
Blood Conservation during Open Heart Surgery: A Literature Review

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Abstract

(*J. Extra-Corpor. Technol.* 18(4) p.198-207 Winter 1986, 74 refs.) Due to the increase of cardiac surgery and cardiopulmonary bypass procedures (CPB) in recent years, tremendous demands have been placed on local blood banking facilities. As a consequence, methods to conserve blood during CPB have proliferated. Indeed, through the many innovations in technique and technology, blood usage has been curtailed to a fraction of what it was less than a decade ago. Oschner et al. report that in 1981, on average, 1.8 units of blood were used per patient per hospital stay, in contrast to approximately 8 units used in 1975. The Cleveland Clinic reports that by the year 1983 average blood usage per patient per hospital stay had decreased to 0.8 units. These numbers show a sharp improvement over the 5-8 units of blood required simply to "prime the pump" in the late sixties and early seventies.

A number of technologies are responsible for this drastic reduction in homologous blood requirements during CPB. More efficient oxygenators, for example, have contributed to lengthened red cell survival. Improved biomaterials have substantially increased the survival of platelets and leukocytes. Prebypass autologous blood withdrawal techniques, which can protect up to 20% of the patient's blood volume from the ravages of CPB, have been used. Autotrans-

fusion devices, which reclaim blood that otherwise would be lost, process it, and then return it to the circulation in a usable form, have also found significant use. The development of molecules of heparin and protamine of increased purity has provided greater control over the coagulation cascade, especially when used in conjunction with activated clotting time and heparin-protamine titration tests. An important development in blood conservation has been that of hemodilution.

Hemodilution Techniques

As early as 1955, Gollan⁵ reported the results of a series of dog experiments in which hemodilution and hypothermia were used. In 1960, Neptune⁶ first described the relevance of hemodilution to CPB, and soon after, Gadbois reported on the physiologic changes that occur when homologous blood is pooled and used to prime the extracorporeal circuit (ECC). These alterations became known as the "homologous blood syndrome," which is manifested by hypotension upon initiation of CPB, thrombocytopenia, leukopenia, sequestration of blood, pulmonary congestion, renal insufficiency, and cerebral changes.⁷ Cooley⁸ found sludging of the erythrocytes and plugging of many of the smaller vascular radicals in the omentum of animals undergoing open heart procedures. He noted further that these changes did not occur when 5% dextrose was used to prime the pump in place of homologous blood. This finding prompted research to develop a better method of priming the ECC. Both Cooley⁸ and Roe⁹

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reported better perfusion with crystalloid primes than with blood primes; Cooley⁸ used 5% dextrose in water and Roe⁹ used a balanced electrolyte solution.

Cooley enumerated the advantages of hemodilution; it: 1) eliminates the need for heparinized blood; 2) provides for economy of personnel and equipment; 3) increases the availability of cardiopulmonary bypass for emergencies; 4) enhances venous return; 5) reduces postoperative bleeding and prevents postoperative renal and pulmonary complications; 6) permits the use of disposable equipment; 7) prevents hematologic complications including incompatibility, hepatitis and thrombocytopenia; 8) conserves the patient's own blood volume; 9) permits safer operations on infants; and 10) permits surgery in patients with religious opposition to blood transfusion.⁸

Thus, a number of very clear advantages to hemodilution were immediately evident, including decreased blood requirements per patient and decreased blood cell destruction as evidenced by lower plasma hemoglobin levels, increased diuresis, and fewer fibrin deposits.⁹ Even with only 50% hemodilution, using a balanced iso-osmolar electrolyte solution with a resultant hematocrit of 18-24%, plasma hemoglobin levels were lower, there was decreased operative bleeding, and fewer renal complications were observed in the absence of the homologous blood syndrome.¹⁰ The oxygen-carrying capacity of hemodiluted blood even at normothermia was sufficient since metabolic acidosis did not occur. Moreover, because of the reduced viscosity of hemodiluted blood, perfusion was improved during hypothermia when the blood normally becomes more viscous.¹¹ Thus, prevention of the homologous blood syndrome through the use of hemodilution, in itself, reduced blood usage in patients by almost 50%.

