have been hindering the development of blood fractionation industry in developing countries. This is also an area which offers good scope for North-South co-operation as well as South-South co-operation. Through technical co-operation among developing countries, programmes related

to blood fractionation could be developed at sub-regional/regional levels. To this extent self sufficiency can be attained which in its turn will result in the conservation of scarce foreign exchange resources.

(b) Raw Materials Used in Plasma Fractionation

R. Perry

Raw materials used in pharmaceutical manufacture are numerous and their control and provision cover a wide range of technical disciplines. Most of the materials carry Pharmacopoeial specifications or the require - ments are well documented elsewhere and thus procedures for their supply and control are well established. Plasma fractionation is one small part of the pharmaceutical industry and differs only in the uniqueness and scarcity of its critical raw material. In this context plasma poses major problems both in its supply and lack of well defined or validaded quality criteria. In the author's view attempts to control the quality of plasma solely through analytical criteria is neither realistic nor practical to implement. However, there is undeniably a need to control and validate the quality of plasma and this is best achieved through a process of procedural control and validation from the point of donation through to its entry into process. The outline specifications presented reflect this philosophy and with an adequate Quality Assurance infrastructure the objectives of specific analytical criteria can be attained. The proposals that have been outlined have extensive implications but unfortunately do not even represent 'the state of the art' as this is changing constantly. They do represent, however, conclusions that can be drawn from the present state of knowledge and lie within the scope of practicability. While individual organisations may not be able to implement such policies fully, they should represent their aspirations.

(c) Tecniques in Use for Plasma Fractionation

H.G.J. Brumelhuis

The methods for the separation of human plasma can be divided into three groups based on differential solubility, differential interaction with solid media and differential interaction with physical fields. The different methods used in each of these groups have been indicated. Among the separation methods based on differential solubility, cryoprecipitation

and neutral organic solvent precipitation with ethanol are used most widely. As regards separation methods based on differential interaction with solid media, these methods are finding increased use specially for the fractionation of trace components. The last group, that is, methods based on differential interaction with physical fields finds limited use. The methods used for confectioning after separation of the protein include gelfiltration, ultrafiltration, lyophilization and thin film evaporation. Liquid-solid separations are critical in order to harvest desired plasma derivatives. For the purpose of polishing, depth filters are used and for sterile filtration membrane filters are used. The sterile filtration is followed by aseptic filling in glass containers, ampoules or bottles.

Many possibilities in fractionation are possible. The performance of the fractionation differs from one to another fractionation centre as well as in the methods and technology used. Details of actual methods used are often not disclosed.

An extended cold-ethanol fractionation followed by the Netherlands' Red Cross Blood Transfusion Service has been described in detail.

(d) Production and Quality Control

J. Vandersande

The expertise required to design, construct and operate a plasma derivatives manufacturing facility will have to be developed with the help of a sponsor organization currently producing such derivatives.

If the manufacturing process selected is the cold ethanol method, the equipment has to be designed to control parameters such as pH, ionic strength, protein concentration, ethanol content and temperature.

In addition, process equipment should be designed to minimize the changes of contamination.

Treatment of final containers and closures should be aimed at particle reduction. Adequate quality control should be performed regardless of financial considerations.

Auxiliary systems, such as water, steam and air should be designed to produce high quality products free of additives.

(e) Case Study of a Production Plant

G Myllylä

The fractionation department of the Finnish Red Cross Blood Tranfusion Service is described as an example of a rather new and small production plant. The fractionation unit is typically a national plant, which is responsible for the preparation of the plasma products needed to cover the domestic demand. The plant was built during 1979 and about 72,000 litres of plasma were fractionated in 1981. The methods, processing equipment, supporting functions and structure of the department are shortly described.

The history of plasma fractionation in Finland is summarized in order to describe the background of the present function; why and for what purposes the production plant was built, how it was planned and what were the costs.

Some relevant tasks in establishing a new fractionation unit are listed. The importance of early contacts to one or a few functioning plants and thorough training of the key persons is emphasized.

