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Intraoperative Blood Conservation—Every Cell is Sacred

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Learning Objectives: To give the reader an understanding of 1) cell salvage efficiency and how it might be optimized, 2) the use of cell salvage in trauma surgery, and 3) the complications associated with cell salvage and how they might be avoided.

Abstract
Awareness of the negative impact of allogeneic blood transfusion on patient outcome is increasing. Many strategies can be used to minimize or eliminate allogeneic transfusion. These strategies include preoperative anemia optimization, intraoperative hemodilution, point of care laboratory testing, and cell salvage. The technique that offers the greatest blood avoidance ability is cell salvage. This article discusses how cell salvage can be maximized, the safety of this technique in trauma surgery, and the complications associated with its application.

In recent years, an evolving understanding of the consequences of allogeneic blood transfusion has resulted in an interest in blood conservation. This understanding includes a recognition of the immunosuppressive effects of allogeneic transfusion,[1] recognition of the constantly changing risks of transmission of bacterial and viral disease,[2] and a growing awareness of transfusion-related acute lung injury.[3] More recently, interest has focused on the effect of stored blood on the microcirculation. It appears from animal models that our goal of enhancing oxygen delivery through transfusion may not actually be improving tissue oxygen levels. In these models, functional capillary density and tissue oxygenation actually fall following the transfusion of stored blood.[4,5] In addition, an allogeneic blood shortage[6] and rising costs of blood products have made many hospital administrators take note of the impact that allogeneic blood has on their balance sheet.

Multiple strategies can be applied to avoid allogeneic transfusion. The primary strategies involve preoperative erythropoietin and iron supplementation, preoperative autologous donation, acute normovolemic hemodilution, and the application of cell salvage systems. These strategies are outlined in Table 1. From mathematical modeling, it would appear that cell salvage offers the greatest ability to help toward avoiding allogeneic blood transfusion.[7] In addition, cell salvage requires no preoperative preparation to effectively implement, making it ideal for a trauma or obstetrical hemorrhage.

Mathematical modeling of cell salvage has revealed that small changes in red cell processing efficiency can make large differences in the blood loss that a patient can sustain prior to needing allogeneic transfusion therapy.[8] These models suggest that a 70-kg patient with a starting hematocrit of 45% and a blood volume of 4,900 mL can sustain a blood loss of 9,600 mL if a transfusion trigger of 21% is used and cell salvage captures 60% of lost red blood cells (Fig. 1). The sustainable blood loss rises to 13,750 mL if 70% red cell recovery is achieved. This implies that a 10% increase in effectively collecting, washing, and returning lost cells results in the ability for a patient to sustain 4,150 mL of greater blood loss without needing allogeneic red cell products. This highlights the importance of optimizing the cell salvage system.

Optimizing Red Cell Return

Optimizing the cell salvage process can occur at multiple points in the processing. The following discussion will elucidate some of the areas where optimization can occur.

Suction. Shear force applied to red cells during suctioning can lead to hemolysis. Shear force is created by turbulence. In general, turbulence destroys red cells. High turbulence results from high suction pressure. So the lowest suction pressure that is tolerable to the surgeon should be applied. The vacuum pressure should be regulated to 80 to 120 torr, which is adequate for most surgical procedures.[9,10] Vacuum level can be temporarily raised to clear the field in the event of massive blood loss, and then reduced to a lower level for lower flows. It is important to remember that if multiple suction lines are attached to a collection reservoir, all of the lines need to be used simultaneously; otherwise, when one suction line is placed in blood and the others are not, then suction pressure will be reduced. Alternatively, a vigilant cell salvage technician can place clamps on

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Table 1: Components of a Perioperative Blood Conservation Program

Blood conservation should be addressed over the entire perioperative course. Components for each stage of the perioperative period are listed below:

Preoperative Period
1. Erythropoietin
2. Androgens
3. Iron, folate, B12 supplements
4. Avoidance of anticoagulant drugs
   a. Nonsteroidal anti-inflammatory drugs
   b. Herbal supplements
   c. Antiplatelet drugs
   d. Heparin/warfarin