Components of the Prime

Balanced electrolyte solutions (Table 1) are favored over 5% dextrose in water because of the possibility of producing severe hyponatremia and hypochloremia. With hypotonic solutions, (e.g., 5% dextrose in water) a severe drop in serum electrolytes can be expected.¹² Due to the hyposmolarity of the diluent, fluid rapidly escapes into the extracellular space as the body attempts to maintain normal plasma protein concentrations. This can be observed as a considerable gain in weight.¹³ At some point between the second and fifth postoperative day, the fluid returns to the vascular space for elimination by the kidneys. This temporary hypervolemia may result in congestive heart failure in patients with limited cardiac reserves.¹⁴

Clinical experience has shown that colloids are important components of the priming solution. About 80-85% of the colloid osmotic pressure is exerted by 50-60% of the low molecular weight (66,300-69,000) plasma proteins, and it is this fraction of the prime that prevents massive extracellular fluid overload. Hallowell et al.¹⁵ concluded that "the principal effect of withholding albumin is to increase net positive water balance..." An approximate 3-5 gm/100 cc albumin concentration is recommended for cardiopulmonary bypass.¹⁶

Synthetic colloids may also be used in the priming solution. Hetastarch,¹⁷ for example, is a synthetic polymer composed of amylopectin. It has an average molecular weight of 450,000 and is supplied in a 6% solution. (Hespan) Hetastarch provides 77 mEq of both sodium and chloride at a pH of 5-7. It possesses colloidal properties that resemble albumin and may be used in the prime as a plasma volume expander. A disadvantage of this agent is its long half-life, as it generally takes one to two weeks for the body to excrete 99% of the administered dose. In some patients this may take as long as 17 weeks. Hetastarch, which coats the platelets, has also been implicated in decreased platelet function, and has resulted in transiently prolonged prothrombin times (PT), partial thromboplastin times (PTT), and clotting times. Kightlinger et al.¹⁸ have substantiated a 66% drop in platelet count when hetastarch was used as a prime component in specific type membrane oxygenators in contrast to a 28% reduction with albumin.

Mannitol has been used as an additive in priming solutions. This osmotic diuretic is a dexahydroxyl alcohol, which affects the glomerular filtrate to such an extent that it hinders the reabsorption of water and

Table 1
Formulation of Crystalloid Prime

Plasma-lyte A
Travenol Labs
Sodium 140 mEq
Potassium 5 mEq
Magnesium 3 mEq
Chloride 98 mEq
Acetate 27 mEq
Gluconate 23 mEq
Approximate pH 7.4 adjusted with Sodium Hydroxide
Approximate milliosmols per liter 294

solutes by the renal tubules. To be properly effective, renal blood flow and glomerular filtration must be maintained to enable the drug to reach the tubules. Increasing the renal blood flow as a result of dilating the vascular segments between the renal artery and glomeruli, lowering the renal vascular resistance, and reducing the blood viscosity may all contribute to the diuretic effect. Mannitol also promotes the excretion of sodium and protects the kidneys from nephrotoxins by preventing the toxins from concentrating in the tubular fluid. Generally speaking, osmotic diuretics cause water to be withdrawn from the cells into the extracellular spaces, or in the case of blood, from the erythrocytes into the plasma. As a result, the extracellular fluid volume, plasma volume, and circulation time are increased, and extracellular stores of sodium are diluted.

The Perfusion Circuit _____

Refinements in the perfusion circuit over the years have also reduced blood trauma and enhanced blood conservation. Improvements have been made not only in the equipment but also in the materials used in the manufacture of this equipment. The development of the oxygenator exemplifies this fact. The technology has progressed from rotating disc oxygenators to bubble oxygenators to membrane oxygenators, with each device offering a distinct advantage over the previous version. The quantity of prime required for the bubble oxygenator was only a fraction of that required for the rotating disc oxygenator, and although the membrane oxygenator required approximately the same priming volume as the rotating disc, it exerted far less trauma on the formed elements of the blood. Heimbecker reported in 1977 a 300% decrease in plasma hemoglobin levels and a savings of six units of blood per patient with the membrane oxygenator.¹⁹ He also realized an almost zero rate in pulmonary complications among this cohort of patients.

