Intra-operative cell salvage: a fresh look at the indications and contraindications

Stephen A. Esper, Jonathan H. Waters

Department of Anesthesiology, Magee Womens Hospital of University of Pittsburgh Medical Center, Pittsburgh, United States of America

Introduction

Numerous approaches are used to avoid transfusion of allogeneic blood. Primary methods include, but are not limited to, erythropoietin and iron supplementation, pre-operative autologous donation, acute normovolaemic haemodilution, haemoglobin-based blood substitutes and infusible oxygen-carrying fluids, and the use of cell salvage systems. While currently unavailable in North America and Europe because of an increased risk of myocardial infarction and death[1,2], research continues in the areas of haemoglobin-based blood substitutes and infusible oxygen-carrying liquids.

Of the accepted strategies mentioned above, cell salvage offers the medical community a safe, resource-saving, and relatively inexpensive method to avoid allogeneic red cell transfusion. Currently, incorrect information and misconceptions regarding the use of cell salvage systems frequently portray them as expensive, ineffective, and inappropriate for use in certain clinical situations. In addition to addressing these misconceptions, this article will discuss indications and contraindications for the use of such systems.

Indications

In the past, the AABB (formerly known as the American Association of Blood Banks) has recommended the following general indications for cell salvage use: the anticipated blood loss is 20% or more of the patient's estimated blood volume; cross-match-compatible blood is unobtainable; the patient is unwilling to accept allogeneic blood, but will give consent to receive blood from intra-operative blood salvage, as in the case of Jehovah's witnesses; more than 10% of patients undergoing the procedure require transfusion; the mean transfusion for the procedure exceeds one unit[1].

These recommendations are derived from a cost comparison between administering allogeneic blood and use of cell salvage. More recently, the cost of administering allogeneic blood has grown, which changes this economic relationship. At the same time, the medical community has gained a much better understanding of the expense associated with cell salvage. For this reason, implementation of cell salvage should be considered when much smaller amounts of blood loss are anticipated.

Because of the difficulty associated with the accurate prediction of substantial blood loss and the possible need for allogeneic transfusion, for the majority of cases it would be appropriate to set up the cell salvage device in a "stand-by" mode. This "stand-by" mode is simply the collection system which includes a cardiotomy reservoir, a suction line and an anticoagulant. The cost of a collection or "stand-by" set-up is comparable to that of the reagents for cross-matching two units of allogeneic blood. While being a sizeable paradigm shift, hospitals might consider implementation of a "stand-by" set-up rather than "type and cross". In cases in which substantial blood loss is certain to occur, such as in a repair of an open thoraco-abdominal aneurysm repair, it is reasonable to bypass the "stand-by" set-up and proceed directly to preparing components necessary to process blood.

Cell salvage may be indicated in numerous types of invasive procedures. The decision to provide cell salvage should be accompanied by clear and appropriate communication between the hospital administrative staff, case-specific surgeon and anaesthesiologist. In many cases, it should be individualised because the patient's starting haemoglobin and haematocrit, gender, age and body weight can all influence the risk of requiring blood

Blood Transfus 2011;9:139-47 DOI 10.2450/2011.0081-10

products[3]. Table I lists many of the surgical procedures that should be considered for implementation of cell salvage.

While a discussion concerning all of the financial permutations for the provision of cell salvage services is well beyond the scope of this article, it is important to mention the following point briefly. Prior to adopting the aforementioned strategic implementation of cell savage, it is important to understand whether the hospital's approach is to contract out the cell salvage to other care providers or to offer the possibility through an in-house service. The economics differ dramatically depending on the model used.

Contraindications

An extensive list of contraindications can be found in Table II. It must be noted that there are very few absolute contraindications. Those that do exist represent a danger to the patient. Anything that results in red cell lysis upon administration of the salvaged blood product is defined as a definite or absolute contraindication. If blood is mixed with fluids such as sterile water, hydrogen peroxide, alcohol, or any hypotonic solution, red cell destruction will occur. End-organ damage can be precipitated if a salvaged product that contains lysed red blood cells is administered[4,5]. It is best to circumvent incorporation of these materials and contaminants to avoid pathological embarrassment to the patient.

Many contraindications to cell salvage are not as definitive as those described above and would be described as relative contraindications. Relative contraindications to cell salvage encompass a wide range of factors that, if incorporated into or associated with the salvaged blood product, could potentially injure the patient upon re-administration. Few data exist to support the danger of the proposed relative contraindications. The risks and benefits of using cell salvage must be weighed against the same risks of allogeneic blood.