Intraoperative Period
1. Red blood cell avoidance
   a. Normovolemic hemodilution
   b. Preoperative autologous donation
   c. Cell salvage
2. Coagulation system avoidance
   a. Component sequestration
   b. Normovolemic hemodilution
3. Adjuncts
   a. Point-of-care testing
   b. Microsampling
   c. Drug therapy
      • Desmopressin
      • Aprotinin
      • ε-Aminocaproic acid
      • Recombinant factor VIIa
   d. Deliberate hypotension
   e. Maintenance of normothermia
   f. Avoidance of normal saline
   g. Appropriate positioning

Postoperative Period
1. Washed or unwashed cell salvage
2. Erythropoietin/iron
3. Hyperbaric oxygen therapy
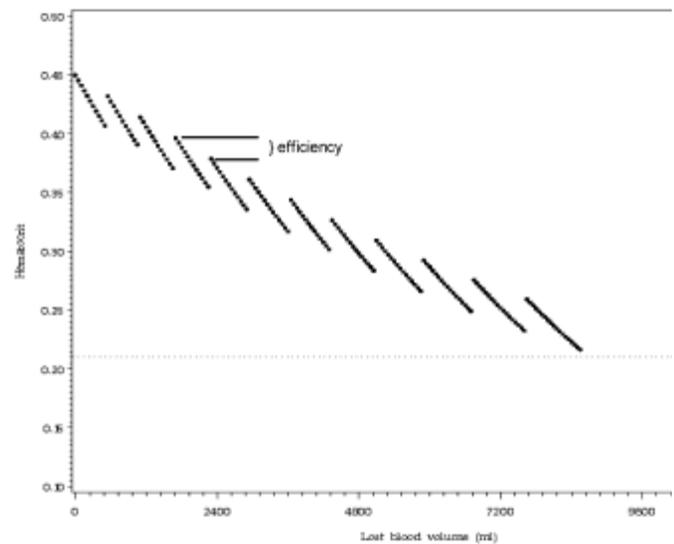4. Minimize phlebotomy

Figure 1. A demonstration of how the hematocrit changes as blood is lost. The saw-tooth pattern represents blood being lost. At a certain point, blood loss has been adequate for cell salvage processing to start. The blood is then returned to the patient, with the hematocrit being raised. The difference between the hematocrit from one cycle to the next is the efficiency of the system. (Adapted from Waters et al.[8])

unused suction lines to maintain adequate pressure with release of the clamps when the surgeon is ready to use a particular line.

The design of the suction tip can also influence turbulence. Tips that have small-caliber openings create high degrees of turbulence at the tip, which can hemolyze cells during collection. If possible, the largest tip opening should be used. This is generally not a problem for trauma surgery.

Rinsing of Surgical Sponges. The next opportunity for optimizing cell salvage efficiency is by rinsing out red cells from lap sponges. Fully soaked gauze pads or lap sponges may contain up to 100 mL of blood.[11] Of this blood, approximately 75% is retrievable. To retrieve these red cells, each sponge should be rinsed in a basin of isotonic solution (normal saline, Ringer's lactate, Hartmann's solution) and wrung out prior to their discard. The rinse solution is periodically sucked into the cardiotomy or collection reservoir when it is noted that the sponges are no longer losing their red discoloration upon rinsing.

Objections to the practice of rinsing sponges arise from two areas. The first fear is that this practice may result in cotton fibers being incorporated into the shed blood. In unpublished work (Potter, Biscotti, Waters, 2003), we soaked lap sponges with blood and subsequently rinsed and wrung the sponges out with normal saline. This red cell rinse solution was then centrifuged, thus concentrating any particulates. On microscopic examination, no cotton fibers were found. Discussion with the manufacturer of these sponges revealed that no fiber shedding is caused by a tight weave of these sponges and a double-washing process that eliminates cotton fiber shedding. This processing is done to eliminate fiber shedding into the surgical wound. If significant concern exists when rinsing sponges, the cardiotomy or collection reservoir typically has a filter, although the reservoir can be purchased without a filter. The filter size varies between 40 and 120 microns, depending on the type of reservoir and the manufacturer. If this is deemed inadequate, a microaggregate filter could be used at the point of administration.