Complement-Mediation _____

Pulmonary dysfunction following bypass is one of the first indications that a complement-mediated allergic reaction is occurring. Numerous causes of complement activation have been identified as arising from CPB. Complement C3a and C5a act as spasmogens, stimulating the release of mast cell histamines which cause smooth muscle contracture and increased vascular per-

meability. The fact that anaphylatoxins are formed during cardiopulmonary bypass is supporting evidence that C3a conversion does occur during these procedures. C5a has the unique ability to interact directly with specific high affinity receptors on peripheral blood neutrophils. Binding of C5a initiates cellular responses including chemotaxis, lysosomal enzyme release, superoxide generation, autoregulation, and increased adherence.

Chenoweth observed an increase in plasma C3a levels within 10 minutes of the initiation of CPB when a nylon tricot containing bubble oxygenator was used and postulated that this may be a universal phenomenon.²⁰ Kreutzer's study appeared to bear this out. One cause of the apparent C3a activation may be blood-gas interface that exists with bubble oxygenation.²¹ Another possibility may lie in the materials used to make the oxygenator. Nylon tricot, like the nylon wool found in leukopheresis devices, serves as a potent complement activator. Hill found increased levels of C3a in patients when a nylon tricot oxygenator was used in comparison with a polyester oxygenator. He also observed a 4.5% postoperative pulmonary complication rate with the nylon oxygenator, whereas only 0.3% pulmonary complication rate occurred with the polyester oxygenator.²²

Platelet Activation and Survival _____

The platelets are also handled roughly during CPB.²³ Platelets react on contact with most foreign surfaces. They adsorb on the surface, and then either desorb or become activated and undergo denucleation.²⁴ Adenosine diphosphate (ADP), adenosine triphosphate (ATP), serotonin, catecholamines, and calcium (Ca^{++}) are released from storage granules within the platelet and can induce other platelets to aggregate.

Blood proteins suffer similar trauma. Any polymer surface exposed to the blood becomes coated with plasma proteins either by direct adsorption, or via mediation on contact with other formed elements, especially platelets. The polymer surface is then either rendered passive, as a consequence of adsorption, or actively thrombogenic.

The search is ongoing for better biomaterials that are less thrombogenic and less biologically active. Some of the least active surface materials include undiluted silicones, silicone rubber, and the polyether-polyurethanes due to their negative charge.²⁵ In qualifying the activity of a biomaterial, surface charge is an important consideration. If the charge is positive, both

the plasma proteins and formed elements, all of which carry a negative charge, will adsorb to it. If the biosurface is negatively charged, only the proteins will still adsorb to it because the surface of a protein is a mosaic of positive and negative charges. Hence, pretreatment with albumin during ECC may help to preserve the platelets and serum proteins, as the positively charged proteins in the albumin molecule will interact electrostatically with the negatively charged polyvinyl chloride and silicone rubber materials to form an albumin monolayer, thereby decreasing platelet destruction.²⁴

Heparin, a strongly negative polymer, is not effective in preventing platelet aggregation during CPB, as it prevents thrombin-induced platelet aggregation only, and platelet reactivity is not significantly altered. Consequently, with the exception of the inhibition of thrombin formation the presence of adequate amounts of heparin during CPB will not stop the interaction of platelets with the biomaterial.²³

Anticoagulant Drugs

The anticoagulant heparin was first isolated from canine liver by Dr. Howell in 1916 and administered to humans in 1935 by Best.^{26,27} Heparin is not a single chemical compound; rather it is a family of compounds which have an average molecular weight of 12,000 daltons. It is an anionic, sulfated glycosaminoglycan found in mast cells, and one of the strongest negatively charged polymers known. The anticoagulant activity of heparin requires the presence of antithrombin III.²⁸ Heparin acts as a catalyst that markedly accelerates the rate at which antithrombin III neutralizes thrombin and inactivates coagulation factor Xa. The form of heparin bound to the antithrombin III co-factor contains about 85% of the total anticoagulant activity. The remaining 15% is unable to bind to antithrombin III. This heparin-antithrombin III complex inhibits the activity of the other coagulation enzymes.²⁹

At least 11 proteins are involved in the coagulation scheme. Of these, six are ultimately activated to serine proteases (prothrombin, factors VII, IX, X, XI, and XII). With the exception of factor VII, also a serine protease, the heparin-antithrombin III complex has been found to be capable of neutralizing all of the other six activated coagulation enzymes. This complex, therefore, also inhibits the activation of fibrin stable-factor which prevents the formation of a stable fibrin clot.