A specific example from the current literature is the administration of pro-coagulants such as thrombin. Furthermore, controversy surrounds the administration of cell salvaged blood products collected during specific types of situations, including cardiac surgery, orthopaedic surgery, emergency trauma situations, procedures involving contaminated or septic wounds, obstetrics, and malignancy. The use of cell salvage in these circumstances is variable from practice to practice. These situations are clouded by a clear divide within the medical community. Some investigators advocate the use of cell salvage claiming that it is safe and effective. Others feel that the danger associated with cell salvage makes it inappropriate to use. In many circumstances, communication between

Table I - General indications for cell salvage.

Specialty	Surgical procedure	Comments
Cardiac	Valve replacement Redo bypass grafting	
Orthopaedics	Major spine surgery Bilateral knee replacement Revision of hip replacement	
Urology	Radical retropubic prostatectomy Cystectomy Nephrectomy	Individualised by surgeon Limited to patients with prior radiation therapy When tumour involves major vessels
Neurosurgery	Giant basilar aneurysm	
Vascular	Thoraco-abdominal aortic aneurysm repair Abdominal aortic aneurysm repair	Should be individualised by surgeon and patient's characteristics
Liver Transplant		
Other	Jehovah's Witnesses Unexpected massive blood loss Red cell antibodies	When accepted by patient

Table II - Relative contraindications to cell salvage.

Pharmacological agents
Clotting agents (Avitene, Surgicel, Gelfoam, etc.)
Irrigating solutions (betadine, antibiotics meant for topical use)
Methylmethacrylate
Contaminants
Urine
Bone chips
Fat
Bowel contents
Infection
Amniotic fluid
Malignancy
Haematological disorders
Sickle cell disease
Thalassaemia
Miscellaneous
Carbon monoxide (electrocautery smoke)
Catecholamines (phaeochromocytoma)
Oxymetazoline (Afrin)
Papaverine

team members, especially the surgeon and anaesthesiologist, should be utilised to make the medical decision to proceed with intra-operative cell salvage.

In all circumstances of possible contamination, the safety of cell salvage may be increased through the use of a double suction set-up. In this set-up, one suction line is connected to the cell salvage reservoir and used for suctioning blood. The other suction line is connected to the regular wall suction and used for aspiration of the contaminant[6-8]. By using separate suction devices, the contamination of the salvaged blood is minimised. Because overall contamination of the salvaged blood product is minimised, the resultant concentration of contaminant in the washed product is also minimised. Generally, processing of the salvage product is capable of removing significant amounts of these contaminants. Nevertheless, a high concentration may overwhelm the system's capabilities. Thus, every effort should be made to minimise the load of the contaminant.

Bacterial contamination

Penetrating, traumatic injury to the large bowel, surgery involving an infected wound, or surgical procedures to the lower portion of the gastrointestinal tract are circumstances that may cause bacterial contamination of salvaged blood. It is generally thought that administration of this contaminated blood will lead to bacteraemia or sepsis in a patient who is otherwise previously healthy. At present, no data supporting this anecdotal conclusion can be found in the literature. What information can be found seems to suggest that cell salvage can be performed safely in these circumstances.

Bacterial contamination of salvaged blood appears to be common. In the setting of cardiac surgery, Bland *et al.* found that 30% of processed and re-administered units obtained by intra-operative blood salvage were contaminated with bacteria[9]. Kang *et al.* reported that 9% of the blood returned to patients during liver transplantation had bacterial contaminants, usually of skin origin[10]. No clinical sequelae were noted in either of these circumstances.

Contrary to the notion that skin flora contamination is inconsequential, contamination of blood by frank stool is thought to be harmful to the patient. This area has been investigated primarily in emergency trauma procedures in which several authors have reported that increased rates of sepsis were not seen in patients who received an infusion of salvaged blood that was contaminated by frank stool[11-13]. These studies would suggest that cell salvage can be done safely in the face of bacterial contamination.

The impact of processing salvaged blood that has been bacterially contaminated was originally studied and reported in an article published in 1983. In this study, Boudreaux *et al*. inoculated expired units of blood with bacteria and subsequently washed them. They found that washing the units resulted in a reduction of contamination to 5-23% of the starting bacterial load[14]. In a similar study done 20 years later, Waters *et al.*[15] found a 99% (approximate) reduction in bacterial contamination when cell washing and

leukocyte depletion filtration were both performed. The same study also considered the importance of differentiating between gross contamination and possible/unobserved contamination as a generated, dose-response curve showed that a 99% reduction of a bacterial load that started at 10^7 still left 10^5 bacteria. This level of contamination was identified to occur in surgical procedures in which gross faecal contamination of the blood was observed, as opposed to unobserved contamination.

