Use of Cellular and Plasma Apheresis in the Critically Ill Patient: Part 1: Technical and Physiological Considerations

Michael L. Linenberger, MD*‡
Thomas H. Price, MD†‡

Apheresis is the process of separating the blood and removing or manipulating a cellular or plasma component for therapeutic benefit. An apheresis procedure, or series of procedures, may be indicated in the critical care setting as primary or adjunctive therapy for certain hematologic, neurologic, renal, and autoimmune/rheumatologic disorders. Optimal management of severely ill patients undergoing apheresis requires a working knowledge of the technical, methodological, and therapeutic considerations. These considerations include instrument hardware and separation methods, vascular access requirements, hemodynamic and hemostatic effects of the procedures, exposure to anticoagulants and homologous blood products, physiological variables affecting blood/plasma processing efficiency, and therapeutic endpoints for specific indications. Part 1 of this review will discuss each of those technological considerations and the basic physiological principles that guide this form of therapy. Part 2 of this series will deal with the clinical indications and applications for specific disorders that are most likely to affect patients in the intensive care unit.

Key words: *apheresis, therapeutic plasma exchange, plateletpheresis, leukapheresis, red cell exchange*

Therapeutic apheresis involves the use of specialized instruments to selectively remove cellular constituents and/or higher molecular weight plasma solutes from the blood. In-line plasma treatment (to separate specific plasma constituents) or cellular immunomodulation methods have also been developed; however, those are either still predominantly investigational, used for special indications on an elective basis, or not widely used in the United States. For some severely ill patients, apheresis serves as the major therapeutic intervention. In other cases, cellular or plasma depletion is only one component of a multifaceted care plan. Indications for therapeutic apheresis have recently been categorized according to the quality of evidence for safety and efficacy from published clinical trials and experience [1]. However, utilization within critical care units may vary, based on availability and affordability of the procedures, regional practice patterns, and options for alternative treatments.

The instruments and treatment protocols used for therapeutic apheresis procedures perform consistently well for patients with stable hemodynamic and physiological parameters. However, such procedures may be inefficient, poorly tolerated, or less effective in a severely ill patient. For this reason, it is essential that the critical care team work closely with the physicians and nurses of the hospital apheresis service in the management of these patients.

From the *Seattle Cancer Care Alliance, Seattle, WA, the †Puget Sound Blood Center, Seattle, WA, and the ‡Department of Medicine, Division of Hematology, University of Washington, Seattle, WA.

Received May 5, 2004, and in revised form Jun 26, 2004. Accepted for publication Jul 9, 2004.

Address correspondence to Michael Linenberger, MD, Apheresis and Cellular Therapy, Seattle Cancer Care Alliance, 825 Eastlake Ave E., PO Box 19023, Seattle, WA 98109, or e-mail: linen@u.washington.edu.

We thank Dr F. Marc Stewart for his critical reading and helpful discussions, Mariola Blonska for her help in preparation of the manuscript, and Joni Kirschenman for assistance with the illustrations.

Linenberger ML, Price TH. Use of cellular and plasma apheresis in the critically ill patient**.** *J Intensive Care Med.* 2005;20:18-27.

DOI: 10.1177/0885066604271394

Apheresis Technology and Procedural Issues

Instruments and Methodologies

The most commonly used instruments for therapeutic apheresis separate the cellular and fluid components of extracorporeal blood by centrifugation, exploiting the relative differences in the specific gravities of the various fractions (Table 1).

Table 1. Relative Densities of Plasma and Peripheral Blood Cellular Components

Component	Relative Specific Gravity	
Plasma	1.025-1.029	LIGHT
Platelets	1.040	
Mononuclear cells (lymphocytes, myeloblasts, monocytes)	1.050-1.066	
Granulocytic precursors	1.070-1.080	
Bands and neutrophils	1.087-1.092	
Erythrocytes	1.078-1.114	HEAVY

Apheresis instruments that use centrifugation physically separate these components based on their relative specific gravities, allowing selective removal of a particular fraction.

Blood flows from the patient to a rapidly spinning centrifuge, the component targeted for removal is diverted to a collection container, and the rest of the blood is returned to the patient [2,3]. Such machines can usually be adapted for either plasmapheresis or cytapheresis procedures.

Centrifugation instruments process blood using either a discontinuous or a continuous method. With discontinuous (or intermittent) apheresis, a discrete volume of blood is drawn into the chamber, separated, collected, and then returned (with replacement fluid) before a subsequent volume of blood is drawn and processed. Continuous-flow methods draw blood without interruption into the extracorporeal circuit while it is being separated, collected, and reinfused. Some instruments can be programmed to perform either a continuous-flow or an intermittent process, whereas others are designed for only one method. The extravascular blood volume requirements differ among the disposable sets used by individual centrifugation instruments for specific applications.

Extracorporeal plasma separation may also be achieved by membrane filtration, with the membrane configured as either a hollow fiber or a flat plate [2,3]. The pore size of such filters, 0.2 to 0.6 microns, excludes erythrocytes, leukocytes, and platelets (which have mean sizes of 7, 10-13, and 3 microns, respectively), allowing separation of the patient's plasma from the other components of the blood. The limitation of the membrane technology is that it can only be used to isolate plasma. Centrifugal based equipment is required for cytapheresis procedures.