Many factors can influence the activity of heparin: 1) dose; 2) mode of administration; 3) tissue source; 4) whether it is a Ca^{++} or Na^+ salt; and 5) molecular weight. Individual patient characteristics will also affect the activity of heparin. For example, platelet factor 4, a substance released from activated platelets, will neutralize heparin. An insufficient amount of antithrombin III will render heparin almost ineffective. In cirrhotic patients, the plasma half-life of heparin is increased, but it is decreased in patients with pulmonary embolism or liver impairment. With regard to the mode of administration, intravenous heparin administration is nearly instantaneous, whereas the subcutaneous route is much slower. There is no difference in blood levels with either Ca^{++} or Na^+ salt during I.V. administration. Na^+ salt heparin is absorbed more slowly from the subcutaneous site than the Ca^{++} salt. By PTT assay, the potencies of both porcine mucosal and lung heparin agree reasonably well. However, there is a marked increase in the potency of lung heparin when analyzed with the anti-Xa clotting assay. Thomas showed that low molecular weight heparin had a lesser effect than high molecular weight heparin.³⁰

The exact mechanism of the metabolism of heparin is not clear, but it is thought to be removed from the circulation by the reticuloendothelial system. Some heparin may localize on the arterial and venous endothelium, and some may be metabolized in the liver to uroheparin. Thomas concluded that "Even if it was possible to test each preparation of heparin in man, the difference between individuals will result in substantially different effects for the same lot of heparin." Therefore, it must be accepted that the heparin effect depends on the individual characteristics of the patient as much as on the concentration measured by an *in vitro* assay.

Other anticoagulant drugs are routinely used, some for their major action, and some for other effects. Aspirin, the salicylate ester of acetic acid, is a non-steroidal, anti-inflammatory drug that inhibits platelet aggregation by inhibiting prostaglandin synthesis. Aspirin also irreversibly acetylates and inactivates the enzyme cyclo-oxygenase in the circulating platelets. This effect lasts for four to seven days, depending on the remaining life span of the affected platelets. It is therefore advised that patients about to undergo CPB remain aspirin-free for seven days prior to surgery.

The effect of Coumadin (sodium warfarin) is slower and somewhat delayed in comparison with heparin. Coumadin interferes with vitamin K metabolism in the

liver, thus altering the synthesis of blood coagulation factor II (prothrombin), VII (proconvertin), IX (plasma thromboplastin), and X (Stuart-Prower). Coumadin prolongs the PT and PTT but can be reversed with adequate doses of vitamin K over several days.

Persantine is a coronary vasodilator which increases coronary blood flow and coronary sinus oxygen saturation. The dilatory effect of this agent is due to the accumulation of adenosine, a potent vasodilator. Persantine inhibits platelet aggregation caused by ADP and may increase the platelet count. It may also prolong platelet survival and has no effect on the prothrombin levels.

Protamine, an antagonist of heparin, is used to neutralize the effect of heparin. This simple, low molecular weight cationic protein acts by complexing with the strongly acidic heparin to form a stable salt. Protamine administration must be carefully monitored. If too small a dose is given, the anticoagulant effect will persist: too much, and protamine will act as an anticoagulant itself. Protamine inhibits the formation of thromboplastin, which in turn prevents the conversion of prothrombin to thrombin. It takes effect within 30 to 60 seconds of IV administration.

When the heparin-protamine salt is metabolized, some free heparin may be released, possibly accounting for the transient elevations in activated clotting times (ACT) seen postbypass. The phenomenon of heparin rebound is thought to be the result of either the metabolism of the salt and/or the relocation of the third-space heparin-containing fluids. Heparin rebound is most often seen 8-9 hours post surgery.