The importance of any remaining bacteria is unknown at this time. The bacterial contamination of platelets in allogeneic blood is related to this issue, which has been of intense interest to the blood banking community. Prior to the implementation of bacterial testing of platelets, 500 to 750 severe reactions or deaths occurred each year from bacterial contamination of blood products[16]. In a surveillance study by Yomtovian *et al.*, eight bacterially contaminated pools of platelets were administered to patients. Five asymptomatic individuals had a bacterial load that ranged from the 10^2 to 10^{11} cfu/mL per individual. The other individuals were symptomatic with a bacterial load that ranged from 10^6 to 10^8 cfu/mL per individual[17]. In addition to other studies that have been published, this study suggests that symptomatic infection is influenced more by the type of bacteria present in the blood rather than the quantity[18-20].

It is important to keep in mind that during the course of most operations, bacteraemia secondary to surgical trauma is already present and broad-spectrum antibiotics such as cefazolin and bactrim are routinely used to manage this bacteraemia. Several studies have suggested that these drugs add additional safety when contaminated salvaged blood is re-administered[21,22].

In a review of controversies surrounding intra-operative blood salvage, Dzik and Sherburne[23] pointed out that allogeneic transfusion leads to an increase in infection rate. They continued, indicating that if cell salvage were to be utilised in a situation in which the blood could possibly be contaminated with bacteria, the clinical situation must govern whether or not the re-administration of such blood is of greater risk or benefit to the patient. It should be remembered that there is a known risk that exists with allogeneic blood, whereas administration of salvaged blood is associated with only a theoretical risk. Until data are generated demonstrating a risk from salvaged blood in these circumstances, it seems reasonable to avoid the known risk of allogeneic blood through the use of cell salvage.

Obstetrics

Cell salvage is useful in the field of obstetrics. One of the leading causes of death during childbirth is uncontrollable haemorrhage with the rates of postpartum haemorrhage and hysterectomy for haemorrhage on the rise[24]. Because cell salvage represents a life-saving opportunity to resupply the mother with previously lost haemoglobin, the use of cell salvage is naturally attractive[25,26]. During the peripartum period, cell salvage blood can be contaminated with bacteria, amniotic fluid and foetal blood. Contamination by foetal blood is a definite concern because of possible antigen-antibody complexes that may form secondary to "Rh" type differences between the mother and the child. Theoretically, the potential to create an iatrogenic amniotic fluid embolus is the greatest fear that accompanies amniotic fluid contamination. Because amniotic fluid emboli syndrome rarely occurs (1:8,000 to 1:30,000 deliveries), a definitive study assessing the risk of amniotic fluid embolus with cell salvage is nearly impossible. We are, therefore, left to look at surrogate markers which might be associated with the syndrome.

A 1991 article indicated that tissue factor is most likely involved in the disseminated intravascular coagulopathy that typically follows the acute embolic event of amniotic fluid embolus[27]. Bernstein and Colleagues evaluated the washout of tissue factor during use of cell salvage and found that all tissue factor activity was eliminated by routine washing[28]. Although this revelation is important, it must be understood that tissue factor may be only one of many components leading to amniotic fluid embolus syndrome. While washing out tissue factor may improve the quality of cell salvage blood for re-administration, it may not completely guarantee that amniotic fluid embolus syndrome would not occur[29,30]. However, several studies assessing the removal of free haemoglobin, bromocreosol green dye, and heparin from salvaged blood suggest that if one factor is effectively removed, the other factors are also removed[31,32]. The information obtained from these studies, therefore, suggests that if tissue factor is effectively removed from salvaged blood

contaminated with amniotic fluid, the other components of amniotic fluid would also be similarly removed or the concentration of such components would be significantly reduced.

The cause of amniotic fluid embolisation itself is controversial. Some investigators feel that particulate contaminants are responsible for amniotic fluid embolisation[33,34]. Durand and colleagues showed that washing salvaged blood did not remove foetal squamous cells[35]. Subsequently, Waters *et al.* demonstrated that leucocyte depletion filters used in concert with cell washing reduced the foetal squamous cell concentration to a level comparable to that of these cells in a maternal blood sample following placental separation[36]. This study went on to conclude that combining cell salvage washing and filtration produced a blood product that was similar to maternal blood. The exception to this conclusion was foetal haemoglobin contamination of maternal blood.

Because of this exposure to foetal haemoglobin, isoimmunisation can lead to erythroblastosis in subsequent pregnancies. ABO incompatibility generally tends to be a minor problem when compared to Rh incompatibility. Anti-D immune globulin, also referred to as Rhogam, is used to prevent isoimmunisation. The dose should be calculated and subsequently administered to the mother after the re-administration of cell salvage blood. This allows the immune globulin dose to reach adequate levels for additional cell neutralisation.