In the United States and Canada, centrifugal cell separators are the dominant technology. Membrane filters are in use, for the most part, in Europe and Asia. Whichever technology is used, the basic scheme of component removal is the same (Fig 1A). Blood is drawn from the patient, mixed with an appropriate amount of anticoagulant, and delivered to the separation device. The component of interest is diverted to a collection bag (in the case of a membrane filtration device, the collected component must be plasma), and the residual blood components are mixed with additional replacement fluid (if appropriate) and returned to the patient. The procedures usually require blood flows of 50 to 150 mL/min and last approximately 2 to 3 hours.

Specialized plasmapheresis methods have also been developed with the goal of more selectively removing the purported pathophysiological substances from the separated plasma (Fig 1B). Some of these techniques are relatively crude. The collected plasma may be passed through a hollow fiber filter apparatus in which the pore size is reduced to retain higher molecular weight substances such as immunoglobulin (Ig) M or immune complexes [4]. Alternatively, the plasma may be cooled to effect the precipitation of cryoproteins, which can then be removed [4,5]. More sophisticated techniques effect the selective removal of specific targeted substances from the patient's plasma by means of physicochemical separation or absorption to an immobilized ligand [2,4,6-11]. Adsorption columns have been designed to remove (1) IgG and immune complexes (using immobilized *Staphylococcus aureus* protein A); (2) low-density lipoprotein (LDL) (using immobilized anti-LDL antibody or dextran sulfate); (3) anti-DNA and anticardiolipin antibodies (using immobilized dextran sulfate); (4) nonspecific Ig (using immobilized anti-Ig antibody); and (5) endotoxin, inflammatory cytokines, and mediators of sepsis (using immobilized polymyxin B or other adsorbers) [7-10]. Aside from the staphylococcal protein A and dextran sulfate columns, which have been approved by the Food and Drug Administration, these systems have been predominantly tested and used outside the United States.

With any of these selective techniques, the advantage over the simple plasma separation procedures is that the treated plasma, from which the harmful substances have been removed, can serve as the replacement fluid, obviating the need to use either albumin solution or allogenic plasma for this purpose. The disadvantages in comparison to simple plasma exchanges are 2-fold: (1) the efficiency of removal of the pathologic substance is lower, and (2) the technique requires that one knows

