IRISH HAEMOPHILIA SOCIETY
BLOOD PRODUCT POLICY

FEBRUARY 1996

INTRODUCTION

Blood Product replacement therapy remains the crucial issue in the treatment of Haemophilia. Many people with Haemophilia have been affected by viral contamination of blood products and therefore, safety of blood products will always be a matter of deep interest and concern to all our members.

In market research carried out in 1994 among people with Haemophilia in Ireland and the UK, the main priority and concern of people with Haemophilia remained safety of blood products. Blood Products and Factor Replacement Therapy for people with Haemophilia are safer now than at any time in the past. However, there have been instances of transmission of Hepatitis and concern with relation to transmission of new and unidentified viruses and agents in the recent past. Therefore vigilance remains vital.

The Irish Haemophilia Society has, over the last several years, looked closely at all aspects of Blood Product therapy, in order to arrive at a cohesive Blood Product policy. The first such policy was produced in October 1992. Several developments in Factor Replacement therapy have taken place since that time. This updated policy reflects those changes.

We strongly believe that all persons with Haemophilia have the right to receive safe, pure and effective Blood Products. These products should be produced and purchased in such a manner as to make them eminently suitable for home treatment. We also believe that children with severe Haemophilia should receive regular prophylactic treatment with blood products to prevent the long-term consequences of bleeding episodes.

This document sets out realistic, practical and achievable objectives for Blood Product therapy in Haemophilia. It is our hope that close liaison and consultation between the National Haemophilia Treatment Centre, the Blood Transfusion Service Board, the Department of Health and the Irish Haemophilia Society on Blood Product Policy will lead to these objectives being attained.

Brian O'Mahony
CHAIRMAN I.H.S.

1. INTRODUCTION

1.1 Replacement therapy in Haemophilia should be based on the provision, in sufficient quantity, of the safest, most effective products that medical knowledge and technology can offer to enable people with Haemophilia to lead full and productive lives.

1.2 Products based on the use of Recombinant DNA technology are now being used for some people with Haemophilia in Ireland. We envisage greater use of such products in the coming years. Consideration such as donor source and testing do not apply to these products but will apply to all products derived from Human Blood or Plasma

1.3 Blood products must be available in sufficient quantities to allow adequate treatment to be given for all bleeding episodes.

1.4 Supply must be sufficient to permit a programme of prophylactic treatment of children with severe Haemophilia to be maintained.

1.5 Supply must be sufficient to allow prophylactic Treatment of adults where clinically indicated.

2. SAFETY AND PURITY

2.1 Safety of blood products is dependent on a number of processes and steps, all of which must be optimised to ensure safety:-

-Selection of donors.
-Testing of donor plasma
-Fractionation and viral inactivation.
-Surveillance and Regulation.

2.2 High purity products with a high specific activity (excluding albumin) should be used for the treatment of all patients with severe Factor VIII and Factor IX deficiency.

2.3 Use of high purity, as opposed to intermediate purity products minimises the amounts of extraneous protein present. This increases the safety of the product, decreases immune modulation, decreases the amount of allogenic proteins and thus leads to less adverse side effects.

2.4 High purity Factor IX should be used in all cases instead of PPSB (exception being where PPSB is specifically indicated for other reasons). This leads to a decreased risk of Thrombogenicity.

2.5 High purity products are more soluble and therefore require a lower reconstitution volume and are easier to administer or be administered.

3. SELECTION OF BLOOD/PLASMA DONORS.

3.1 The optimum source plasma for these blood products is plasma from Irish voluntary unpaid donations, derived from routine donations and plasmapheresis programmes.

3.2 Plasma self-sufficiency is an important element in blood product policy, but use of products sourced from other plasma must be allowed if self sufficiency leaves a shortfall in treatment requirements.

3.3 If the amount of Plasma collected in Ireland for this purpose is not sufficient to manufacture the amount of concentrates required, additional concentrates should be sourced from the same manufacturer providing that the plasma collection system used by the Manufacturer is suitably validated.