(f) Development of a national fractionation industry

J Uhler

KabiVitrum is manufacturing blood products by means of Cohn fractionation. Today's manufacturing process, however, comprises in addition to alcohol precipitation a variety of chromatographic purification steps, now in use for the production of all blood products. Close co-operation with Swedish scientists and other manufacturers has given the opportunity to introduce the main blood products simultaneously or in some cases even before the appearance of the corresponding products on the world market. New products as well as process development have been heavily dependent upon the supply of different qualities of blood plasma. The lack of domestically produced plasma has thus been a major factor limiting the operation.

The market demands of the different blood products have never corresponded to equal amounts of plasma. As the cost of raw material is a heavy burden for blood fractionation, efforts to establish a demand and supply balance is vital to the economy of the operation.

KabiVitrum is producing a number of different products biological as well as synthetic. The area of blood products has benefited from experience made for other products in research, production and marketing. Particularly so from the total R and D operation. The quality demands on modern production of pharmaceuticals require a large number of expert functions. For the manufacture of biological drugs like blood products a daily engagement of these expert depart - ments is necessary. To establish and maintain the expertise, national as well as international co-operation and an active exchange of information is vital.

Dr. Tcheknavorian summarized the proceedings on Blood Plasma Fractionation as follows :

All countries should have a well established Blood Transfusion Service and adequate plasma transport and storage facilities.

Plasma is one of the major products in such a transfusion unit.

50 percent of the cost of the plasma products is plasma source itself.

Consequently the countries with well established blood transfusion service should start the fractionation of plasma.

The design and equipment should be chosen according to the technology available and suitable to their requirement and infra - structure.

A fractionation unit could start with a small investment and could be upgraded step wise.

It is advisable that such a fractionation unit be established by guidance and advise of experienced persons.

The training of personnel is crucial and it takes time to have a team trained in all disciplines of fractionation.

Countries which have insufficient plasma for establishing an independent unit, should as a first step contact other fractionating unit for processing and receiving products in return.

These countries can in the meantime improve collection and separation of blood and arrive at a stage when they can start their own unit.

The economics should not be the main guiding principle to start a fractionation unit. Training and accumulation of knowledge are more important and when these are attained, the economics could be achieved in a shorter time.

One can compromise on equipment but never on quality. Quality standards should be maintained throughout from the stage of blood collection through processing and final product.

It should be aimed to process the collected plasma within one month but not later than 6 months. Outdated plasma should also be used but retrieval of biological products is much less.

The fractionation unit need not be in the vicinity of blood collection unit. It could very well be located in a well organized pharmaceutical industry and share common services such as control and maintenance.

V STRATEGY FOR NATIONAL OR REGIONAL SELF-RELIANCE IN BLOOD DERIVATIVES

Case Study

G. Miksche

S. Sjölin

A case study of a non-existing nation "Plasmania" was presented. This country has a per capita consumption of US$10 per year on Pharmaceuticals, which include plasma solutions, plasma expanders

albumin, etc. Blood donation is exclusively provided by public sector. 90 percent of donations are at eight blood banks and the blood is mostly transferred to patients in the same hospital. There is no organized exchange of blood or blood components between hospitals. Erythrocytes are normally given as whole blood. The collection costs for all whole blood produced in the country amount to US$ 2.8 million. The import cost for plasma products and plasma comes to US$ 3.0 million. Together they correspond to 3 percent share in US$ 200 million pharmaceutical market. If the expenditure on imported plasma substitutes and infusion solutions is added to this figure, their share comes to about 9 percent, most of which is contributed by imports. There are no local facilities for the production of infusion solutions. There are two plants for the production of basic pharmaceuticals meeting 40 percent of local requirements.