The second fear is that the sponges might introduce bacteria into the collected blood. This does not seem to be a reasonable fear because any bacterial contamination that is present must have come from the surgical wound. Thus, the patient has already been exposed to the bacteria. It is well described that cell salvage blood is routinely contaminated.[12,13] This contamination has not been correlated with clinical sequelae. If sponges are suspected to be contaminated, they should simply be discarded rather than rinsed.

Anticoagulant. As blood is suctioned from the surgical field, an anticoagulant should be mixed with the blood. The purpose of the anticoagulant is to prevent clot formation in the collection reservoir or processing system. Clotting of blood in the collection system will result in loss of otherwise recoverable blood, as well as the need for reservoir and bowl replacement when large clots obstruct blood flow through the system. Either citrate or heparin can be used for anticoagulation during cell salvage. Because of its low cost and ready availability, heparin is most commonly used. Added to a

carrier such as normal saline at a dosage of 30,000 units/L of heparin, the solution is titrated through the aspiration suction system at a rate of 15 mL per 100 mL of collected blood. It is better to err on the high side rather than risk underadministration and loss of red cells to clotting. Overadministration of heparin during shed blood salvage is of no consequence in a cell-washing system. Adequate washout will remove all but a trace of heparin, with less than 10 units residual remaining in the final blood product.

Citrate has also been used as an anticoagulant. Some controversy exists as to which anticoagulant is best.[14,15] The administration rate for citrate-bearing anticoagulants (such as acid-citrate-dextrose [ACD] and citrate-phosphate-dextrose [CPD]) is also 15 mL per 100 mL of collected blood. Again, overuse of citrate anticoagulants is better than inadequate doses. On reinfusion, rapid liver metabolism makes citrate toxicity a difficult state to achieve. In compromised liver function, correction with small doses of calcium provides immediate and nontoxic reversal. At the Mayo Clinic in Rochester, Minnesota, 15,000 units/L of heparin is mixed with a liter of the citrate solution. Use of this solution has been noted to eliminate the cellular and protein deposits that are frequently seen coating the interior surface of the processing bowl.

If a leukocyte-depletion filter is to be used during cell salvage processing, some thought might be given to the use of heparin rather than citrate. The degree of deformability of leukocytes is reduced in the presence of calcium.[16] If a leukocyte-depletion filter is being used to remove bacteria, cancer cells, or amniotic fluid contaminants, this decreased deformability might also affect these contaminants. By decreasing the deformability of these cells, the ability to filter them out of the blood product may be enhanced. This is an area where further research is needed.

Collection Reservoir. The reservoir is the collection site for blood as it awaits processing. Residual clot can form within the reservoir if blood loss exceeds the ability of the anticoagulant to stop clot formation, or cells can be trapped by macroaggregate material such as bone fragments or fat. These red cells can be retrieved by mechanically agitating the reservoir while rapidly infusing normal saline or Ringer's lactate solution into the collection reservoir. This can be performed by using one of the suction lines, or infusing saline directly into the reservoir through ports on the top of the reservoir. These ports are available on some manufacturer's reservoirs, but not all of them. Surprisingly large quantities of red cells can be retrieved through this mechanical agitation.

Cell Salvage and Trauma

Bowel surgery, penetrating trauma to the abdomen, or surgery where an infected wound is involved present a circumstance where shed blood might be contaminated with bacteria. In this scenario, readministration of cell salvaged blood is feared to lead to bacteremia or sepsis. No supportive data of this fear can be found in the literature. What can be found would suggest that cell salvage in these environments can be performed safely.

Surprisingly, bacterial contamination of cell salvaged blood appears to be routine. Bland et al[13] found that bacterial contamination of cell salvaged blood in cardiac surgery approaches 30% of the units processed and readministered. Kang et al[12] reported that 9% of the blood returned to liver transplant patients had bacterial contaminants, usually of skin origin. In these circumstances of bacterial contamination, no clinical sequelae were noted. Contamination from skin flora has been assumed to be inconsequential, but the contaminants of frank stool have been thought to be different. This area has also been investigated primarily in trauma, where several authors have reported on frank

stool contamination of reinfused, salvaged blood, yet no increased sepsis rates were noted.[17-19] These studies would suggest that cell salvage in the face of bacterial contamination can be done safely.