Support for the use of cell salvage in obstetric haemorrhage is now provided by 390 reported cases in which blood contaminated with amniotic fluid has been washed and re-administered without filtration[37-39]. In addition, the American College of Obstetricians and Gynecologists[40], the Obstetric Anaesthetists Association of Great Britain[41], and the British Confidential Enquiry into Maternal and Child Health[42] have advocated the use of blood salvage in obstetrics.

Malignancy

Surgical procedures involving resection of cancerous tumours are a source of major controversy. As mentioned earlier, immunomodulation occurs with allogeneic transfusion. The issue of whether this immunomodulation affects tumour growth is unresolved. At the same time, there is evidence to suggest that there is a worse outcome for patients who receive allogeneic blood in the setting of cancer surgery[43-45]. These findings would suggest that avoidance of allogeneic blood is of great importance. Likewise, re-administration of cell salvage blood that contains many tumour cells would also seem to be contradictory to a good patient outcome; however, during tumour surgery, studies have shown that haematogenous dissemination of cancer cells is common[46-48]. In fact, it has been demonstrated that a high percentage of patients presenting for cancer surgery have circulating tumour cells, but this presence does not appear to correlate well with patient survival[49]. It has been estimated that only 0.01%-0.000001% of circulating tumour cells have the potential to form metastatic lesions[50]. With this in mind, it is appropriate to question the importance of tumour cell administration via cell salvage blood.

With this understanding, the use of leucocyte depletion filters is currently advocated for removal of tumour cells during cancer surgery. These devices have been used for filtration of tumour cells from cell salvage blood for urologic surgery[51,52], pulmonary surgery[53], and in a variety of cell lines that were used to contaminate discarded blood[54,55]. All of these studies concluded that leucocyte depletion filters were highly effective at removing contaminating tumour cells from cell salvage blood.

Cell salvage during tumour surgery has been studied in hepatic resection for malignancy and urologic oncology[56-58]. In these uncontrolled studies, the actual outcome was compared to the expected outcome. There was no increase in metastasis or mortality. This information suggests that diffuse cancer metastasis does not occur following re-administration of cell salvage blood. It should also be added that no mention was made of the use of leucocyte depletion filters in these studies.

Two controlled studies were recently performed to evaluate the use of cell salvage: one was prospective while the other was retrospective[59,60]. In both of these studies, patients undergoing radical retropubic prostatectomy who were given cell salvage blood were compared to those who received transfusions of pre-operatively donated autologous blood. Both studies demonstrated that the outcome of the two groups was equivalent. Again, this would suggest that massive metastasis does not occur due to the use of cell salvage.

Collagen haemostatic agents

There has been a debate as to whether the use of microfibrillar collagen haemostats is a contraindication to the use of intra-operative blood salvage. McClure *et al*.[61] reported that microfibrillar collagen haemostat was able to pass through a 40-micron microaggregate filter and maintain its ability to promote platelet aggregation; the phenomenon was related to the dose administered. In the same article, McClure indicated that the findings supported the view that blood contaminated with microfibrillar collagen haemostat should not be returned to the patient's circulation. However, approximately 8 years later, Orr *et al.* specifically studied the possible removal of Avitene microfibrillar collagen haemostat by an early generation leucocyte depletion filter (Pall RC100) as well as the microaggregate filter which would filter to 20 microns (Statlabs 20 micron)[62]. Ninety-seven percent of the total collagen was removed by each filter and the collagen that was able to pass through the filters did not seem to promote platelet aggregation. Thus, the article indicated that the risk of platelet aggregation and blood clotting can be significantly reduced by using blood-transfusion filters.

As there are no randomised controlled trials *in vivo*, it cannot be determined with certainty that one result disproves the other. At the same time, it does seem that as filter technology within the field of intra-operative blood salvage progresses, the threshold of safety for re-administration of cell salvage blood will continue to increase.

Sickle cell disease and thalassaemia

Intra-operative blood salvage from patients who have sickle cell disease is an issue that is debated in the medical community. The underlying concern is the possibility that cell salvage blood re-administered to the patient in question will sickle and further reduce oxygen-carrying capacity. There are no trials to support this concern, but, at the same time, the only evidence that supports the administration of cell salvage blood lies in case reports.

In a paper published with two case reports of obstetric patients who had sickle cell carrier status, Okunga and Skelton indicated that the patients received cell salvage blood and made recoveries that did not reveal any pathological embarrassment as a result[63].