There are several known reactions to protamine.³¹ Patients with a history of seafood or fish intolerance should be highly suspected. The allergic reaction to protamine is manifested by rapidly developing hypotension due to vasodilation.³² Kurusz reported two patients having this type of reaction to protamine.³³ These individuals were also taking NPH insulin, and Kurusz theorized that because of the presence of protamine in NPH insulin, they had already become sensitized to it; hence the anaphylactic response when given the large dose of protamine necessary to reverse systemic heparinization. If protamine must be given to a patient who is suspect for a reaction, it should be administered intra-arterially.³²

Clotting Determination Techniques _____

An accurate means of determining the status of the patient's coagulation potential is extremely important

during CPB. Many different types of clotting tests have been used. The *Lee-White* whole blood clotting time was the first test introduced to measure anticoagulation. This test is unsatisfactory for a number of reasons. In the first place, it is extremely time consuming and the results are easily skewed with abnormalities in contact activation.

The activated partial thromboplastin time (APTT),³⁴ a commonly used coagulation assay, is sensitive to small amounts of circulating heparin, but shows considerable variation in the face of large heparin doses.

The activated clotting time (ACT) described by Hattersley³⁵ is performed on whole blood. The assay is terminated when a blood clot forms. The ACT was introduced in 1969 as a replacement for the Lee-White test. The normal range is 102-142 seconds (± 10) and the mean is 122 seconds on normal, unheparinized blood. The ACT permits quantitative analysis on discrete blood samples. The celite-activated test tube causes an intrinsically initiated clot. This test suffers somewhat in the presence of hemodilution, hypothermia, platelet dysfunction, and hypofibrinogen anemia,^{36,37} but data supplied by Congdon show that the ACT is linear throughout the range of heparin levels encountered.³⁴

Pharmacokinetics and Pharmacodynamics _____

The questions, how much heparin to give a patient in order to achieve systemic anticoagulation, or how much heparin antagonist to administer, are important issues in blood conservation. Properly controlled, little blood need be lost, but mishandled, monumental problems can occur. An empirical approach to heparin-protamine management is really not sufficient if the best of these protocols is only good enough to adequately protect 99% of the patients.³⁸ Bull et al.³⁹ advanced the technique of using dose-response curves to guide the administration of heparin. Constructing the dose-response curve for individual patients is really quite simple. Using the ACT (celite-activated clotting time), an initial control sample is measured and plotted on a graph. A dose of heparin, generally 2 mg/kg, is given and five minutes later another ACT is done to measure the patient's response.

Since the ACT is linear throughout the range of heparin levels, a straight line drawn between these two points can then be extrapolated outward until it intersects the desired ACT axis. From this, one can deter-

mine the amount of heparin required to reach a specific ACT level. Periodically throughout the procedure, an ACT is drawn, the results located on the dose-response curve, and the precise amount of heparin given to establish the acceptable ACT is known. By fitting a linear heparin-protamine titration curve along one axis, the amount of protamine necessary to reverse a given effect can also be predicted. Dearing et al.⁴⁰ reported that the individualization in management afforded by this technique significantly improved blood conservation. They reported a 50% reduction in blood usage using the dose-response curve technique.

Since the ACT is variously affected by hemodilution and hypothermia — two modalities common to CPB — its reliability during perfusion is somewhat questionable. Moreover, under these circumstances its use in conjunction with the heparin dose-response curve has been strongly criticized, since the heparin dose-response curve depends upon the ACT to calculate the neutralizing dose of protamine. Culliford,⁴¹ writing in 1980, found that the ACT neither accurately reflected the plasma heparin concentration, nor accurately predicted the necessary dose of protamine. In fact, they reported a 43% over-prediction for protamine and recommended an empirical approach to heparin neutralization.