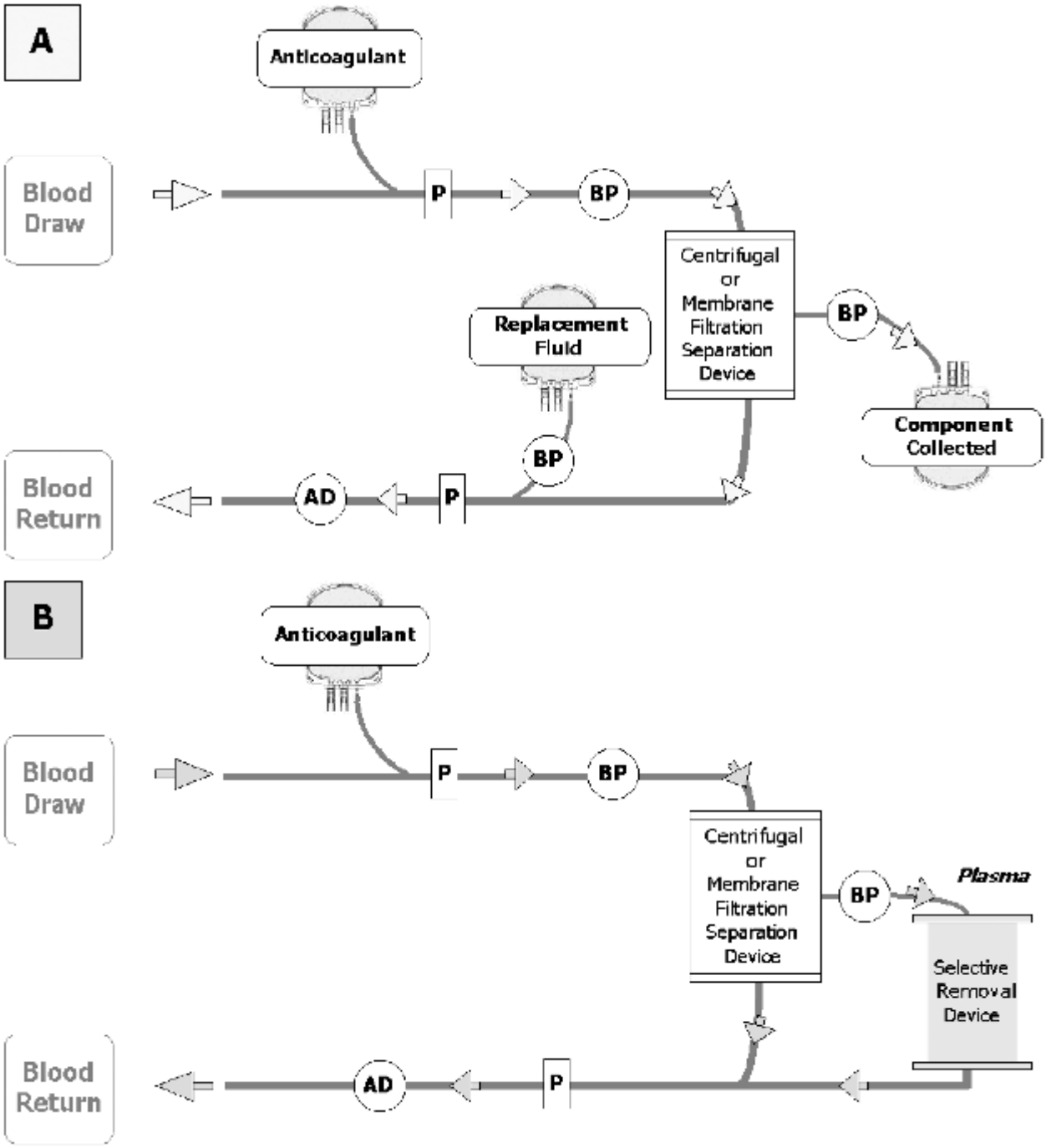

Fig 1. (A) Basic scheme of component removal in therapeutic apheresis procedure. An anticoagulant is added to the patient's blood as it is drawn and pumped to the separation device. The component to be collected is pumped from the device to a collection bag, and the remainder of the blood is returned, along with appropriate replacement fluid, to the patient. (B) Scheme for selective removal of pathogenic substance from the patient's plasma. The patient's anticoagulated blood is pumped to the separation device, and separated plasma is then delivered to the selective removal device. The purified plasma is then combined with the cellular portion of the patient's blood and returned to the patient. P = pressure monitor; BP = blood pump; AD = air detector.

what one is trying to remove. Unfortunately, the nature of the inciting substance is not well understood in many of the disorders treated by these apheresis procedures. In some centers, plasma separation methods have been combined with hemodialysis, hemoperfusion, or hemofiltration to

treat acute fulminant hepatic failure or sepsis syndrome [6,12-14].

Vascular Access

Adequate venous access is required to accommodate the high flow rates necessary to process at least 1 blood volume over the course of a few hours. Intermittent apheresis procedures require a single large vein. Continuous-flow procedures require 2 venous access sites. With either method, the draw site must withstand the negative pressures associated with inlet rates ranging from 50 to 150 mL/min. Similarly, the return vessel must accommodate flow rates of up to 120 mL/min.

Antecubital and forearm veins may be adequate for patients with large veins and for whom large numbers of procedures are not required. For adults, a 16- to 18-gauge Teflon or silicone coated steel, back-eye apheresis or dialysis-type needle is required for the draw line. For pediatric patients, an 18-gauge butterfly may be used. A 16- to 20-gauge needle, a plastic peripheral venous catheter, or a central catheter port may be used for the return line. If a continuous-flow procedure is required and only one extremity is available, the return line should be placed in a vein that is proximal to the draw line to avoid recirculation. Plastic peripheral or central venous catheters (eg, peripherally inserted central catheter lines) are not suitable for draw access because they collapse under the high inlet negative pressure.

A large-bore central venous catheter is required for patients with inadequate peripheral venous access and is usually necessary to efficiently treat critically ill patients [15]. Fluoroscopic or sonographic guidance optimizes the chances for successful placement with a single pass (≥80%) and minimizes the complication rate (<5%) [16]. The physician should consider a number of clinical factors in determining the type of catheter to be placed. For urgent procedures, short-term therapy, and pediatric patients, a femoral line may be the best option. For patients with nonurgent indications who are likely to require long-term therapy, placement of a tunneled catheter will minimize the likelihood of needing a second line placement. Double-lumen apheresis or dialysis catheters are ideal for continuous-flow procedures, whereas a single-lumen catheter is adequate for intermittent processing. For continuous-flow procedures, the proximal port serves as the draw line and the distal port for blood return. Catheters for adults or children weighing more than 40 kg should be at least 11.5 F. Children weighing 20 to 40 kg or less than 20 kg can be treated using 10-F or 8-F catheters, respectively. A 13.5-F tunneled double-lumen apheresis catheter (eg, placed to collect peripheral blood stem cells for an autologous transplant) or an arteriovenous fistula or graft, created for dialysis access, can be used for therapeutic apheresis.

Anticoagulants

To prevent extracorporeal clotting, an anticoagulant is usually added to the patient's blood as it is withdrawn. A buffered dextrose solution containing citrate (acid citrate dextrose [ACD]), which chelates ionized plasma calcium, is the most commonly used anticoagulant for centrifugation apheresis procedures. Unfractionated heparin may also be used, either alone or in combination with ACD. Heparin is the anticoagulant of choice for membrane plasma separation methods. Under special circumstances, a patient may be systemically anticoagulated with heparin, thereby obviating the need for extracorporeal anticoagulation. This latter approach requires careful monitoring and incurs a higher potential risk of bleeding.