Cook *et al*. and Fox *et al.*, in two separate case reports, described that cell salvage blood was re-administered to a patient during hip arthroplasty and progressive scoliosis repair, respectively, both of whom were homozygous for sickle cell trait[64,65]. However, in the paper by Okunga *et al*., it was pointed out that 20% of the cells were altered (but not sickled) in one patient's salvaged blood and 15-20% of the cells were sickled in the other patient's salvaged blood. Brajtbord *et al.* reported that blood samples taken from a patient known to have sickle cell disease, showed no indication of sickling prior to processing[66]. After processing, 50% of the cells were seen to have sickled and the blood was not, therefore, transfused.

An editorial by Hulatt *et al.* discussed some of these issues in reference to the Association of Anaesthetists of Great Britain and Ireland (AAGBI) safety guidelines on the use of intra-operative cell salvage, and indicated that in the Royal Berkshire Hospital in Reading, UK, they advise against the use of cell salvage for those individuals who may require cell salvage during their operation. They also make the statement that determination of the re-administration of cell salvage blood should be examined more on a case to case and individual basis with appropriate and informed consent[67].

β-thalassaemia is a haematological disease with reduced or absent production of b chains leading to an excess of α globin chains. Red blood cell survival is shortened in β-thalassaemia. This is directly correlated with the degree of α globin chain excess in the red blood cell. The excess of α globin chains produces changes in the red blood cell which can result in haemolysis and anaemia[68].

Waters *et al.* explored the issue of β-thalassaemia in a case report involving an obstetric patient who required intra-operative blood salvage secondary to discovery of placenta accreta[69]. The patient received cell salvage blood without any untoward effects. Certainly, further study is required in this area. At the same time, when considering the use of cell salvage, the decision should be made according to risk/benefit determinations on an individual patient basis.

Carbon monoxide

Carbon monoxide binds haemoglobin with a greater affinity than does oxygen and can, therefore, significantly reduce the oxygen-carrying capacity of

haemoglobin. It has been shown that there is increased production of carbon monoxide with electrocautery use[70]. This is of importance since electrocautery is used in many patients, some of whom require intra-operative blood salvage.

Controversy exists as to whether it is appropriate to transfuse cell salvage blood to patients who have had electrocautery given the possible increase in carbon dioxide and significant decrease in oxygen-carrying capacity. Slucky *et al.* investigated this in a study involving four patients for whom data regarding carbon monoxide levels and clinical outcome were available[71]. It was shown that while carbon monoxide rose in the cell salvage blood, this was not clinically relevant.

Phaeochromocytoma

A phaeochromocytoma is a tumour of the adrenal medulla that secretes vasoactive substances of the sympathetic nervous system, including noradrenaline and adrenaline. After the secretion of noradrenaline from a nerve terminal, the catecholamine can be removed by one of three methods: re-uptake into the adrenergic nerve terminal by active transport; diffusion away from nerve endings; destruction of small amounts by tissue enzymes including monoamine oxidase (MAO, present at nerve terminals) and catechol-O-methyl transferase (COMT, diffusely present in all tissues). At the same time, noradrenaline and adrenaline secreted from the adrenal medulla remain active until they diffuse into tissues where they are degraded by COMT, which occurs mainly in the liver. The activity of these molecules can be upwards of several minutes[72].

The controversy here is that if cell salvage blood is re-administered to a patient undergoing adrenalectomy because of a phaeochromocytoma, the vasoactive molecules (the width and mass of which would be smaller than the smallest transfusion filter) would still be active because they would not have been enzymatically inactivated and destroyed. If great quantities of these molecules are active, it could be expected that the patient might develop hypertension and an increase in myocardial oxygen demand, and end-organ damage could perhaps follow.

Tsunobuchi *et al.* published a case report in 1995 that examined this issue in a patient undergoing adrenalectomy for a phaeochromocytoma[73]. Pre-operative and intra-operative catecholamine levels, pre-washing and post-washing, were measured. There did not seem to be a significant decrease in the amount of catecholamines after washing and the authors of the paper stated that hypertension was predictable, following autotransfusion. Tsunobuchi and his colleagues went on to state that haemodynamic monitoring should be conducted constantly during these cases. It would follow from these results that further study is certainly required and that perhaps the presence of these vasoactive substances in the cell salvage blood puts the patient at a higher risk to the patient than that produced by receiving allogeneic blood transfusion.

Anecdotally, the authors have seen haemodynamic effects when blood has been aspirated which contained oxymetazoline (Afrin) during sinus surgery and papaverine during vascular surgery. As a result of this observation, caution should be used when any vasoactive drugs are used topically within the surgical field.

Keywords: autotransfusion, cell salvage, erythrocytes, allogeneic transfusion, blood conservation.