Vertrees et al.⁴² realized advantages using Protamine Titration to derive protamine dosages. Hepcon^{®a} assays the amount of circulating heparin by means of heparin-protamine titration. Since protamine is an anticoagulant itself, an overabundance of either agent will impede clot formation.⁴³

In a comparison study of the Hepcon method and the empiric approach to heparin neutralization, Vertrees obtained the following results. In the empirical group (n = 36) 241 units of platelets and 113 units of fresh frozen plasma were required. Three patients (10%) were reoperated for bleeding (10%). Using Hepcon (n = 26), only 24 units of platelets and 18 units of fresh frozen plasma were used. No patients were returned to the operating room for bleeding. They also realized a 66% reduction in blood usage, from 7.3 to 4.8 units of RBC's per patient. Kemna has found that lower protamine doses and fewer reoperations due to bleeding were required when the heparin concentration was monitored with the Hepcon-heparin titration protocol.⁴⁴

Planning and Management in Blood Conservation Autotransfusion Systems (ATS)

If blood must be shed in the course of CPB, it makes sense that as much of it as possible should be salvaged and reused. In 1968, Klebanoff et al. invented a device that utilized a roller pump to return shed blood to a patient through a standard transfusion filter. This report signaled the beginning of the era of autotransfusion and the development of autotransfusion systems (ATS).⁴⁵

The first commercially available autotransfusion device, marketed by Bentley Laboratories, was an adaptation of Dr. Kelbanoff's device. The most serious draw-back of this ATS device was that it required a skilled technician in its operation. The patient was inadvertently systemically anticoagulated since heparin was used to keep the device free of clots. Instances of air and particulate emboli have been reported.⁴⁶ Although most problems with this device were probably due to operator error, it is no longer used or manufactured.

Noon and Sorenson Research developed a system in which a special aspiration tip was used to create an anticoagulation mixture of seven parts citrate to one part blood.⁴⁷ This mixture was in turn used to anticoagulate the collection chamber. After collection the chamber was disassembled and a portion of the mixture was then de-aired and reinfused back into the patient. The unit was recalled because of inconsistencies in delivering the proper citrate-phosphate-dextrose (CPD) ratio. Nevertheless, the Noon-Sorenson device had some favorable aspects. It caused little alteration in coagulation assays and only minor changes in hematocrit.⁴⁸

Subsequent alterations in the device resulted in the Sorenson Trauma ATS,^b which has been useful in collecting mediastinal drainage from chest tubes for reuse by the patient. Schaff et al. were able to reduce homologous blood use by nearly 50%, from 8.4 units to 4.2 units per patient.⁴⁹ Thurer et al. confirmed the safety of the Sorenson ATS, although they did not realize the tremendous savings in blood reported by Schaff.⁵⁰

At the 1985 meeting of the American Academy of Cardiovascular Perfusion, Toomasian et al. reported preliminary studies with an ATS^c currently in development in their laboratory.⁵¹ Toomasian and colleagues, studying 11 animals, have found little change in hema-

a Hepcon System 10, Hemotec, Inc., Englewood, CO 80112

b Sorenson Research Co., Inc., Salt Lake City, UT 84107

c Thoratec Bloodstat[™], Thoratec Laboratories, Berkeley, CA 94708

tology or coagulation profiles after 3 transfusions of total estimated blood volumes. ACT determinations have been only slightly prolonged, electrolytes have stayed within normal ranges, and no significant histopathologic changes have been noted.⁵²

Centrifugation Systems _____

Centrifugation and cell washing systems currently are the autotransfusion technique of choice.⁵³ Systems available include the Haemonetics Cell Saver^d and the Dideco Cell Saver.^e Some advantages of this form of cell recovery are the:

1. rapid availability of autologous blood
2. absence of transfusion disease
3. avoidance of transfusion reactions
4. reduction in net intra-operative blood loss
5. decreased demands on local blood banks
6. general acceptance by Jehovah's Witnesses

The proposed advantages of cell washing are that it removes 1) excess water, heparin, serum hemoglobin, bacteria, potassium, and other cellular debris, and 2) the cell concentrates usually have hematocrits in the range of 60-70% when infused.⁵⁴ Cell washing is not recommended, however, in the presence of contamination. Breyer et al. noticed a more complete removal of potassium and recommended cell washing particularly when potassium elimination is desired.⁵⁵

Centrifugation is one of the most commonly used form of red cell concentration. Not only does it permit the use of autologous red cells, but in doing so it also eliminates residual prime and washes out 88% of the heparin and microemboli. Some possible complications include the removal of formed elements and proteins lighter than the red blood cells (RBC), for example, serum proteins, white blood cells (WBC), free hemoglobin, fibrinogen, and other plasma coagulation factors.^{48,56-58} Unrestricted use of the centrifuge could possibly result in large serum protein losses, as well as a depletion of clotting factors. It does, however, sustain red cell volume without producing volume overload.