Heparin is metabolized within 30 to 60 minutes after completion of the procedure. The half-life of citrate is approximately 30 minutes in patients with normal liver and renal function. Citrate metabolism is severely impaired and plasma ionized calcium levels are significantly reduced in patients with acute hepatic failure undergoing therapeutic plasma exchange [17]. Citrate-induced metabolic alkalosis can develop in patients with renal failure. In contrast to heparin, citrate infusion does not induce an anticoagulant effect in vivo.

The adverse effects of extracorporeal anticoagulant drugs relate to their concentration in the reinfusate and rate of delivery [18]. More citrate is delivered with procedures requiring a larger process volume, longer duration, and use of homologous blood and/or plasma products (which are collected and stored in citrate). Although modern apheresis instruments automatically adjust the extracorporeal ACD infusion rate when homologous blood products are a part of the return fluid, clinical signs of toxicity occur in roughly 0.8% to 1.2% of therapeutic procedures [19-21].

Symptoms and signs of citrate toxicity include a metallic taste in the mouth, perioral numbness, distal paresthesia, muscle twitching, spasm, nausea, tetany, and prolonged Q-T interval. Hypokalemia and hypomagnesemia may also occur [18,21]. In

noncommunicative critically ill patients, a decrease in blood pressure, subtle electrocardiographic change, arrhythmia, or agitation may be the only clues to citrate toxicity. Mild signs and symptoms usually resolve by simply lowering the blood flow rate. Interrupting the blood flow for a few minutes allows time for metabolism of the citrate. In more symptomatic patients or those at greater risk of adverse effects, ionized calcium should be monitored and/or prophylactic or supplemental infusions of calcium chloride or calcium gluconate should be given [22,23]. These infusions should be administered through the distal return line and not mixed with citrate-containing return fluid. Albumin replacement fluid does not contain citrate but may lead to hypocalcemia because of avid calcium binding [20,23]. For this reason, supplemental calcium is often added to albumin return fluid during plasma exchange procedures.

Continuous reinfusion of extracorporeal heparin during apheresis procedures prolongs the clotting time. Patients at high risk for bleeding (eg, those with coagulopathies or with severe thrombocytopenia) or with concerns of heparin sensitivity (eg, heparin-induced thrombocytopenia) should undergo apheresis exclusively with ACD. If heparin is required in a patient with a high risk of bleeding, the activated clotting time should be closely monitored. Heparin-induced bleeding may be reversed with protamine.

Extracorporeal Blood Volume Processing and Fluid Balance

Minor shifts in intravascular volume and/or oxygen-carrying capacity must be considered in the procedure plans for severely ill patients requiring therapeutic apheresis [24]. The American Association of Blood Banks has recommended that the extracorporeal volume not exceed 15% of the total blood volume (TBV) for general procedures and blood collection. Even this limit may not be tolerated by patients with preexisting hemodynamic instability and/or those requiring ongoing vasopressor support. Recent large retrospective surveys revealed that hypotension or vasovagal phenomena occur in roughly 0.5% to 1% of therapeutic apheresis procedures [19,20]. Higher rates occur during intermittent flow procedures because the extracorporeal volumes are larger and because maximum and minimum extracorporeal volumes are experienced with each cycle.

Table 2. Weight-Based Determination of Total Blood Volume

	Blood Volume (mL/kg of Body Weight)			
	Fat	Thin	Normal	Muscular
Male	60	65	70	75
Female	55	60	65	70

Children: preterm: 100; birth to 4 months: 85; 4 months to 10 years: 80; >10 years: 75

The total blood volume (TBV) is calculated using a conversion factor determined by age (in children) or sex and body habitus (TBV = weight × blood volume conversion factor).
Adapted from Gilcher RO. Apheresis: principles and practices. In: Rossi EC, Simon TL, Moss GS, Gould SA, eds. *Principles of Transfusion Medicine*. 2nd ed. Baltimore, Md: Williams & Wilkins; 1996:537-545.

Total blood volume is calculated according to sex, age, and body habitus (Table 2). The red cell volume is a product of the hematocrit and TBV (ie, TBV × hematocrit ÷ 100). The separation chambers in centrifugal apheresis instruments require specific volumes of packed red cells to establish and maintain the separation gradients [2]. These values vary widely among the available instruments, and different separation chambers designed for a single instrument often require different red cell volumes. The expected maximum extracorporeal volume for the procedure depends on this red cell value as well as the patient's hematocrit. For example, if the extracorporeal red cell volume required by the instrument is 200 mL and the patient's hematocrit is 40%, 500 mL of the patient's blood must be removed before the interface is established, an amount usually well tolerated by a hemodynamically stable 60-kg adult. On the other hand, if the patient's hematocrit is 20%, the extracorporeal volume required to fill the separation chamber will be 1000 mL, an amount not so easily tolerated.

If the volume of the patient's blood needed to fill the separation chamber is excessive, 2 options are available. The first is to administer additional fluid to the patient, either colloid or crystalloid, while the patient's blood is filling the chamber. With this technique, the patient is more euvolemic during the procedure. However, one needs to consider the patient's ability to tolerate the expansion of intravascular volume when red cells in the separation chamber are reinfused at the completion of the procedure. A second option is to prime the separation chamber with allogenic red cells and to discard the red cells in the separation chamber at the end

of the procedure. The advantage of this option is that the patient can be maintained essentially euvolemic through to completion of the procedure. The disadvantage is that the patient is exposed to an allogenic blood component. This second method is most appropriately used in children, usually those who weigh less than 25 kg, in whom large shifts in intravascular volume are less well tolerated.

