COUNCIL OF EUROPE
COMMITTEE OF MINISTERS

RECOMMENDATION No. R (80) 5

OF THE COMMITTEE OF MINISTERS TO MEMBER STATES CONCERNING BLOOD PRODUCTS FOR THE TREATMENT OF HAEMOPHILIACS

(Adopted by the Committee of Ministers on 30 April 1980 at the 318th meeting of the Ministers' Deputies)

The Committee of Ministers, under the terms of Article 15.*b* of the Statute of the Council of Europe,

Considering that the aim of the Council of Europe is to achieve a greater unity between its members and that this aim may be pursued, *inter alia*, by the adoption of common regulations in the public health field ;

Considering that ethical and economic reasons necessitate optimal use of blood and all blood components to cater for the needs of haemophiliacs, and aware of the resulting implications with regard to the organisation of blood collection, fractionation and therapeutic use ;

Taking note of the fact that the risks of transmission of infectious diseases, in particular viral hepatitis, may vary from one area to another ;

Recalling the recommendation of the World Health Organisation, the League of Red Cross Societies and the International Society of Blood Transfusion concerning the promotion of voluntary non-remunerated blood and plasma donations, the Agreements of the Council of Europe Nos. 26, 38 and 84 and the Protocols thereto, as well as the technical recommendations of the WHO Expert Committee on Biological Standardisation and of the Task Force of the International Society for Haemostasis and Thrombosis,

Recommends the governments of member states to :

I. *a.* establish minimal criteria for the quality, packaging, labelling and control of blood products for the treatment of haemophiliacs ;

b. ensure that the available products are put to optimal use from a medical and socio-economic point of view ;

c. inform all concerned in haemophilia therapy of the problems arising from the procurement and rational use of blood components concerned in order to balance the needs and resources ;

d. provide, in so far as possible, a national haemophilia register.

II. Pursue the implementation of the recommendations indicated in the appendix hereafter with a view to reaching, as far as possible, self-sufficiency of the member states and their medical professions, both in respect of antihaemophilia products and blood plasma required for their preparation.

Appendix to Recommendation No. R (80) 5

Ethical and economical reasons as well as the medical needs require optimal use of blood and of all its components. This requirement should guide the various responsible organisations of blood collection, fractionation and therapeutic use in the choice of the methods of collection, production and treatment. It also demands a regional, national and international co-ordination policy.

This co-ordination necessitates in particular :

- the combination of whole blood donation and plasmapheresis, so as to achieve an optimal use ;

- the increase of whole blood collections and the development of plasmapheresis, according to the needs for plasma derivatives as a source of Factor VIII, albumin and specific immunoglobulins ;

- the optimal use of red cell concentrates, albumin and plasma protein solutions, according to the recommendations of previous reports ;[1]

- a limited use of fresh-frozen and freeze-dried plasma, to take into account the needs of Factor VIII, albumin and plasma protein solutions ;

- the use of frozen cryoprecipitates only when other preparations of Factor VIII of controlled potency are not available with satisfactory conditions of efficiency, safety and cost.

The geographical origin and the type of donor population (remunerated or non-remunerated) of the plasma used for coagulation factor concentrates should be indicated on every vial, in view of the fact that the risks of transmission of infectious diseases, in particular viral hepatitis, may vary from one area to another and according to the conditions of recruitment of the donors. From an ethical point of view, with respect to the health of the donor and the recipient, the recommendations of WHO and of the League of Red Cross Societies concerning the promotion of voluntary non-remunerated blood and plasma donations should be followed.

The logistic system of blood collection methods and use of blood and plasma should ensure a maximum availability of Factor VIII. Therefore it is advisable :

1. to separate the plasma from the blood cell components as early and as completely as possible ;

2. to rapidly freeze the plasma and to store it at low temperature, if possible below minus 30°C.

The methods of thawing and harvesting cryoprecipitates as final product or as starting material for further purification should yield a product containing an adequate potency of Factor VIII. Rapid thawing appears to be more efficient. The size of the pools should be determined after having considered the necessity of warranting a minimal potency, of avoiding waste by overdose and of ensuring maximal safety. As far as possible, each pool should only contain products from the same centre or area.

Quality control should take into account the recommendations of the Council of Europe, the WHO Expert Committee on Biological Standardisation and the Task Force of the International Society for Haemostasis and Thrombosis. Special efforts should be made to reduce the risk of transmission of hepatitis by controlling each batch and each unit of plasma used for the preparation of coagulation factor concentrates and by using sensitive methods (RIA or equivalent methods for HBsAg, other available methods for other hepatitis viruses).

For individual and small pool (maximum twelve donors) cryoprecipitates (frozen or freeze-dried), controls of potency, solubility and stability should be frequent. It is recommended that the potency of all products in regular use should be confirmed *in vivo* for several batches in several patients, and for new products a more thorough investigation should be carried out including half-disappearance time.

Factor IX concentrates should moreover be specially controlled for the presence of activated coagulation factors by *in vitro* or *in vivo* tests.

Information concerning the general method of preparation, added substances, the minimum concentration of the relevant coagulation factors, solubility time of the product and the mean recovery and survival *in vivo* should be supplied to the user.

1. "The production and use of cellular blood components for transfusion", Council of Europe, Strasbourg 1976, and "Indications for the use of albumin, plasma protein solutions and plasma substitutes", Council of Europe, Strasbourg 1978.

Within a rational blood component therapy and a balanced public health policy, the indication for the various types of concentrates might be the following :

a. The less purified Factor VIII concentrates (3-20 I.U/ml reconstituted solution) for usual treatment of haemophilia A and von Willebrand's disease : these concentrates may be used for home therapy, on demand or in episodic or continuous prophylaxis.

b. The more concentrated preparations of Factor VIII (more than 15 I.U/ml solution) for major surgery and for haemophiliacs with severe inhibitors in case of serious haemorrhage, or risk of serious haemorrhage.

c. The more purified preparations of Factor VIII (more than 0.5 I.U/mg protein) in case of intolerance of less purified preparations.

More purified preparations of Factor VIII should not be used in von Willebrand's disease, unless it has been ascertained that the product is able to correct the observed abnormalities of the disease.

d. Factor IX concentrates in haemophilia B, severe constitutional deficiencies of Factors II, X (and VII, if sufficient amount of this factor is contained in the preparation).

e. Concentrates containing the four Factors II, VII, IX and X, in acquired deficiencies due to severe lack of vitamin K or overdose of anti-vitamin K, if it is not possible to wait for the effect of vitamin K administration. The risk of transmission of viral hepatitis must be especially emphasised in such patients. Frozen or dried plasma can also be useful in this situation.

In acquired deficiencies due to severe hepatic failure, Factor IX concentrates are not to be advised because of the risk of thrombotic accidents. Platelet-rich plasma, fresh-frozen plasma or freeze-dried plasma are preferable in such cases.

Generally speaking, it seems desirable for each member state :

1. to establish a national inventory of the cases of haemophilia A and B ;

2. to attempt to find within its own population the necessary quantities of anti-haemophilic factors, or the required quantities of plasma for their preparation ;

3. to establish minimal criteria for presentation and quality ;

4. to ensure for users that the available products have a fair price-quality ratio, the most expensive ones being reserved for medically justified situations ;

5. to give the necessary information to all concerned in haemophilia therapy regarding the problems arising from the procurement and rational use of products ; it must be realised that a balance should be achieved between the available resources and the justified needs of haemophiliacs.