References

1) Natanson C, Kern SJ, Lurie P, et al. Cell-free hemoglobin-based blood substitutes and risk of myocardial infarction and death: a meta-analysis. JAMA. 2008; **299**: 2304-12.
2) Guidelines for blood recovery and reinfusion in surgery and trauma. American Association of Blood Banks Autologous Transfusion Committee 1996-1997 Committee.
3) Scott BH, Seifert FC, Glass PS, Grimson R. Blood use in patients undergoing coronary artery bypass surgery: impact of cardiopulmonary bypass pump, hematocrit, gender, age, and body weight. Anesth Analg 2003; **97**: 958-63.
4) Pierce LR, Gaines A, Varricchio F, Epstein J. Hemolysis and renal failure associated with use of sterile water for injection to dilute 25% human albumin solution. Am J Health Syst Pharm 1998; **55**: 1057-70.
5) Anonymous. From the Centers for Disease Control and Prevention. Hemolysis associated with 25% human albumin diluted with sterile water--United States, 1994-1998. JAMA 1999; **281**: 1076-7.
6) Fong J, Gurewitsch ED, Kump L, Klein R. Clearance of fetal products and subsequent immunoreactivity of blood salvaged at Cesarean delivery. Obstet Gynecol 1999; **93**: 968-72.
7) Potter PS, Waters JH, Burger GA, Mraovic B.