An additional consideration is the net fluid balance at the end of the procedure. The volumes of fluids extracted and returned during apheresis can be adjusted by the operator, or automatically, to achieve a final net positive, even, or negative balance. Retention fluid, which is collected and discarded, may consist of red cells, platelet-rich plasma, leukocytes, and/or platelet-poor plasma. The reinfusate consists of replacement fluid, including anticoagulant solution, auxiliary crystalloid, colloid solution, or allogenic red cell or plasma products, along with the autologous blood cells and plasma that are not retained. The final fluid balance equals the volume of reinfusate fluids minus the volume of retained components. A safe, acceptable end-positive or end-negative net fluid balance, for patients without concerns for hypovolemia or circulatory volume overload, is ±10% to 15% of the TBV. For patients with baseline dehydration or hypovolemia, such as might occur with nephrotic syndrome, additional crystalloid or colloid can easily be supplied as part of the procedure. Allogenic red cells could also be given to severely anemic patients with the replacement fluid, but these are more appropriately transfused before (preferable) or after the procedure. It is usually not possible to remove large amounts of fluid (ie, >200-400 mL, or volumes achievable with hemodialysis) with plasma exchange procedures because the deficit is colloid rather than crystalloid, and hypotension is likely to occur. Patients with decompensated congestive heart failure, pulmonary edema, or anuric renal failure are usually managed by methods to maintain euvolemia during the procedure, as outlined previously.

Blood Product Exposure and Pharmacological Considerations

Allogenic blood products may be required for various therapeutic apheresis procedures in the critical care setting. Red cells are administered during therapeutic red cell exchange. Fresh frozen plasma (FFP) or cryo-poor plasma may be indicated as part of the replacement fluid during plasma exchange. These components are infused rapidly, and the apheresis operator and critical care team must be vigilant for signs of transfusion reactions that may be difficult to differentiate from circulatory overload, infection, or disease-related complications [25]. Patients with anemia, thrombocytopenia, or certain coagulopathies may require adjunctive transfusions of red cells, platelets, plasma, or cryoprecipitate. In most cases, these components are best transfused after the apheresis procedure has been completed.

The half-life and efficacy of certain pharmaceutical drugs may be affected by the removal of large amounts of plasma during plasma exchange. In general, this applies to drugs that are highly protein bound. Because of the high volume of distribution, agents that are free in the plasma or lipid-soluble are not appreciably altered. These relationships are not well understood for most drugs. It is thus generally prudent, when possible, to administer drugs after the plasma exchange has been completed. Another pharmacological consideration is that patients using angiotensin-converting enzyme (ACE) inhibitors are predisposed to profound bradykinin release, resulting in flushing, hypotension, nausea, and vomiting when treated with staphylococcal protein A immunoadsorption [23]. For that reason, ACE inhibitors should be held for 48 hours before those procedures.

Apheresis Physiological Principles

The ability of an apheresis procedure to effectively reduce a pathological cellular or plasma constituent depends on the intravascular (vs extravascular) distribution of the target constituent and the kinetics of production and catabolism (ie, intravascular half-life) [26,27]. Soluble macromolecules with predominant intravascular distribution are more rapidly depleted by daily plasma exchanges than solutes that distribute widely in the extravascular tissues. Extravascular molecules are inaccessible to removal by apheresis, and they serve as reservoirs to replenish the circulation (by reequilibration). Normal IgM, IgD, and fibrinogen have relatively large intravascular fractions (75% to 80%), whereas IgG, IgA, albumin, and the C3 component of complement are more balanced between the 2 compartments (ie, 47% to 60% intravascular distributions).

Because plasma exchange removes large molecules at a rate that greatly exceeds their natural syn-

thetic and clearance rates, a simple "1-compartment" mathematical model has been used to predict the depletion of soluble plasma substances [26,27]. This model assumes that the intravascular compartment is unaffected by the homeostatic influx or catabolism of constituents. As an example, a single 1-vol plasma exchange (ie, approximately 40 mL/kg), using a continuous flow method with 5% albumin replacement fluid, will remove approximately 63% of the IgM and IgG found in the intravascular compartment [27]. More important, the whole-body IgM and IgG levels will be reduced by only 47% and 28%, respectively, because of the contribution of extravascular proteins. By comparison, a 1.5-vol plasma exchange (ie, approximately 60 mL/kg) will remove roughly 78% of the intravascular immunoglobulins [27] and will decrease the whole-body IgM and IgG levels by 59% and 35%, respectively.