In centrifugal ATS, the blood flows continuously into a spinning Latham bowl. The revolutions cause the erythrocytes, leukocytes, platelets, and plasma to separate. In separating the formed elements from the plasma, the lighter constituents are displaced first as more volume is added to the spinning bowl. Reaves et

al. in 1976 used the IBM cell processor to salvage about 1,200 cc of blood from the oxygenator post-bypass.⁵⁹ From this salvaged volume, they were able to recover the equivalent of 2-3 units of red cells. They also noticed that in the process of washing the cells, they were able to eliminate much of the microemboli often found in dilute blood and the diluent itself. At approximately the same time, Tucker and Cohn, using the Haemonetics Cell Saver, reported a reduction in homologous blood requirements from 12 units per patient in 1970 to 4.8 units in 1973.⁶⁰ They reported that the Haemonetics Cell Saver was particularly useful for increasing the hematocrit. Moran et al. reported on the ability of the Haemonetics device to rapidly concentrate red cells.⁶¹ The average hematocrit of their post-centrifuged blood was 56%. They also found no significant red cell destruction or change in red cell integrity. Furthermore, 88% of electrolytes and heparin contained in the initial volume was eliminated. All told, they realized a 17% reduction in homologous blood usage.

Orr and Blanko demonstrated higher 2,3-diphosphoglycerate levels in centrifuged blood than in banked blood.⁶² They further demonstrated that the salvaged red cells had a greater resistance to osmotic stress than either banked blood or fresh erythrocytes. Lodge found that by using the cell saver and judiciously controlling the blood loss they were able to reduce blood usage from 4.3 units per patient to 1.9 units per patient in a pediatric population.

Vertrees et al. reported, in 1979, blood usage among cardiac surgery patients was decreased by 32% with the introduction of the cell saver.⁶³ The cell saver was used throughout the entire procedure for all suctioned blood, except for the cardiotomy suction. In 1981, Crodell and Lavender⁵⁴ compared three groups. In Group 1, no salvage techniques were used; in Group 2, blood salvage was performed before and after bypass and from shed mediastinal blood with a Sorenson Receptal ATS Mediastinal system; and in Group 3, blood salvage before and after bypass and postoperatively was accomplished with the cell saver. They showed that Group 2 (cell saver and ATS) and Group 3 (cell saver) required only one-third the amount of whole blood and one-fourth the amount of packed cells as Group 1 (no blood conservation techniques). There was no difference in hemoglobin or hematocrit or other laboratory data among the three groups, and no difference in costs. Nevertheless, Group 3 (centrifuge) required increased amounts of colloid.

^d Haemonetics Corporation, Braintree, MA 02184
^e Autotrans[®] bt7951A, Electromedics, Inc., Englewood, CO 80112

Breyer, in a prospective nonrandomized study carried out in 1985, compared 2 groups of patients. A group of 89 patients did not have the cell saver and required an average of 4-6 units of blood per patient postoperatively. A second group of 52 patients in which the cell saver was used required an average of only 3.0 units of blood per patient postoperatively. This is a savings of 35% in the cell saver group of patients, with no difference between these two groups for other blood products.⁶⁴

Hemofiltration

This technique has been borrowed from renal dialysis. Hemofiltration, also known as ultrafiltration or hemoconcentration, involves the selective removal of plasma water and dissolved solutes by ultrafiltration. This is a diffusive process with smaller molecules diffusing more rapidly than larger ones.⁶⁵ During its application, the cellular and protein content of the blood are preserved while plasma water and crystalloid solutes are eliminated. The technique of ultrafiltration, or hemoconcentration, is a convective process with plasma and dissolved solutes filtering at the same rate, limited only by the pore size of the device. Transmembrane pressure (TMP) is the driving force.

