NATIONAL SELF-SUFFICIENCY IN BLOOD AND BLOOD PRODUCTS

H H Gunson

Main cellular components and plasma products that can be isolated from a donation of whole blood

Self-sufficiency in blood and blood products means that a nation is able to provide from within its own population enough blood and plasma to meet the clinical need for the products derived from them. At the World Health Assembly in 1975 member states were urged to "promote the development of national blood services based on voluntary non-remunerated donation of blood." Stemming from this proposal, countries were encouraged to achieve self-sufficiency from voluntary unpaid donations rather than relying on donations collected by commercial companies from paid donors.

The government of this country opted for self-sufficiency from voluntary and unpaid donors to preserve the system that has operated since blood collection started here.

Blood is collected as whole blood, which can be divided into two parts, the cellular components and plasma. The cellular products are red cells, platelets, and white cells. Plasma is composed of many substances, a number of which have therapeutic value and can be purified by fractionation.

Immunoglobulin products.

Although local shortages of whole blood, red cells, and platelets do occur when heavy demand coincides with low rates of collection, the United Kingdom as a whole has always been self-sufficient. This has not been the case for some fractionated plasma products in England and Wales, particularly the coagulation factor VIII (used in the treatment of patients with haemophilia) and albumin products (widely used in many surgical, medical, and obstetric procedures). All over the world these two products have been the most needed blood products; if the requirements for factor VIII and albumin can be satisfied, then there will be enough plasma available to provide all the other products such as coagulation factor IX and immunoglobulins. This can be achieved by sequential fractionation of a pool of plasma from which one product can be separated, followed by others.

Demand for factor VIII concentrates

Coagulation factors.

The pattern of treatment of patients with haemophilia has changed during the past 15 years. An increasing number of patients are now being treated at home, operations can now be performed successfully when the patient is being treated with factor VIII, and year by year the requirement for factor VIII is increasing.

As the incidence of haemophilia is reasonably constant throughout the world, the use of factor VIII can be expressed in relation to the size of the population. Between 1975 and 1980 it was estimated that one unit of factor VIII concentrate for each inhabitant of the country was required. In 1981 the directors of the haemophilia centres in the United Kingdom estimated

More than 100 million units of factor VIII will be used each year in the 1990s

that, before 1990, 100 million units of factor VIII would be needed in this country (about two units for each inhabitant). In 1987 more than 90 million units of factor VIII were used, so this target seems to be realistic. There is considerable variation among countries in the amount of factor VIII that is used, however, and in some it has already risen to 3.5 units/inhabitant. There is no reason why the amount used in the United Kingdom should not exceed 100 million units in the 1990s.

Demand for albumin products

Human albumin solutions.

During the decade 1975-85 albumin was probably the most widely used of fractionated products, particularly in West Germany, Japan, and the United States. There has been a decline, however, since the use of crystalloid and gelatinous solutions for the emergency restoration of blood volume has increased. It is now recognised that if enough factor VIII can be produced, then there will be sufficient albumin to meet our national requirements.

Plasma supply to satisfy the demand for factor VIII

Production of 4.5% albumin solution.

I presented a paper to a meeting of the International Society of Blood Transfusion in 1983 and at that time, knowing the yield of factor VIII/kg plasma, it was possible to calculate that a country would require between 8000 and 9000 kg plasma/million inhabitants to provide two units of factor VIII/inhabitant. I said that the volume of plasma needed for self-sufficiency could be modified in the future.

This prophecy did not take long to be fulfilled. Haemophiliac patients were already contracting AIDS, and during 1984 measures had to be taken to ensure that factor VIII concentrates (as well as those of other coagulation factors) could not transmit HIV. Heat treatment of the products had been the commonly used method of preventing transmission of HIV. Many products of intermediate purity produced at that time, however, could not be heat treated satisfactorily. Further steps in purification had to be taken.

Both the purification and heating are at the expense of the yield of factor VIII, which has halved since 1983. Considerable attempts are being made to increase this yield and this, together with paying attention to the quality of the plasma, are essential features in any programme designed to provide self-sufficiency of fractionated coagulation factors.

More plasma is needed to satisfy the demand for factor VIII

Supply of plasma in England and Wales

Blood Products Laboratory, Elstree.

Plasma from the regional transfusion centres in England and Wales is fractionated at the Blood Products Laboratory, Elstree. This factory was designed in 1981, construction began in 1982, and it was commissioned during 1988. Its capacity is sufficient to permit the production of 100 million units of factor VIII, as well as enough albumin and other plasma products, to treat all patients in the United Kingdom.