Complete reequilibration of macromolecules occurs between the extravascular and intravascular compartments roughly 48 hours after a plasma exchange. The effect of repeated procedures can, therefore, be predicted using the 1-compartment model (Fig 2A). For example, a therapeutic endpoint for some autoimmune neurological diseases, such as acute inflammatory demyelinating polyradiculopathy (ie, Guillain-Barré syndrome), is to reduce the whole body Ig levels by 85% to 90% [28]. Based on predictions of a 1-compartment model, three to four 1-vol plasma exchanges will be required to deplete whole-body IgM, whereas 6 to 7 procedures will be required to reduce IgG by that amount. By comparison, 1.5-vol exchanges will achieve those levels of IgM and IgG after only 3 and 5 procedures, respectively (Fig 2B). The 1-compartment model is less reliable at predicting the therapeutic benefit for molecules with rapid synthetic rates and for cases with "rebound" Ig production [29].

The efficiency of cell depletion by cytapheresis is less predictable than solute removal by plasma exchange. Leukemic blasts or abnormal platelets may be inaccessible because of their propensity to sequester within the spleen and/or to adhere to the vascular endothelium. Depletion efficiency is also affected by the TBV of the patient, the rates of production and release from extravascular sites, and the volume of blood processed. Despite the uncertainty, a cytapheresis procedure that processes 1.5 to 2 blood volumes can be expected to remove roughly 35% to 85% of the leukocytes or platelets [30]. Effective therapeutic red cell exchange may also be somewhat unpredictable because of splenic sequestration, which occurs in young patients with sickle cell crisis or in patients with massive intravascular hemolysis due to erythrocyte protozoal infection (eg, with *Plasmodium falciparum* and *Babesia* species) [31].

Effects of Apheresis on Hemostasis

With most plasma exchange procedures, the replacement fluid, usually a combination of albumin and saline, contains no coagulation factors. As a result, plasma levels of these factors are reduced in proportion to the intensity of the exchange. With a typical 1.3-vol plasma exchange, one can expect the immediate postexchange levels of most factors to be approximately 25% of their preprocedure values. The exceptions are factors VIII and IX, which are reduced to lesser degrees, because of their increased vascular distribution and/or mobilization during the exchange procedure. Subsequent recovery of these factor levels is largely dependent on the normal synthetic rate of the individual factor. Most factors will have returned to their baseline values by 24 hours. Fibrinogen, the factor with the longest synthetic half-life, usually takes about 3 days. Lower factor levels may be encountered when additional plasma exchanges are performed before the factor levels have returned to baseline. Because fibrinogen levels are the most severely affected over the course of a series of plasma exchanges, preprocedure fibrinogen levels should be monitored to determine the risk of hemostatic compromise.

The importance of coagulation factor depletion by plasma exchange depends on the clinical situation. Most patients with no underlying hemostatic risk tolerate these changes well and require no supplementation with coagulation factors. In these cases, it is sufficient to monitor the preexchange fibrinogen levels; if less than 140 to 150 mg/dL, the volume of the exchange should be reduced, the frequency should be decreased, or FFP should be included as part of the replacement fluid. In patients with underlying increased bleeding risk (eg, severe thrombocytopenia, pulmonary hemorrhage), it is reasonable to include 25% FFP replacement to ensure adequate postexchange hemostasis.

A particularly challenging problem arises when plasma exchange is required for a patient who is anticoagulated with warfarin. Ideally, one would like to maintain a steady therapeutic level of anticoagulation. Exchange without incorporating FFP into the replacement fluid will substantially reduce