The impact of cell salvage processing on blood that has been bacterially contaminated was first investigated by Boudreaux et al,[20] who inoculated expired units of blood with bacteria and found that washing was capable of reducing contamination to 5% to 23% of the starting contamination. In a similar study, Waters et al[21] found an approximately 99% reduction in bacterial contamination when the combination of cell washing and a leukocyte-depletion filtration was performed. In the same report, a dose-response curve was generated that showed that a 99% reduction of a starting load of bacteria of 10^7 still left 10^5 bacteria. This level of contamination was identified to occur in surgical procedures in which gross fecal contamination of the blood was observed. Thus, differentiating between gross contamination and possible or unobserved contamination is important.

The importance of any remaining bacteria is unknown at this time. Related to this issue is that of bacterial contamination of allogeneic blood, primarily platelets. This issue has been of intense interest to the blood banking community because of the 500 to 750 severe reactions or death that occur each year from bacterial contamination of blood products.[22] In a surveillance study by Yomtovian et al,[23] eight bacterially contaminated pools of platelets were administered to patients; five had no symptoms with bacterial loads ranging from the 10^2 to 10^{11} cfu/mL, and the others had symptoms with bacterial loads ranging from 10^6 to 10^8 cfu/mL. This study plus others suggest that the type of bacteria is more important than the quantity.[24-26]

It is important to keep in mind that, during the course of most operations, bacteremia is present that is related to the surgical trauma. Broad-spectrum antibiotics are routinely used to manage this bacteremia. Several studies have suggested that these drugs add additional safety when contaminated cell salvage blood is readministered.[27]

Dzik and Sherburne,[31] in a review of the controversies surrounding cell salvage, pointed out that allogeneic tranfusion leads to an increase in infection rate and that, when faced with bacterial contamination of cell salvaged blood, a clinical decision needs to be made as to which therapy offers the least risk to the patient. Known risk exists with allogeneic blood, but only theoretical risk is associated with cell-salvaged blood. Until data are generated supporting the theoretical risk of cell salvage in these circumstances, it seems reasonable to avoid the known risk of allogeneic blood through the use of cell salvage.

Complications to Cell Salvage

Air Embolism. The worst possible complication that has been associated with cell salvage is that of air embolus. This is a totally preventable complication. When blood is first pumped into the processing system, air is pushed out into the waste bag. When the blood is finished processing, some of this air can enter the primary reinfusion bag. Over time, the amount of air can become significant. It is imperative that blood not be reinfused from the primary reinfusion bag. Instead, blood should be transferred into a secondary reinfusion bag or a transfer bag, which then has the air burped back into the primary reinfusion bag (Fig. 2). The secondary bag is then disconnected from the system and can be used or pressurized like any other blood product. If the primary reinfusion system is pressurized directly into the patient, the patient could have the accumulated air transfused, resulting in air embolus.
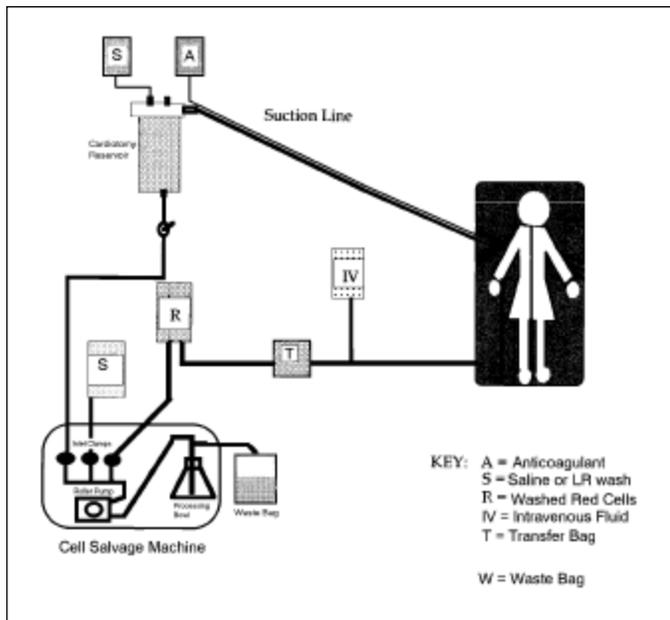
Figure 2. This schematic demonstrates the processing steps of cell salvage. Red cells should never be administered from the primary reinfusion bag (R). They should always be placed into a secondary bag (T), which has the air removed followed by its isolation from the cell salvage system either by disconnection or by clamping.

