Red Cell Banking and the Production of a Factor VIII Concentrate

R. A. CUMMING, S. H. DAVIES, D. ELLIS and W. GRANT
Regional Blood Transfusion Centre and Blood Products Unit, Edinburgh

The main purpose of this paper is to describe a procedure for the preparation of a human antihaemophilic Cohn Fraction I for routine clinical use. Experimental quantities of the fraction were made in the Scottish Blood Products Unit between 1952 and 1956 and thereafter its manufacture was developed. In 1960 the volume of fresh plasma fractionated was 320 l, derived from blood from a total of 1,425 donors. It was felt at this time that it was no longer reasonable to discard the red cells produced and an investigation was initiated to ascertain whether they could be safely recovered, "banked", and utilized for clinical purposes. The results of this investigation and the preparation and use of the antihaemophilic fraction are described below.

Methods

Equipment and reagents. Standard British transfusion equipment was used throughout. "Vickap" bottle-top covers (Viscose Development Company Ltd., London) were autoclaved before use in a solution of 1 in 1,000 aqueous "Hibitane" antiseptic (chlorhexidine diacetate: Imperial Chemical Industries), as recommended by James [14]. Centrifugation was carried out in MSE "Major" refrigerated centrifuges with six-place blood bottle heads, and fitted with motors capable of giving 2,000 rpm with full load.

The "transfer set" consisted of a 12 gauge needle (British Standard Wire Gauge), 10 cm long, joined by 35 cm of 6 mm plastic tubing (Capon Heaton, Birmingham) to a second 12 gauge needle, 22 cm long which was protected by a loose sleeve of Paul’s drainage tubing (12.5 mm), weighted with 3 cm of glass tubing O.D. 8 mm. The shorter needle was protected by a removable plastic tubing guard and the whole was double-wrapped for sterilisation along with two guarded six-way needles (16 gauge) each of which was fitted with a cotton wool air filter. Protein precipitate pastes were re-suspended with Vibro-mixer stirrers (AG, für Chemie-Apparatebau, Männedorf ZR, Switzerland). "Stirrer assemblies" consisting of a 35 cm shaft
with a 22 mm stainless steel disc (23 mm disc reduced), were placed in a blood bottle, with the shaft passing through a rubber diaphragm seal. The latter was held in place with a standard aluminium screw-cap, and the whole was autoclaved before use.

“Ethanol-bicarbonate solution”, sterilized by filtration, was distributed in bottles each of which contained 82 ml 53.3% v/v ethanol plus 3 ml 0.5 M NaHCO₃. “Dilute citrate-saline” contained 3% sodium chloride and 0.63% trisodium citrate (5H₂O), adjusted to pH 6.80±0.05 with N HCl, and sterilized by autoclaving. This solution is equivalent to a 1:1 dilution of “physiological” citrate-saline. “Ethanol-glycine mixture” contained 6.5% v/v ethanol and 1M glycine adjusted to pH 6.80±0.05 with N HCl and sterilized by filtration. All reagents were made up in freshly distilled pyrogen-free water, and distributed in bottles fitted with sterile rubber wads, perforated aluminium screw-caps, and paper covers.

Cold room operations were carried out in a “sterile cold room”, in which the air was continuously circulated through a bacteriological air filter (Yokes Ltd., Guildford, Surrey). In addition, the room was sprayed once per day with a 1 in 10,000 aqueous solution of Hibitane. Air filtration was discontinued for some hours following spraying to allow settling of droplets. The temperatures of this room and of the cold baths were controlled (±0.5°C) by mechanical refrigeration. Staff were, in addition to warm clothing, sterile masks, hair covers and operating theatre gowns, and “scrubbed up” their hands before entering the cold room. Sterile rubber gloves were worn when appropriate. “Hibitane swabs” consisted of sterile 7.5 x 7.5 cm eight-ply gauze swabs soaked in a solution of 1% Hibitane in 70% ethanol.

Bleeding of donors. Standard donations of 400 ml of blood were collected by gravity flow through plastic taking sets from normal blood donors with reasonably accessible veins. Each blood bottle was silicone-treated, and contained 2 g sodium dihydrogen citrate (1/2H₂O) and 3 g dextrose in 100 ml water. During bleeding good mixing of the blood and anti-coagulant solution was maintained by swirling the bottle by hand at intervals not exceeding one minute. This was facilitated by a suspension arrangement in which the bottle-holders hung from a rubber harness. The time required for bleeding was 3 to 5 min.