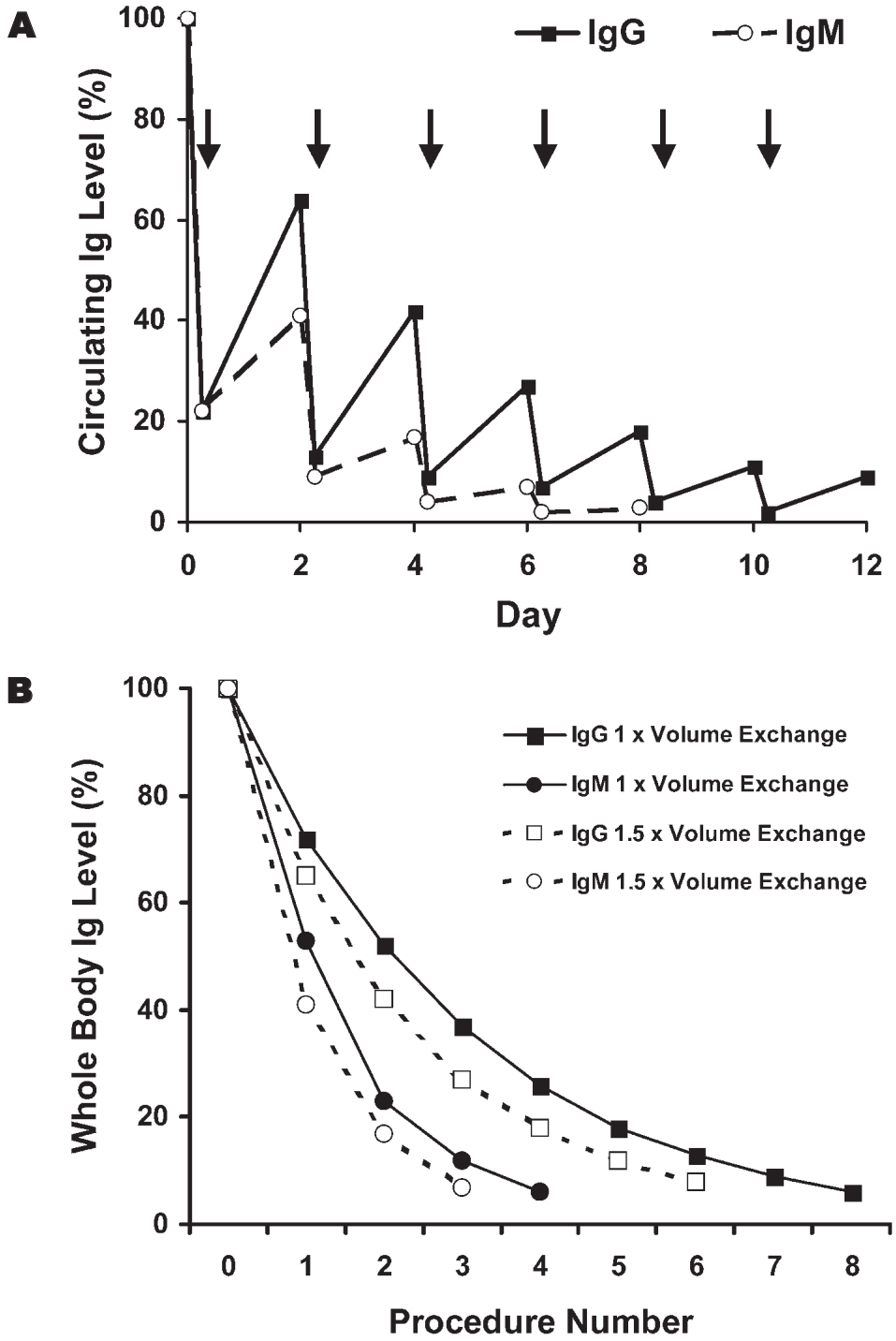

Fig 2. Hypothetical depletion of whole body immunoglobulin (Ig) levels by therapeutic plasma exchange (TPE), using a continuous flow method, performed every 2 days, as predicted by a 1-compartment model and using known intravascular/extravascular distribution ratios for IgM and IgG (see text). (A) Decreases in Ig levels after 1.5-vol exchanges (designated by arrows) and the effects of reequilibration prior to the next exchange. (B) Progressive depletion of whole-body Ig levels with 1-vol or 1.5-vol TPE. These curves assume that there is negligible input or loss to the whole-body Ig levels by synthesis or catabolism.

the levels of coagulation factors and will result in an excessively anticoagulated patient. Alternatively, too much FFP replacement will leave the patient inadequately anticoagulated. It is difficult to predict with confidence where the balance lies, but a reasonable estimate is that using FFP as replacement

for the last 10% to 15% of the exchange will likely leave the patient in the desired range. Preexchange and postexchange coagulation screen measurements allow one to titrate the volume of plasma to the desired amount. Another approach to this problem is to switch the patient to heparin anticoagulation and determine the amount of plasma replacement required by monitoring the fibrinogen level, as discussed previously.

Plasma exchange may also reduce the patient's platelet count by 10% to 20% because the platelets are not completely separated from the plasma in the apheresis machine. Similarly, therapeutic leukapheresis, which might be indicated for leukostasis complications associated with acute myeloid leukemia, retains a significant number of platelets and reduces the patient's platelet count by 30% to 50%. These effects must be anticipated in patients starting an apheresis procedure with significant thrombocytopenia, and preparations should be made for platelet transfusion support, as indicated, after a procedure is completed.

Consultation With the Apheresis Service

Although the critical care physician should have a basic understanding of the issues discussed here, it is essential that apheresis therapy be a cooperative effort between the patient's physician and the physicians and nurses of the hospital apheresis service. The apheresis service may reside in a hospital clinical department, within the hospital transfusion service, or perhaps at the regional blood center. The first step is usually a consultation with the apheresis medical director to discuss the patient's diagnosis and general clinical condition, hemostatic issues, evidence that apheresis is likely to be beneficial, treatment plan, impact of apheresis on other treatment modalities, volume management, use of blood components, and vascular access. This partnership must then continue through the patient's course so that appropriate adjustments can be made to optimize the therapy.