The participants were asked to solve the country's problem regarding self-reliance in blood and blood products. The following suggestions were put forward by the participants :

- Problem in the recruitment of adequate number of donors
- Lack of political support
- A question of proper organization
- The Minister of Health should provide adequate funds
- There is need to create a supporting structure including planning, propaganda and political support
- Should establish a pilot unit for plasma fractionation

PLAN OF ACTION

Introduction

Blood and blood derivatives are essential components in the health care programmes of any country. However, some developing countries depend entirely on imports of these products. The cost of imported material is often prohibitive and well beyond the reach of many: in some countries a bottle of imported albumin concentrate was costing in 1980 half the annual income of an average rural family. Further the imports of these items would mean the depletion of scarce foreign exchange resources at the disposal of these countries, apart from posing transport problems. Consequently, the developing countries are unable to meet even a fraction of their demand for blood and blood derivatives. This is obvious from the fact that the average consumption of albumin per one million inhabitants varies several fold between developing countries and Europe or the USA.

The Lima Declaration and Plan of Action for economic co-operation and development calls for the share of developing countries in total world industrial production to increase to at least 25% by the year 2000. From the foregoing it is clear that there exists a very wide gap between the present level of production capability with respect to blood and blood derivatives in developing countries and the target embodied in the Lima Declaration. According to the Lima Declaration, the Governments of developing countries have been urged to adopt all measures to exercise their national sovereignity over their natural resources and the further utilization of those resources and of human and material potential at their disposal. Besides, the Alma Ata Declaration on primary health care envisages the attaintment of

"health for all by the year 2000". Since blood is the basic raw material available in all the developing countries and as blood and blood derivatives form one of the essential elements in health care programmes it is obvious that the developing countries should give serious consideration to achieving self-reliance to the extent possible in this sphere.

In doing so, it should be appreciated that in certain cases this could result in local production at a higher cost compared to the imported product. In this connection the social benefits conferred by local production should also be taken into account.

In the light of above, UNIDO and the Committee for National Cooperation on Pharmaceuticals of the Swedish Ministry of Health and Social Affairs, Sweden together with World Health Organization and the League of the Red Cross Societies have organized the above Seminar with a view to acquaint representatives of developing countries with the various facets of blood transfusion services and the plasma fractionation industry. Experts prepared background papers on relevant topics and presented them. This was followed by interesting discussions.

During the discussions, it was appreciated that the issue of blood and blood derivatives could be considered broadly at three levels as indicated below :

(i) Blood (whole)

(ii) Blood components (can be prepared by a blood transfusion service, includes cell concentrate, cryoglobulin, fresh frozen plasma).

(iii) Plasma derivatives (done on an industrial scale from pooled plasma includes albumin, immunoglobulins, coagulation factor concentrates)

While the activities under items (i) and (ii) above could be carried out at the National level, the one under item (iii) could be accomplished at national/UN sub-regional/UN regional level.

The implementation of the Plan of Action could be carried through co-operation between the Governments of developing and developed countries and industry as well as co-operation between developing countries themselves at all levels either directly or through the United Nations system.

The following Plan of Action was adopted :

I Action at National Level

A. Governments of developing countries should formulate a clear policy and get involved in programmes for blood collection, preservation, quality control and production depending on their own situation according to the following priorities :

(i) Provision of whole blood
(ii) Provision of components
(iii) Plasma fractionation

B. Depending on the status of development in this particular field and infrastructure available, developing countries could be grouped as follows :

(i) Countries which have no organized national blood programme and no facilities/experience for production of blood derivatives. Countries in this category should start with the organization of national blood programmes and concentrate on priorities A (i) and (ii).

(ii) Countries which have organized national blood programmes and some infrastructure and knowledge of fractionation on a laboratory scale but do not possess adequate plasma for taking up production of blood derivatives on a bigger scale.

These countries should widen their scope of services of blood components. As far as plasma fractionation is concerned, they should increase national or UN sub-regional/regional supply of plasma for establishing production on industrial level.

(iii) Countries which possess well established national blood programmes and sufficient plasma, infrastructure and experience to take up production on laboratory/pilot plant scale. They should enter into industrial level production of plasma derivatives.

C. Governments with insufficient resources and which can not organize national blood programmes on a large scale should enter into UN sub-regional co-operation with a view to pool their capabilities and raw materials to take up plasma fractionation on a UN sub-regional/regional level and receive finished products at production cost in return for raw material supplied by them.