Application of cell-salvage during Cesarean section. Anesthesiology 1999; **90**: 619-21.
8) Rebarber A, Lonser R, Jackson S, et al. The safety of intraoperative autologous blood collection and autotransfusion during Cesarean section. Am J Obstet Gynecol 1998; **179**: 715-20.
9) Bland LA, Villarino ME, Arduino MJ, et al. Bacteriologic and endotoxin analysis of salvaged blood used in autologous transfusions during cardiac operations. J Thorac Cardiovasc Surg 1992; **103**: 582-8.
10) Kang Y, Aggarwal S, Pasculle AW, et al. Bacteriologic study of autotransfusion during liver transplantation. Transpl Proceed 1989; **21**: 35-8.
11) Ozman V, McSwain NE, Nichols RL, et al. Autotransfusion of potentially culture-positive blood in abdominal trauma: preliminary data from a prospective study. J Trauma 1992; **32**: 36-9.
12) Schwieger IM, Gallager CJ, Finlayson DC, et al. Incidence of cell saver contamination during cardiopulmonary bypass. Ann Thorac Surg 1989; **48**: 51-3.
13) Timberlake GA, McSwain NE. Autotransfusion of blood contaminated by enteric contents: a potentially life-saving measure in the massively hemorrhaging trauma patient. J Trauma 1988; **28**: 855-7.
14) Boudreaux JP, Bornside GH, Cohn I Jr. Emergency autotransfusion: partial cleansing of bacteria-laden blood by cell washing. J Trauma 1983;**23**:31-5.
15) Waters JH, Tuohy MJ, Hobson DF, Procop G. Bacterial reduction by cell salvage washing and leukocyte depletion filtration. Anesthesiology 2003; **99**: 652-5.
16) Jacobs MR, Palavecino E, Yomtovian R. Don't bug me: the problem of bacterial contamination of blood components-challenges and solutions. Transfusion 2001; **41**: 1331-4.
17) Yomtovian R, Lazarus HM, Goodnough LT, et al. A prospective microbiologic surveillance program to detect and prevent the transfusion of bacterially contaminated platelets. Transfusion 1993; **33**: 902-9.
18) Do A, Jarvid WR. *Transfusion-related infection*. In: Schlossberg D, ed. Current Therapy for Infectious Disease. St. Louis, MO: Mosby-Yearbook; 1996. p. 340-3.
19) Sapatnekar S, Wood EM, Miller JP, et al. Methicillin-resistant staphylococcus aureus sepsis associated with the transfusion of contaminated platelets: a case report. Transfusion 2001; **41**: 1426-30.
20) Kuehnert MJ, Jarvis WR, Schaffer DA, Chaffin DJ. Platelet transfusion reaction due to Yersinia enterocolitica. JAMA 1997; **278**: 550-1.
21) Smith RN, Yaw PB, Glover JL. Autotransfusion of contaminated intraperitoneal blood: an experimental study. J Trauma 1978; **18**: 341-4.
22) Wollinsky KH, Oethinger M, Büchele M, et al. Autotransfusion-bacterial contamination during hip arthroplasty and efficacy of cefuroxime prophylaxis. Acta Orthop Scand 1997; **68**: 225-30.
23) Dzik WH, Sherburne B. Intraoperative blood salvage: medical controversies. Transfus Med Rev 1990; **4**: 208-35.
24) Joseph KS, Rouleau J, Kramer MS, et al. Maternal Health Study Group of the Canadian Perinatal Surveillance System. Investigation of an increase in postpartum haemorrhage in Canada. BJOG 2007; **114**: 751-9.
25) Berg CJ. Chang J. Callaghan WM. Whitehead SJ. Pregnancy-related mortality in the United States, 1991-1997. Obstet Gynecol 2003; **101**: 289-96.
26) Chang J, Elam-Evans LD, Berg CJ, et al. Pregnancy-related mortality surveillance - United States, 1991-1999. MMWR Surveill Summ 2003; **52**: 1-8.
27) Lockwood CJ, Bach R, Guha A, et al. Amniotic fluid contains tissue factor, a potent initiator of coagulation. Am J Obstet Gynecol 1991; **165**: 1335-41.
28) Bernstein HH, Rosenblatt MA, Gettes M, Lockwood C. The ability of the Haemonetics 4 cell saver system to remove tissue factor from blood contaminated with amniotic fluid. Anesth Analg 1997; **85**: 831-3.
29) Halmagyi DFJ, Starzecki B, Shearman RP. Experimental amniotic fluid embolism: mechanism and treatment. Am J Obstet Gynecol 1962; **84**: 251-6.
30) Morgan M. Amniotic fluid embolism. Anaesthesia 1979; **34**: 20-32.
31) Kling D, Börner U, Bormann v. B, Hempelmann G. Heparin-elimination und freies Hämoglobin nach Zellseparation und waschen autologen blutes mit dem Cell Saver® 4. Anaesth Intensivther Notfallmed 1988; **23**: 88-90.
32) Umlas J, O'Neill TP. Heparin removal in an autotransfusor device. Transfusion 1981; **21**: 70-3.
33) Maleck WH, Petroianu GA. Autologous blood transfusion. Br J Anaesth 1999; **82**: 154.
34) Petroianu GA, Altmannsberger SHG, Maleck WH, et al. Meconium and amniotic fluid embolism: effects on coagulation in pregnant mini-pigs. Crit Care Med 1999; **27**: 348-55.
35) Durand F, Duchesne-Gueguen M, Le Bervet JY, et al. Rheologic and cytologic study of autologous blood collected with Cell Saver 4 during Çesarean. Revue Française de Transfusion et d Hemobiologie 1989;**32**:179-91.
36) Waters JH, Biscotti C, Potter P, Phillipson E. Amniotic fluid removal during cell-salvage in the Cesarean section patient. Anesthesiology 2000; **92**: 1531-6.
37) Rainaldi MP, Tazzari PL, Scagliarini G, et al. Blood salvage during Caesarean section. Br J Anaesth 1998; **80**: 195-8.
38) Grimes DA. A simplified device for intraoperative autotransfusion. Obstet Gynecol 1988; **72**: 947-50.
39) Jackson SH, Lonser RE. Safety and effectiveness of intracesarean blood salvage [letter]. Transfusion 1993; **33**: 181.
40) ACOG Committee Opinion. Placenta accrete. Number 266, January 2002. American College of Obstetricians and Gynecologists. Int J Gynecol Obstet 2002; **77**: 77-8.
41) OAA/AAGBI Guidelines for Obstetric Anaesthetic Services. Revised Edition: OAA/AAGBI, London; 2005. p. 25.
42) Why mothers die. Confidential Enquiry into Maternal and Child Health 2000-2002. London, RCOG, 2004.
43) Francis DM. Relationship between blood transfusion and tumour behavior. Br J Surg 1991;**78**:1420-8.