Achievement of plasma collection

"Recovered" plasma—from donations
"Apheresed" plasma—plasmapheresis

Plasma can be presented for fractionation in various containers, and obtained by different methods. That obtained from blood donations is called "recovered" plasma and that obtained by plasmapheresis "apheresed" plasma. The pooling of plasma from about 30 donations into a 5 kg pool under sterile conditions and the separation of 180-200 ml plasma from each donation of blood into single packs were the traditional means of obtaining plasma until 1984.

The introduction of nutrient additive solutions of which saline, adenine, glucose, and mannitol (SAG-M) is the one in common use in this country, has been an important advance. The addition of the solution to the red cells

permits their storage for up to 35 days and allows the removal of all the plasma from the donation. This means that instead of 200 ml, about 280-300 ml plasma can be separated from each donation.

Plasmapheresis means that the red cells of the donor are automatically returned, and the plasma is harvested by either a centrifugal or a filtration technique. If plasma is collected in this way it means that more frequent donations can be made (up to 15 l/year compared with 2-3 l/whole blood) because time does not have to be allowed for the donor's red cells to regenerate.

The quantity of plasma sent from the regional transfusion centres in England and Wales to the Blood Products Laboratory in 5 litre and single plasma packs has been decreasing since 1983-4, and the principal rise in recovered plasma has resulted from the use of nutrient additive solutions. There has also been a rise in the quantity of apheresed plasma, which now accounts for 13% of the total. Almost 350 000 kg plasma were sent in 1988, and it is hoped that this will increase over the next two years to allow for self-sufficiency of fractionated plasma products.

Future prospects

Currently about 60% of all blood donations are processed for recovered plasma. In order to provide a suitable balance of products for hospitals it is unlikely that more than 70% of the two million blood donations collected in England and Wales will be processed to recover plasma, but this will provide a maximum of about 450 000 kg. The balance—to a maximum of about 550 000 kg—will have to be provided by plasmapheresis.

Achieving this level of plasma collection will be challenging, because it calls for a threefold increase in the current rate of plasmapheresis and this will demand considerable investment. Whether it will provide enough factor VIII for self-sufficiency will depend on the yield and the amount of factor VIII in the plasma and demand.

Biotechnology may eventually assist the process of satisfying demand for factor VIII by finding a way to produce this material with recombinant DNA. When recombinant DNA factor VIII becomes available it is likely to be the preferred product for treatment. It is unlikely, however, that the demand for products derived from plasma will cease immediately, as a safe product made from plasma is now available. The two products could be used concurrently for several years to meet the goal of self-sufficiency.

Self-sufficiency in England and Wales is now a realistic prospect. A great deal has already been achieved, particularly with the increased production of fractionated therapeutic plasma products during the past year at the Blood Products Laboratory. It is hoped that clinicians who use them will recognise their high quality and regard them as preferred products, so that self-sufficiency from voluntary unpaid donations can be achieved.

To provide enough factor VIII concentrate:

- We will need 550 tonnes plasma/year
- We get 450 tonnes from donations

To make up the balance we must have a threefold increase in the current rate of plasmapheresis

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ANY QUESTIONS

Are there any contraindications to giving betahistine hydrochloride for vertigo together with ranitidine when there is a history of healed duodenal ulcer?

There are two subclasses of histamine receptor, H_1 and H_2 . Some of the effects of histamine, such as bronchoconstriction and contraction of the gut, are mediated by H_1 receptors, and others, most notably gastric secretion, involve activation of H_2 receptors. Betahistine is a moderately selective H_1 receptor agonist with an approximate relative activity at the two receptor sites of 40:1 (H_1 : H_2). It is used clinically as a vasodilator to improve blood flow to the labyrinths and brain stem.

Ranitidine is a highly selective H_2 receptor blocker and is virtually without effect on H_1 receptors. H_2 blockers interfere remarkably little with physiological function other than gastric secretion, which implies that extragastric H_2 receptors are of minor physiological importance. They do, however, inhibit effects on cardiovascular and other systems elicited by exogenous or endogenous histamine. It seems unlikely that ranitidine would interfere with the action of betahistine. Similarly, because of the specificity of betahistine for H_1 receptors, any effect on gastric secretion must be negligible and easily antagonised by ranitidine.—J R BENNETT, consultant physician, and ELEANOR DAKKAK, principal pharmacist, Hull