D. There should be close co-operation between the Ministry of Health, and Government authorities and such organization as National Red Cross/Red Crescent, in the field of collection, utilization and fractionation of blood and plasma.

E. Governments could consider the production of test materials such as reagents and other relevant materials.

F. The attention of Governments of developing countries is drawn to the importance of training which is essential for above programmes.

II Action by International Organizations

a) To assist Governments in establishing National Blood Programmes and expanding/improving preparation of blood components.

b) To help developing countries in establishing/improving quality assurance systems/techniques/standards.

c) To train personnel at all levels in national blood programmes, production of blood derivatives and quality assurance.

d) To assist Governments in developing programmes in the area of blood plasma fractionation.

The above assistance could be provided by WHO/Red Cross/ ISBT/UNIDO

e) To assess/evaluate the technology for production of plasma fractions as required by developing countries.

f) To advise and transfer technology for establishing/ expanding/improving plasma fractionation on small/medium/large industrial scale in developing countries.

g) Identification of appropriate technology for plasma fractionation.

h) UNIDO should carry out a survey of existing facilities, infrastructure and availability of plasma for fractionation appropriate for developing countries.

i) UNIDO should carry out a study of requirements for production of additional materials such as containers for blood and plasma fractionation in countries within a UN sub-region/region to make the production of plasma derivatives more advantageous.

UNIDO could provide assistance on recommendation e to i.

j) To provide information and organize Seminars/workshops on blood and plasma fractions for the countries in the interests of the developing countries.

WHO/UNIDO/Red Cross/ISBT

III Action at UN Sub-Regional/Regional Level

a) Developing countries which do not have sufficient plasma and infrastructure for industrial level production should pool their raw materials and capabilities in order to achieve feasible industrial scale production possible.

b) It emerged from the discussions during the Seminar that it is crucial to train a large number of personnel from developing countries at all levels in different disciplines starting from blood collection, preservation to plasma fractionation. As it is not feasible to train such a large number of personnel abroad, it was considered appropriate to establish a regional centre equipped with laboratory/pilot plant facilities for collection, preservation and fractionation thus combining all the relevant activities. Such a centre can also take up Research and Development activities for the benefit of the region and render specific technical assistance to the countries in solving problems pertaining to different activities.

It is recommended that such a centre should be established. For this purpose, the existing facilities relating to blood banks, preservation and production be suitably expanded to serve regional needs.

It is recommended that the first priority should be given to the region which needs it most.

c) To establish production of all relevant materials for activities concerning blood and plasma fractions on a sub - regional/regional level to meet the requirements of the concerned countries.

d) The Governments should have a special consideration as to measures to reduce customs and taxes on materials that are aimed at increasing the self-reliance in the area of blood transfusion and plasma fractionation.

The assistance for the above activities can be provided by WHO/UNIDO.

IV Possible Action which may be Taken by Host Country (Sweden)

a) To transfer or to help transfer of technology to the developing countries either directly or through WHO/UNIDO in the area of establishing blood banks, plasma fractionation plus quality assurance.

b) To encourage or to enter into joint ventures with the developing countries to establish production of plasma fractions.

c) To provide and to support a general transfer of information on all aspects of blood collection, preservation and fractionation to the developing countries.

d) To co-operate with WHO/UNIDO in the establishment of UN sub-regional/regional centres equipped with facilities for production/quality assurance for training personnel at all levels in various disciplines relating to blood collection, preservation and fractionation.

e) To offer training facilities to personnel whenever feasible at all levels from the developing countries in various disciplines starting from blood collection, preservation to plasma fractionation.

V It is recommended that the above Plan of Action be called "Stockholm Declaration 1982 and Plan of Action".

VI Follow-Up Action

In order to secure the follow-up of the above Seminar and Plan of Action, it is recommended that WHO/UNIDO should take initiative in constituting a Committee composed of the organizers/Governments/Experts who contributed to the above Seminar.

VII Vote of Thanks

The distinguished participants expressed their appreciation to the Swedish Government for their role in the organization of the Seminar.