On removing the taking set needle and airway from the bottle the top surface was wiped with a “Hibitane swab” and covered with a sterile Viskap. The bottles were then either immediately loaded into pre-cooled centrifuge cups or placed in a stirred cooling bath at 4° to 10°C.

Separation of the plasma from the red cells. The bottles were spun at 2,000 rpm (1,200 x G, radius measured to inside bottom of the bottle) and +2°C for 2 h. At the end of the centrifugation the spinning head was allowed to stop without braking. Plasma separation and all subsequent steps were carried out in the specially prepared “sterile cold room” at +1°C, using aseptic non-touch needle-piercing techniques throughout. The Viskaps were removed from the tops of the bottles and each was covered with a “Hibitane swab”. Using “transfer sets”, 225 ml of plasma was then siphoned from each of two bottles of blood to give 450 ml of platelet-poor plasma in a sterile receiving bottle. Particular care was taken not to disturb the sedimented cells and buffy coat before or during aspiration of the plasma. The suction was moderate (10 to 15 cm Hg) to prevent over-rapid aspiration and hence frothing. A fresh “transfer set” was used for each bottle of blood. On completion of the plasma separation the red cell concentrate bottles were re-covered with sterile.
Viskaps, mixed by inversion, and transferred to the blood bank at +4°C to await labelling by blood group. Their hematocrit was 65 to 70%.

**Preparation of Cohn Fraction I.** To ensure a pre-alcohol addition temperature of 0°C the plasma was cooled by inversion at a rate of 0.5°C/min. Each plasma bottle was connected by a "transfer set" to a bottle containing 85 ml of pre-cooled "ethanol-bicarbonate solution" at −25°C and the contents of the latter were drawn over as rapidly as possible, using a vacuum of 30 to 40 cm Hg. The needle in the plasma bottle was directed in such a way that the alcohol was delivered in a strong stream down through the centre of the plasma to the bottom of the bottle; because of the lower specific gravity of the alcohol good convection mixing occurred. After removal of the alcohol-addition and airway needles, the bottle was immediately covered with a sterile Viskap, inverted twice to ensure completion of the mixing, and placed in a refrigerated bath. Following equilibration (pH 7.2, ethanol 8% v/v, −3°C) for 2 h or overnight, the bottles of Fraction I suspension were centrifuged at −3°C and 2,000 rpm for 30 min. The supernatants were siphoned off, pooled and stored at +1°C for subsequent processing to gamma globulin and albumin.

Approximately 100 ml sterile "dilute citrate-saline" at 0°C was added to the precipitates, and after partial mixing, the suspensions from three bottles were combined in one and made up to 400 ml. The cap of this bottle was exchanged for a sterile Vibro-mixer "stirrer assembly" and the contents were stirred for 5 to 10 min to give a fine dispersion of the precipitate, which was then brought into solution by warming in a water bath at +30°C for 15 to 20 min with occasional gentle mixing by hand. Following the removal, in a sterile room, of samples for bacteriological and analytical tests the solution was shell-frozen, and stored at −40°C. The time interval between placing at +30°C and shell-freezing did not exceed one hour.

In the subsequent freeze-drying [12] heat input was controlled to give a temperature not exceeding −20°C in the frozen material; the maximum temperature reached in the drying product was +35°C; the final residual moisture content was less than 0.5%; and the dry powder was sealed in dry nitrogen.

Each bottle contained Cohn Fraction I derived from 1,350 ml of fresh ACD plasma. This is the quantity recovered by the above method from 6 bottles or one centrifuge-load of blood and is convenient from the point of view of production, record keeping and therapeutic use. Half quantities were also prepared. Each full bottle contained approximately 3.4 g total protein of which 2.0 g was clottable, and was reconstituted for use with 200 ml sterile distilled water.

**Preparation of glycine-extracted Fraction I.** To prepare a fraction similar to Blomback I-O [2], the Fraction I paste was extracted twice at 0°C by stirring for 15 min with a 6.5% ethanol - 1M glycine mixture at 0°C and then centrifuging at −3°C. Following the second centrifugation and removal of the extracting fluid the final paste was dissolved in "dilute citrate-saline" and processed to a freeze-dried product as described for the Cohn Fraction I. In this case the protein per container was 2.2 g of which 1.9 g was clottable.