44) Vamvakas EC. Perioperative blood transfusion and cancer recurrence: meta-analysis for explanation. Transfusion 1995; **35**: 760-8.
45) Blumberg N, Heal JM. Effects of transfusion on immune function. Cancer recurrence and infection. Arch Pathol Lab Med 1994; **118**: 371-9.
46) Oefelein MG, Kaul K, Herz B, et al. Molecular detection of prostate epithelial cells from the surgical field and peripheral circulation during radical prostatectomy. J Urol 1996; **155**: 238-42.
47) Roberts S, Watne A, McGrath R, et al. Technique and results of isolation of cancer cells from the circulating blood. Arch Surg 1958; **76**: 334-6.
48) Fisher ER.Turnbull RB, Jr. Cytologic demonstration and significance of tumor cells in the mesenteric venous blood in patients with colorectal carcinoma. Surg Gynec Obstet 1955; **100**: 102-5.
49) Klimberg IW. Autotransfusion and blood conservation in urologic oncology. Sem Surg Oncol 1989; **5**: 286-92.
50) Weiss L. Metastatic inefficiency: causes and consequences. Cancer Rev 1986; **3**: 1-24.
51) Edelman MJ, Potter P, Mahaffey KG, et al. The potential for reintroduction of tumor cells during intraoperative blood salvage: reduction of risk with use of the RC-400 leukocyte depletion filter. Urology 1996; **47**: 179-81.
52) Wiesel M, Gudemann C, Hoever KH, et al. Separation of urologic tumor cells from red blood cells by the use of a cell-saver and membrane filters. Investig Urol 1994; **5**: 244-8.
53) Perseghin P, Vigano M, Rocco G, et al. Effectiveness of leukocyte filters in reducing tumor cell contamination after intraoperative blood salvage in lung cancer patients. Vox Sang 1997; **72**: 221-4.
54) Kongsgaard UE, Wang MY, Kvalheim G. Leucocyte depletion filter removes cancer cells in human blood. Acta Anaesthesiol Scand 1996; **40**: 118-20.
55) Torre GC, Ferrari M, Favre A, et al. A new technique for intraoperative blood recovery in the cancer patient. Eur J Surg Oncol 1994; **20**: 565-70.
56) Zulim RA, Rocco M, Goodnight JE, et al. Intraoperative autotransfusion in hepatic resection for malignancy. Arch Surg 1993; **128**: 206-11.
57) Klimberg I, Sirois R, Wajsman Z, Baker J. Intraoperative autotransfusion in urologic oncology. Arch Surg 1986; **121**: 1326-9.
58) Hart OJ, Klimberg IW, Wajsman Z, Baker J. Intraoperative autotransfusion in radical cystectomy for carcinoma of the bladder. Surg Gyne Obstet 1989; **168**: 302-6.
59) Gray CL, Amling CL, Polston GR, et al. Intraoperative cell salvage in radical retropubic prostatectomy. Urology 2001; **58**: 740-5.
60) Davis M, Sofer M, Gomez-Marin O, et al. The use of cell salvage during radical retropubic prostatectomy: does it influence cancer recurrence? Br J Urol 2003; **91**: 474-6.
61) McClure M, Duncan GD, Born GV, Robicsek F. In vitro effect of a microfibrillar collagen hemostat on platelets. Haemostasis 1987; **17**: 349-52.
62) Orr MD, Ferdman AG, Maresh JG. Removal of Avitene microfibrillar collagen hemostat by use of suitable transfusion filters. Ann Thorac Surg 1994; **57**: 1007-11.
63) Okunuga A, Skelton VA. Use of cell salvage in patients with sickle cell trait. Int J Obstet Anesth 2009; **18**: 90-1.
64) Cook A, Hanowell LH. Intraoperative autotransfusion for a patient with homozygous sickle cell disease. Anesthesiology 1990;**73**:177-9.
65) Fox JS, Amaranath L, Hoeltge GA, Andrish JT. Autologous blood transfusion and intraoperative cell salvage in a patient with homozygous sickle cell disease. Cleve Clin J Med 1994; **61**: 137-40.
66) Brajtbord D, Johnson D, Ramsay M, et al. Use of the cell saver in patents with sickle cell trait. Anesthesiology 1989; **70**: 878-9.
67) Hulatt LJ, Fisher W. Intra-operative cell salvage and sickle cell carrier status. Anaesthesia 2010; **65**: 646-56.
68) Polliack A, Rachmilewich EA. Ultrastructural studies in β-thalassemia major. Br J Haematol 1973; **24**: 319.
69) Waters JH, Lukauskiene E, Anderson ME. Intraoperative blood salvage during Cesarean delivery in a patient with β thalassemia intermedia. Anesth Analg 2003; **97**: 1808-9.
70) Beebe DS, Swica H, Carlson N, et al. High levels of carbon monoxide are produced by electrocautery of tissues during laparoscopic cholecystectomy. Anesth Analg 1993; **77**: 338-41.
71) Slucky AV, Eismont FJ. Carbon monoxide levels in cell saver salvaged blood exposed to electrocautery during lumbar spine surgery. J Spinal Disorder 1996; **5**; 404-8.
72) Guyton AC, Hall JE. *Textbook of Medical Physiology*. 11th ed. Elsevier Inc; 2006. p. 752-3.
73) Tsunobuchi H, Katoh H, Takada M et al. The catecholamine concentrations of collected autologous blood during adrenalectomy for pheochromocytoma. Masui-Japanese J Anesthesiol 1995; **44**: 256-9.

Received: 12 September 2010 - Revision accepted: 15 October 2010
Correspondence: Jonathan H. Waters
Department of Anesthesiology
Magee Women's Hospital, Suite 3510
300 Halket St.
Pittsburgh, PA 15213, USA
e-mail: watejh@upmc.edu