3.4 The Blood Transfusion Board should have a policy of rigorous self-exclusion of high risk donors and should encourage repeat donors especially for plasmapheresis.

3.5 Because of the currently undetermined nature of the risk of Creutzfeldt-Jakob Disease transmission by blood or blood products, the Blood Transfusion Service Board should be notified where a donor has died of CJD and any plasma or plasma pool into which this donor has donated should not be used for any single use or concentrate manufacture. This may require a change in Regulations to enable these persons to be identified to the Authorities.

4. TESTING OF DONOR PLASMA

4.1 All plasma used must be tested for the presence of HIV 1, 2, Hepatitis B and Hepatitis C viruses using appropriate tests.

4.2 Alanine Aminotransferase (ALT) tests must be carried out on all plasma donors.

4.3 New or more sophisticated tests should be used as they are developed for new and existing pathogenic viruses. This may include tests for Parvovirus or new Hepatitis viruses.

4.4 The usefullness of carrying out HIV Antigen tests (P24 Antigen) to detect donors in the Window period should be implemented if appropriate.

4.5 The feasibility of using a validated polymerase chain reaction (PCR) test of Plasma Pools, to check for removal of HIV, Hepatitis B and Hepatitis C viruses should be examined. This could be carried out either by the Blood Transfusion Service Board or by the Contract Fractionator. If it is found to be appropriate it should be implemented immediately.

4.6 A system of plasma quarantine or inventory hold for a period of up to six months should be in place to diminish the risk of transmission of viruses by donors who are in the Window period and who may test negative for the viruses on donation.

5. FRACTIONATION OF BLOOD PRODUCTS

5.1 The plasma collected in Ireland is fractionated by a commercial company and the concentrate returned.

5.2 The fractionation and viral inactivation procedures used must be validated and must conform to the highest available standards.

5.3 The blood products produced by Contract Fractionation should fulfill the following criteria:-

5.3 (a) Products should be safe from all known dangerous viruses and bacteria.

5.3 (b) Product should be efficacious with a good half life and recovery.

5.3 (c) Product should not lead to an increased risk of inhibitors.

5.3 (d) Product should be of high purity with high specific activity.

5.3 (e) Product should be licenced by the Irish Medicines Board.

6. SURVEILLANCE AND REGULATION

6.1 Post use surveillance should be carried out by the National Haemophilia Treatment Centre when any new product is used. Patients should be monitored for the appearance of any viral contamination and for inhibitors to Factor VIII or Factor IX.

6.2 The Blood Transfusion Service Board and the Company responsible for the Contract Fractionation should operate according to the highest standards of good manufacturing practice. The Blood Transfusion Service Board and the Fractionation Company should be subject to Licencing Regulation and unannounced inspection by the Irish Authorities and also by relevant European Community Bodies.

6.3 Products regularly used for the treatment of Haemophilia should be licenced by the Irish Medicines Board. New products being considered for use should be licenced by the European Medicines Evaluation Agency (EMEA).

7. RECOMBINANT PRODUCTS.

7.1 Recombinant Factor VIII produced by DNA technology is currently being used in Ireland for the treatment of children with Haemophilia. This product is not derived from Human Plasma, but does contain albumin for stabilization.

7.2 Developments in Recombinant technology for the treatment of Haemophilia should be closely monitored. The developments currently in hand are:-

7.2 (1) Production of a second generation Recombinant Factor VIII Concentrate, which will not require Albumin stabilization, thereby making it totally synthetic.

7.2 (2) Production of a Recombinant Factor IX Concentrate which will also be totally synthetic.

7.2 (3) Recombinant Factor VIIa is available for the treatment of Factor VIII Inhibitors.

7.2 (4) Production of a Recombinant Von Willebrand Factor is at a very early stage of development.