**Tests and assays.** Culture tests on red cell concentrates were carried out on unopened bottles which had been allowed to stand at room temperature for at least 3 days before testing. The caps were removed in a sterile room and 1 ml samples of the well-mixed contents were transferred to each of 2 bottles containing 10 ml of Robertson's cooked meat medium, which were incubated at 20°C and at 37°C.
respectively for 3 to 4 days. The bottles were then sub-cultured on blood agar plates aerobically and anaerobically at 20°C and 37°C.

Factor VIII assays were carried out by the method of BIGGS, EYELING and RICHARDS [1]. A plasma pool from 4 normal donors was used as standard as described. The Factor VIII activity of such a pool was taken as 100%. The theoretical activity, assuming complete recovery in the reconstituted fraction, was 608%, relative to this standard (corrected for dilutions).

Results and Discussion

Contamination rate in cell concentrates. It is known [33, 34, 8, 31] that centrifuged red cells prepared from fresh blood are satisfactory for transfusion purposes, and show good post-transfusion in vivo survival after up to 21 days storage, as measured by radioactive tagging. There is however one difficulty to "banking" red cell concentrates: the risk of bacterial contamination when the plasma is aspirated. Because of the possibility of subsequent bacterial proliferation, the time of storage, after plasma removal, is usually limited to 12 or 24 h (British and United States Pharmacopoeias). In re-opening the question of red cell banking in relation to large scale antihaemophilic factor production the problem was therefore primarily one of finding a procedure for removing the plasma without adding to the risk of bacterial contamination.

From experience gained in the manipulation of sterile solutions while developing methods of preparing antihaemophilic fraction it seemed to us that it might be possible, by using similar techniques, to develop a procedure which would result in red cells which were as safe from this point of view as the whole blood in routine use.

The procedure adopted utilizes basic "aseptic", needle-piercing, non-touch techniques which are standard in plasma processing work. However the operation was carried out in a central unit by specially trained staff, working in a suitably maintained "sterile" processing cold room, and using a carefully defined procedure. During the first year of the trial the cells were prepared and immediately cultured, but were not used clinically. Of 344 bottles, 1 or 0.3% was contaminated. In attempting to compare this rate with published figures for whole blood the effect of the age of the blood at the time of sampling must be taken into account. It is known that while a considerable number of bottles contain organisms immediately after collection, many of these die off during storage at +4°C, due partly to the bac-
and the Production of a Factor VIII Concentrate

...tericidal action of fresh blood and partly to the low temperature. Thus while 2% or more of units are contaminated at the time of collection, rates as low as 0.13% have been reported [14] for blood which has been stored for 3 weeks at +4°C. This is illustrated in Table I, which summarises the literature reports on contamination rates in whole blood, listed in order of increasing storage time. Our rate of 0.3% for the packed cells can be considered satisfactory in relation to a figure of 2.24%, reported by Braude et al. for whole blood cultured after 24 h storage at +4°C [5].

As this figure was encouraging, clinical use of the banked cells was introduced. Cells which were not used within a few days were cultured. Of 618 such bottles 1 or 0.16% was contaminated; this figure again bears comparison with published figures for whole blood cultured after a similar storage period.

TABLE I

<table>
<thead>
<tr>
<th>Time at +4°C before culture</th>
<th>Total cultured</th>
<th>Total cultured</th>
<th>% contain.</th>
<th>Containers</th>
<th>Refs.</th>
</tr>
</thead>
<tbody>
<tr>
<td>24 hours</td>
<td>1697</td>
<td>38</td>
<td>2.24%</td>
<td>Bottles</td>
<td>(9)</td>
</tr>
<tr>
<td>4 days</td>
<td>497</td>
<td>47</td>
<td>1.04%</td>
<td>Plastic bags</td>
<td>(10)</td>
</tr>
<tr>
<td>1-7 days</td>
<td>406</td>
<td>1</td>
<td>0.25%</td>
<td>Bottles</td>
<td>(11)</td>
</tr>
<tr>
<td>6 days</td>
<td>3000</td>
<td>6</td>
<td>0.20%</td>
<td>Bottles</td>
<td>(12)</td>
</tr>
<tr>
<td>&quot;stored&quot;</td>
<td>—</td>
<td>—</td>
<td>0.13%</td>
<td>Bottles</td>
<td>(13)</td>
</tr>
<tr>
<td>&quot;outdated&quot;</td>
<td>313</td>
<td>0</td>
<td>0.00%</td>
<td>Bottles</td>
<td>(13)</td>
</tr>
</tbody>
</table>