Wrong Wash Solution. Generally, normal saline is used as the wash solution. Using 3-liter bags of the wash solution allows for minimal changing of the bag. Many types of solutions are used in the operating room. These solutions include normal saline, glycine, and sterile water. It is important to store these different solutions in different locations so that the appropriate solution is used. If sterile water is inadvertently substituted for normal saline, the red cells will be completely lysed during processing. If lysed red cells in sterile water were to be readministered to the patient, it potentially could be fatal. Glycine-washed cells would still be intact, but glycine has been reported to cause transient blindness and death.[30]

Cell Salvage Syndrome. Attention to optimizing the quality of the product being readministered is required. Salvaged blood that has been poorly processed can result in adverse patient outcome. Inadequate washing has been described by Bull and Bull[32] and has been labeled "the cell salvage syndrome." Inadequate washing and concentration of the cell-salvaged blood can lead to complications such as disseminated intravascular coagulation or acute renal failure. In a study of the "salvaged blood syndrome" incorporating 36,000 cases, Tawes et al[33] concluded that this problem occurs with inadequate bowl filling and inexperienced personnel.

To prevent the occurrence of processing such as described, the American Association of Blood Banks has developed standards for perioperative autotransfusion.[34] Among the standards is a requirement for personnel who are trained and dedicated to the management of the equipment. In addition, monitoring of the quality of the product is required. A measure of adequate concentration of the blood is recommended, which would be reflected by the hematocrit of the product, and a measure of the quality of the wash process is recommended. An appropriate measure of wash quality has not been agreed on. Some of the suggested measures include periodic measurement of heparin washout, potassium washout, albumin washout, and measurement of free hemoglobin.

Conclusion

For the trauma patient, a goal for optimizing patient outcome should be to minimize the transfusion of allogeneic products. For this patient population, the probability of developing postoperative infectious complications rises with every unit of allogeneic blood received.[35] It is difficult to avoid transfusion altogether, but minimizing allogeneic transfusion is imperative. Cell salvage in the trauma environment offers significant ability to do this. An understanding of the parameters that can alter the efficiency of cell salvage systems is important to achieve maximum allogeneic transfusion avoidance. Knowledge of how to produce a quality product is mandatory prior to implementing this technology.

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Massive Transfusion for Trauma is Appropriate

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Learning Objectives: 1) To review the history of blood transfusion and the science of blood banking. 2) To review the literature regarding massive blood transfusion and outcome. 3) To understand adverse consequences of massive blood transfusion, including hemostatic, metabolic, electrolyte, and immune. 4) To understand the epidemiology, pathogenesis, clinical manifestation, and treatment of transfusion-related acute lung injury. 5) To review an example of a massive transfusion protocol and understand when to activate such a protocol, and who should be responsible for activating the protocol.

Abstract
The history of blood transfusion dates back to the mid-17th century. Scientific advances in transfusion therapy still persist today. Major developments have included blood typing, preservation, storage, fractionation, and the emergence of component therapy. Although early reported survival rates following massive transfusion were dismal (6.6%), recent literature shows survival rates of 40% to 60%. Improved survival has been attributed to improvement in trauma care provision, improved rewarming techniques, damage control celiotomy, and improved blood banking technology. With massive transfusion, the recognition of blood as a form of temporary organ transplantation has been realized. The adverse consequences associated with massive transfusion are now diagnosed and treated earlier. This article reviews the history, outcome, and potential complications associated with massive blood transfusions.

History of Blood Transfusion and Component Therapy

The history of blood transfusion dates back to 1628 when William Harvey, an English physician, discovered the circulation of blood (Table 1). Soon thereafter, the earliest known blood transfusion was attempted. The first successful blood transfusion occurred in 1665, and the first claim of successful human blood transfusion was made by the American physician Philip Syng Physick in 1795. Later milestones include the first successful whole blood transfusion, antiseptics to control infection during transfusions, and saline as a "blood substitute."

Although blood transfusions were becoming more common, the adverse consequences arising from donor-recipient incompatibility