8. HOME TREATMENT

8.1 Most people in Ireland with Haemophilia infuse themselves at home.

8.2 This should be borne in mind when the products are produced and packaged.

8.3 Product should be available in different amounts in vials, in order to minimise infusion volumes.

8.4 Factor VIII should be available in 250iu, 500iu, 1000iu vials.

8.5 Factor IX should be available in 500iu and 1000iu vials. Appropriate vials should be distributed to patients.

8.6 Home treatment kits should be designed to ensure that instructions for use, syringes, and other paraphernalia are adequate. Package inserts should contain adequate warning to end users with regard to the risks of viral transmission.

8.7 Kits should be neatly packaged. Bulky kits are difficult to store and transport in sufficient quantities.

8.8 People with Haemophilia should be consultated via the Irish Haemophilia Society when the packaging of Home Care kits is being considered or changed.

9. MILD/MODERATE HAEMOPHILIA AND VON WILLEBRANDS DISEASE

9.1 All patients with mild to moderate Haemophilia and mild Von Willebrands disease should be assessed for response to DDAVP.

9.2 Where it is effective, patients should be treated with DDAVP as it reduces the patients risk of unnecessary exposure to blood products.

9.3 Von Willebrand patients who require treatment with blood products should have access to the safest possible blood products which contain Von Willebrand Factor.

10. COST OF TREATMENT

10.1 Cost of treatment is a consideration, but safety, efficacy and purity of product are paramount.

10.2 Cost can only be considered after these requirements are met. Safety is the main concern. A cheaper product which might be deficient in terms of safety would be a false economy as the consequent viral problems (such as HIV and Hepatitis in the past) would be more expensive in the long term than purchasing the correct product initially.

10.3 By preventing spontaneous bleeding episodes and thus preventing damage to joints, future treatment of arthropathy and orthopaedic surgery may be avoided. Therefore, prophylactic treatment, in itself is cost effective.

11. CURRENT AND FUTURE TREATMENT

11.1 The Concentrates used currently for the treatment of Haemophilia in Ireland are:-

Factor VIII: a Monoclonal Antibody and Solvent Detergent inactivated high purity Concentrate;
:Recombinant Factor VIII for children;

Factor IX: ion exchange chromatography solvent detergent and nanofiltration inactivated concentrate;

Von Willebrands: pasteurised concentrate.

11.2 The Plasma derived Factor VIII and Factor IX are produced by Contract Fractionation from Irish Plasma. If the amount produced is not sufficient to meet requirements, additional concentrates of the same type are purchased from the same manufacturer.

11.3 We envisage that the future trend in Haemophilia Therapy in Ireland would be as follows:-

11.3 (1) Gradual increase in the use of Recombinant Factor VIII until all Haemophilia A patients are using this product by the year 2000.

11.3 (2) Introduction of improved Recombinant Factor VIII and Recombinant Factor IX products, if these are seen to be safe, efficacious and if they are licenced for use.

11.3 (4) Introduction of safer and purer products for the treatment of Von Willebrand Disease as they become available.

12. CONCLUSION

12.1 It is our view that all blood products used for the treatment of Haemophilia must be safe, efficacious and pure and also produced and packaged to ensure ease of use.

12.2 Feedback from product users should be taken into consideration. This feedback can be channelled through the Irish Haemophilia Society and communicated to the Blood Transfusion Service Board and National Haemophilia Treatment Centres.

12.3 It is the view of the Irish Haemophilia Society that the products used, the method of Fractionation used and the supplier should not be changed without prior notice to, and consultation with the Society. An informal group consisting of representatives of the National Haemophilia Treatment Centre, the Blood Transfusion Service Board, the Department of Health and the Irish Haemophilia Society should meet when necessary and at least twice a year, to review current policy in relation to provision of blood product.

12.4 The National Haemophilia Treatment Centre and the Blood Transfusion Service Board may, if they wish, use the Society's publications as a means of communicating information to people with Haemophilia.

12.5 It is our view that close liaison between the National Haemophilia Treatment Centre, the Blood Transfusion Service Board, the Department of Health and the Irish Haemophilia Society is of paramount importance in ensuring that the blood products supplied are optimal and respond to the needs of the people with Haemophilia and in ensuring that all concerned with Haemophilia are well informed and satisfied with the treatment provided.

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