Incidence of reactions to cell concentrates. Reactions reported during an 18 months period totalled 9 out of 4,635 or 0.2% as compared with 35 out of 39,651 or 0.09% for whole blood. A slightly higher incidence of reactions is expected to occur with packed cells, due to the nature of the clinical conditions of the patients. All of the reactions were of a mild pyrexial or allergic type. No positive follow-up was carried out, so that the above figures will exclude mild reactions not reported back to the Transfusion Centre. The residues in the 9 bottles of cells which had caused reactions were cultured and found sterile. In the case of the whole blood 1 of the 35 bottles causing a reaction was contaminated.

It is concluded that, provided adequate precautions are taken, the contamination rate of cells prepared by a needle-piercing technique...
is not significantly different from that of the whole blood in routine use; it is probably much lower than that of whole blood collected under adverse conditions (as at a withdrawal session away from a blood transfusion centre).

During the period of the trial the permitted storage of the cells has been limited to a maximum of 7 days. It was found that most of the cells could be utilized without a longer dating, and there is thus no necessity to extend the period.

In a survey of the available literature on serious reactions due to contaminated blood [32, 6, 23, 3] sixteen cases were noted in which the age of the blood transfused was known. In all sixteen the blood was at least 12 days old. Eight of the sixteen cases were fatal. A number of other cases have been reported where the blood was less old, but in all of these the contamination arose following a massive inoculation with bacteria due to the use of unsterilized equipment or solutions [32, 6, 29].

Further, from a number of studies [6, 23, 10, 30, 4] of the properties of typical cold-growing organisms it can be concluded (a) that the minimum lethal concentration is of the order of $10^5$ to $10^6$ organisms per ml, and (b) that the time required for this concentration to be reached in blood containing an inoculum of say 5 organisms per ml is 12 to 14 days (at +4° to +6°C). It appears likely that provided the cell concentrate is adequately refrigerated, and the initial inoculum is small, the main risk from bacterial contamination develops only after 10 to 12 days of storage. It is thus desirable to limit storage of the red cells, to less than 10 days, and it would also be desirable, if it were possible, to similarly limit the permitted storage of whole blood, as suggested by McEntegart [23].

In recent years plastic bags have become available for the collection of blood, and in the form of a "double pack", these permit the separation of the plasma from the red cells within a totally enclosed system, so that there is no question of an added risk of bacterial contamination [11]. Elaborate sterility precautions are unnecessary, and such packs are therefore preferable. However in situations where the high basic cost of the packs is a significant factor, the needle-piercing procedure described, may offer a workable alternative.

Preparation of factor VIII concentrate. The preparation of a product for clinical use was reported in 1957 by Kekwick and Wolf [19], and in a slightly modified form by Holman and Wolf [13], diethyl ether being used as the protein precipitant rather than ethanol; the successful clinical use of this fraction in the treatment of haemorrhage and the cover of dental extraction has been reported by Maycock et al. [22]. Bломбак [2], in 1958, described the preparation, using ethanol, of a Fraction I-O, derived from Cohn Fraction I, which gave a good recovery of Factor VIII and was effective in the treatment of haemophilia [26]. The preparation and use of washed
and the Production of a Factor VIII Concentrate or extracted Fraction I has also been reported by McMillan, Diamond and Sturgenor [24] and by Johnson et al. [16].

In the preparation of these products the Cohn Fraction I initially obtained was subjected to extraction procedures with a view to removing other coagulation factors, which were thought to decrease the stability of the Factor VIII, and thus cause loss of activity during processing and storage.

In our procedure, on the other hand, we have concentrated, not on removing such impurities, but on minimizing their effects. To achieve this, precautions were taken to avoid influences which might tend to activate or accelerate the early stages of the clotting mechanism. These were 1) Avoidance of tissue thromboplastin: donors with very deep or difficult veins were rejected, entry into the vein was as direct as possible, and bottles of blood were rejected when the flow had been slow (more than 6 min), or interrupted, 2) Rapid processing and controlled low temperatures: this included the immediate chilling of the blood on completion of bleeding, 3) Early removal of platelets: the use of the single 2-h centrifugation described, rather than re-centrifugation of the plasma, had the advantage that the platelets were removed from the plasma at an early stage when there had been minimum exposure to "foreign" surfaces, 4) Omission of a sterilizing filtration: by using the aseptic techniques described a low contamination rate was maintained.