$$TMP = \frac{P_A + P_V + |P_N|}{2}$$

P_A = arterial (inlet) pressure mmHg
 P_V = venous (outlet) pressure mmHg
 $|P_N|$ = absolute pressure of any suction on the ultrafiltrate outlet

The rate of ultrafiltrate removal is a function of the TMP and pore size. The greater the TMP, the faster the rate of fluid removal. However, too great a TMP will cause significant red cell lysis. To avoid this problem it is probably sufficient to hold the TMP below 600 mmHg. The size of the pore through which the filtrate passes varies among manufacturers. One of these devices has a cut-off point of 16,000 daltons and the other, about 50,000 daltons. It is obvious that more blood elements will escape through the larger pore size. So, a careful choice includes the knowledge of what it is you wish to eliminate.

Currently, there are two general types of hemoconcentrator available, the parallel plate, and the hollow fiber (HF) instrument. The hollow fiber hemoconcentrator is more widely accepted because it is easy to use

and permits a larger surface area-to-volume perfusate, which results in more rapid elimination. No absolute contraindications have been found for this technique.

In 1976, Romagnoli et al. used an HF ultrafilter in 24 children and found 31% extraction of the diluting fluids in 11.4 minutes without any apparent changes in lab values.⁶⁶ Wolpoth et al., working on laboratory animals, found significant increases in the hematocrit (19 to 29%) and protein concentration (2.7 to 5.4 gm%) and no hemodynamic changes associated with the ultrafilter.⁶⁷ Russel and O'Bryan, using an ultrafiltration device, realized a 41.5% increase in hemoglobin values postbypass.⁶⁸ Breyer, Engelman, and associates were able to eliminate up to 5 liters of ultrafiltrate during double valve replacement.⁵⁵ This volume represented was due to the large amount of cardioplegia employed.⁶⁹

Sanford et al. considered the loss of plasma-containing clotting factors and platelets to be a disadvantage to the centrifugal means of salvage.⁷⁰ Thus, they were pleased with the platelet levels they were able to maintain using the hemoconcentrator (230,000 cm in the inflow line and 190,000 cm in the outflow line). The total protein rose from 3.3 to 6.7 gm%. They also experienced a rise of plasma-free hemoglobin from 91 to 283 mgm%, thought to be due to the concentration effects. Hopeck et al.⁷¹ found no difference in plasma-free hemoglobin levels. This could possibly be because of better control of the TMP. O'Gella reported no changes in ACT results in his series of patients.⁷²

In 1984 Tamari studied the effects of an ultrafilter to concentrate the contents of the oxygenator.⁷³ They attempted to concentrate the blood by 50% and experienced no increase in the plasma hemoglobin level. They also experienced no losses in hemoglobin, albumin, or fibrinogen, and only a 15% loss in platelets in the hemoconcentrator effluent blood.

Breyer et al. also observed a significant higher plasma-free hemoglobin level in the concentrates produced by the hemoconcentrator versus the cell saver (142 mg/dl vs. 35 mg/dl).⁵⁵ Nevertheless, the plasma levels in the two groups following bypass were essentially identical, 57.1 mg/dl in the cell saver versus 55.3 mg/dl in the ultrafilter group. The blood usage in the two groups was about 3.5 units per patient per stay in comparison to almost 6 units prior to the advent of either of these techniques.

Conclusion

Webster defines the term *conservation* as *the careful*

preservation and protection of something; as planned management of a natural resource, to prevent destruction.⁷⁴ This definition lies at the very heart of blood conservation, and efforts to conserve this natural human resource during operative procedures, such as CPB, assume ever increasing importance as funds to deliver medical technology and patient care become scarce resources in themselves. This review has focused on two aspects of blood conservation in cardiac surgery: 1) the technology, which has clearly proliferated, and 2) the planning and management required on the part of physicians, perfusionists and other health care workers to make the technology work. Dramatic reductions in average blood usage per patient per hospital stay in the current decade speak well for the application of blood conservation technology. Nevertheless, significant variation in data and opinion as to the best modality to use in a given clinical circumstance point to the need for continued dialogue and clinical documentation of the efficacy and use of blood conservation measures.

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