References

1. Smith JW, Weinstein R, for the AABB Hemapheresis Committee KL. Therapeutic apheresis: a summary of current indication categories endorsed by the American Association of Blood Banks and the American Society for Apheresis. *Transfusion*. 2003;43:820-822.
2. Burgstaler EA. Current instrumentation for apheresis. In: McLeod BC, Price TH, Weinstein R, eds. *Apheresis: Principles and Practice*. 2nd ed. Bethesda, Md: American Association of Blood Banks; 2003:95-130.
3. Madore F. Plasmapheresis. Technical aspects and indications. *Crit Care Clin*. 2002;18:375-392.
4. Siami GA, Siami FS. Membrane plasmapheresis in the United States: a review over the last 20 years. *Ther Apher*. 2001;5:315-320.
5. Drew MJ. Plasmapheresis in the dysproteinemias. *Ther Apher*. 2002;6:45-52.
6. Hirasawa H, Sugai T, Oda S, et al. Efficacy and limitation of apheresis therapy in critical care. *Ther Apher*. 1997;1:228-232.
7. Hart GK. Plasmapheresis in intensive care. Part 2 of 2: indications for plasmapheresis and plasma exchange in the intensive care unit. *Intensive Care World*. 1990;7:80-84.
8. Schmidt J, Mann S, Mohr VD, Lambert R, Firla U, Zirngibl H. Plasmapheresis combined with continuous venovenous hemofiltration in surgical patients with sepsis. *Intensive Care Med*. 2000;26:532-537.
9. Reeves JH, Butt WW, Shann F, et al. Continuous plasmafiltration in sepsis syndrome. Plasmafiltration in Sepsis Study Group. *Crit Care Med*. 1999;27:2096-2104.
10. Hart GK. Plasmapheresis in intensive care. Part 1 of 2: history, techniques and complications. *Intensive Care World*. 1990;7:21-25.
11. Kodama M, Hanasawa K, Tani T. Blood purification for critical care medicine: endotoxin adsorption. *Ther Apher*. 1997;1:224-227.
12. Yang KS, Kenpe K, Yamaji K, Tsuda H, Hasimoto H. Plasma adsorption in critical care. *Ther Apher*. 2002;6:184-188.
13. Stegmayr BG. Apheresis as therapy for patients with severe sepsis and multiorgan dysfunction syndrome. *Ther Apher*. 2001;5:123-127.
14. Vamvakas EC, Pineda AA. Selective extraction of plasma constituents. In: McLeod BC, Price TH, Weinstein R, eds. *Apheresis: Principles and Practice*. 2nd ed. Bethesda, Md: American Association of Blood Banks; 2003:437-476.
15. Schonermarck U, Bosch T. Vascular access for apheresis in intensive care patients. *Ther Apher Dial*. 2003;7:215-220.
16. Sadler DJ, Saliken JC, So CB, Gray RR. Apheresis: another indication for radiologically placed central venous catheters. *Can Assoc Radiol J*. 1999;50:177-181.
17. Apsner R, Schwarzenhofer M, Derfler K, Zauner C, Ratheiser K, Kranz A. Impairment of citrate metabolism in acute hepatic failure. *Wien Klin Wochenschr*. 1997;109:123-127.
18. Crookston KP, Simon TL. Physiology of apheresis. In: McLeod BC, Price TH, Weinstein R, eds. *Apheresis: Principles and Practice*. 2nd ed. Bethesda, Md: American Association of Blood Banks; 2003:71-94.
19. McLeod BC, Sniecinski I, Ciavarella D, et al. Frequency of immediate adverse effects associated with therapeutic apheresis. *Transfusion*. 1999;39:282-288.
20. Korach JM, Berger P, Giraud C, Le Perff-Desman C, Chillet P. Role of replacement fluids in the immediate complications of plasma exchange. French Registry Cooperative Group. *Intensive Care Med*. 1998;24:452-458.
21. Schlenke P, Frohn C, Steinhardt MM, Kirchner H, Kluter H. Clinically relevant hypokalaemia, hypocalcaemia, and loss of hemoglobin and platelets during stem cell apheresis. *J Clin Apheresis*. 2000;15:230-235.
22. Mokrzycki MH, Kaplan AA. Therapeutic plasma exchange: complications and management. *Am J Kidney Dis*. 1994; 23:817-827.
23. Weinstein R. Hypocalcemic toxicity and atypical reactions in therapeutic plasma exchange. *J Clin Apheresis*. 2001;16:210-211.
24. Jones HG, Bandarenko N. Management of the therapeutic apheresis patient. In: McLeod BC, Price TH, Weinstein R, eds. *Apheresis: Principles and Practice*. 2nd ed. Bethesda, Md: American Association of Blood Banks; 2003:253-282.

25. Goodnough LT, Brecher ME, Kanter MH, Au Buchon JP. Transfusion medicine. First of two parts—blood transfusion. *N Engl J Med*. 1999;340:438-447.
26. Weinstein R. Basic principles of therapeutic blood exchange. In: McLeod BC, Price TH, Weinstein R, eds. *Apheresis: Principles and Practice*. 2nd ed. Bethesda, Md: American Association of Blood Banks; 2003:295-320.
27. Brecher ME. Plasma exchange: why we do what we do. *J Clin Apheresis*. 2002;17:207-211.
28. McLeod BC. Therapeutic plasma exchange in neurologic disorders. In: McLeod BC, Price TH, Weinstein R, eds. *Apheresis: Principles and Practice*. 2nd ed. Bethesda, Md: American Association of Blood Banks; 2003:321-344.
29. Dau PC. Immunologic rebound. *J Clin Apheresis*. 1995;10:210-217.
30. Hester J. Therapeutic cell depletion. In: McLeod BC, Price TH, Weinstein R, eds. *Apheresis: Principles and Practice*. 2nd ed. Bethesda, Md: American Association of Blood Banks; 2003:283-294.
31. Pepkowitz S. Red cell exchange and other therapeutic alterations of red cell mass. In: McLeod BC, Price TH, Weinstein R, eds. *Apheresis: Principles and Practice*. 2nd ed. Bethesda, Md: American Association of Blood Banks; 2003:411-436.