Initially fractionation was carried out as a closed-system sterile operation in 3 l pools in glass precipitation vessels, similar to those described by Kekwick and Mackay for plasma protein fractionation by the ether method [18]. In 1957 Nitschmann, Kistler and Joss [28] described a technique for the preparation of Cohn Fraction I for use as fibrinogen, in which the alcohol precipitation was effected by injecting the alcohol directly from a syringe into plasma in standard blood bottles. As this procedure has advantages over precipitation in larger vessels we investigated the possibility of adapting it for the preparation of an antihemophilic Fraction I. It was found that, applied as described in the experimental section, this method gave a satisfactory product. Nitschmann and Kistler [20, 27] have since reported that Fraction I prepared as described for fibrinogen has in fact been used successfully as a source of Factor VIII, although the activity was variable and only selected batches were used clinically.

Table II shows Factor VIII assay results obtained on aliquots taken before freeze-drying from a series of bottles of Cohn Fraction I.
TABLE II

Activity and Storage Stability of Fraction I

Activities are expressed as percentages of the activity of a fresh citrated plasma standard. A yield of 100% in the Fraction would give 608% as the assay result. Storage was at +4°C in dried form.

<table>
<thead>
<tr>
<th>Unit No.</th>
<th>Aliquots</th>
<th>Months of storage</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>3</td>
<td>6</td>
</tr>
<tr>
<td>1040</td>
<td>569</td>
<td>639</td>
</tr>
<tr>
<td>1063</td>
<td>720</td>
<td>660</td>
</tr>
<tr>
<td>1070</td>
<td>400</td>
<td>427</td>
</tr>
<tr>
<td>1081</td>
<td>600</td>
<td>580</td>
</tr>
<tr>
<td>1116</td>
<td>842</td>
<td>800</td>
</tr>
<tr>
<td>1322</td>
<td>599</td>
<td>600</td>
</tr>
<tr>
<td>1441</td>
<td>600</td>
<td>800</td>
</tr>
<tr>
<td>1495</td>
<td>580</td>
<td>593</td>
</tr>
<tr>
<td>1525</td>
<td>400</td>
<td>520</td>
</tr>
<tr>
<td><strong>Average:</strong></td>
<td>589</td>
<td>595</td>
</tr>
<tr>
<td><strong>Average recovery:</strong></td>
<td>95%</td>
<td>97.5%</td>
</tr>
</tbody>
</table>

which had been produced routinely for clinical use. The Table includes all the assays on a consecutive series of sampled bottles. It can be seen that the average yield of Factor VIII activity, based on the volume of plasma fractionated is 95% and that there is no major loss of activity in the units assayed, during the first 9 months of storage. Variability in the individual results (range 393 to 843 or 64.5% to 138% recovery) could be due to, (a) variation in Factor VIII levels in the donors of the standard plasma, (b) loss of activity in handling the standard plasma pools, (c) variability of the assay, (d) loss of activity in individual fraction aliquots. We do not as yet have sufficient data to distinguish between the above possibilities.

It was observed that Fraction I prepared from blood which was not immediately chilled and centrifuged was slightly less stable, the average activity (12 units assayed) falling from an initial 571% (93.5% recovery) to 465% (76% recovery) during 9 months of storage.

For purposes of comparison the small-pool equipment and handling procedures were also applied to the preparation of a glycine-
washed Fraction I similar to Blombäck Fraction I-O [2]. Assays on aliquots from a series of units of this product gave similar results to those obtained with the Cohn Fraction I, the average recovery again being over 90%, with no significant loss of activity in 9 months of storage. Such recoveries are in agreement with those reported by Blombäck for the I-O Fraction [2].

Activity measurements on a series of reconstituted whole units of the Cohn Fraction I gave a slightly lower average figure of 487% (80% recovery). However these assays were carried out on residues remaining after clinical use and it is possible that exposure to room temperature for several hours was the cause of some activity loss.

When administered pre-operatively, in absence of a bleeding site, and without blood or plasma transfusions, the Cohn Fraction I gave approximately the expected rises in Factor VIII activity in the patient's plasma and was effectively haemostatic. Thus in three patients given the Fraction pre-operatively, and assayed 10 min later, the rises were 78%, 85% and 117% of those expected on the basis of the in vitro activity of the Fraction and the plasma volume of the patients (estimated on a weight basis). The rises were similar to those obtained on intravenous injection of the I-O type Fraction which had been prepared as a basis of comparison.

The Cohn Fraction described has been used with satisfactory clinical results in the treatment of a wide range of cases. Its application in a series of dental cases was reported by Middleton et al. [32], and other uses include (a) arrest of haemorrhage in haematuria; in gastrointestinal, joint and intracerebral bleeding; and in sublingual and retropharyngeal haematoma, (b) cover of investigative procedures such as percutaneous carotid angiography and air encephalography, (c) operative cover in bilateral achilles tenotomy and in open reduction and pinning of an avulsed radial epiphysis. In general it has been found that in a severe haemophiliac (Factor VIII less than 1%), who is at rest and who is not actively consuming Factor VIII at a site of haemorrhage, the administration of one unit of the Cohn Fraction every 6 to 8 hours will maintain a haemostatic level. The combined use of animal Factor VIII concentrate [21], and the human product has been successful in certain major operations. These included (a) nephrectomy, (b) major exploration of buttock, (c) major exploration of calf, (d) craniotomy and intracranial ligation of traumatic arterial aneurysm. The operation and early post-operative period were controlled with the animal concentrate, and on
development of sensitization to the animal protein immediate change to the human product was made. This procedure was valuable when the human fraction was in short supply. The use of the human material at this point made it unnecessary to resort to the use of Fraction from a second animal species in order to complete the treatment.

A low incidence of mild pyrexial reactions (0.3%) was observed with the Cohn Fraction. This is similar to the experience of Nilsson, Blomback and Ramgren [26] for the I-O Fraction, and in contrast to a high incidence reported by Maycock et al. [22] for the other Fraction. However it is possible that the high rate reported by the latter authors may have been due to the rapid administration rates used.

From earlier work on the use of Cohn Fraction I, Frommeier, Epstein and Taylor [9] concluded that there was a greater risk of the development of circulating anticoagulants to Factor VIII, than with blood or plasma. However later workers have not confirmed this finding. Nilsson, Blomback and Ramgren [26] in their series using Fraction I-O report that none of their patients developed circulating anticoagulants despite prolonged therapy in a number of cases. In our series one case has been observed in which a transient circulating anticoagulant to Factor VIII developed, disappearing following cessation of treatment.

It appears from these results that it is possible to prepare a safe and reasonably active Cohn Fraction I, provided suitable precautions are taken during processing. The rather variable activity reported for this fraction by other workers may be due to minor differences in processing, such as speed of operation, temperature control, or procedure for platelet removal.

Jones et al. [17] report that effective platelet removal by double centrifugation is essential if maximum activity of Fraction I-O is to be achieved; it is possible that the early removal of platelets, before they have been submitted to the trauma of a plasma aspiration step may contribute to the stability of the Factor VIII in our Fraction I.

Because of the risk of transmitting serum hepatitis, small-pool operation is preferable, in preparing antihaemophiliic fractions. The simplicity of the procedure described is thus an advantage in large-scale production.
Summary

The preparation of an antihaemophilic small-pool Cohn Fraction I is described, together with a procedure for the recovery and banking of the red cell concentrates available as a by-product. More than 2,000 unit doses of the Fraction and more than 10,000 bottles of red cell concentrates have been used clinically with satisfactory results. The method of preparation of the Fraction is simple, and its activity appears to be sufficiently high, uniform and stable for practical purposes.

Résumé

Les auteurs décrient le processus de préparation d’une fraction I de Cohn antihémmophiiique provenant de pool réduit et une méthode pour la récupération et le stockage des sédiments érythrocytaires qui peuvent être utilisés comme produits secondaires. Plus de 2000 unités de fractions I et plus de 10000 flacons de sédiments érythrocytaires ont été utilisés pour les besoins cliniques avec des résultats satisfaisants. La méthode de préparation de la fraction est simple, et l’activité du produit semble être suffisamment haute, uniforme et stable pour les besoins cliniques.

Zusammenfassung


References

and the Production of a Factor VIII Concentrate


Authors' address: Dr. R. A. Cumming, Dr. D. Ellis and Mr. W. Green, Regional Blood Transfusion Centre and Blood Products Unit, Royal Infirmary, Edinburgh, 3; Dr. S. H. Davies, Department of Haematology, Royal Infirmary, Edinburgh, 3 (Scotland).