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REVIEW ARTICLES

Cell salvage as part of a blood conservation strategy in anaesthesia

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Key points

- Cell salvage reduces the requirement for allogenic blood transfusion.
- It should be considered for surgery with an anticipated blood loss of >1000 ml.
- It can be used in cancer surgery, but a leucocyte depletion filter is recommended.
- Evidence from cardiac and orthopaedic surgery is reasonable but is limited for other surgery.
- There is still a need for large prospective randomized controlled trials.

Summary. The use of intraoperative cell salvage and autologous blood transfusion has become an important method of blood conservation. The main aim of autologous transfusion is to reduce the need for allogeneic blood transfusion and its associated complications. Allogeneic blood transfusion has been associated with increased risk of tumour recurrence, postoperative infection, acute lung injury, perioperative myocardial infarction, postoperative low-output cardiac failure, and increased mortality. We have reviewed the current evidence for cell salvage in modern surgical practice and examined the controversial issues, such as the use of cell salvage in obstetrics, and in patients with malignancy, or intra-abdominal or systemic sepsis. Cell salvage has been demonstrated to be safe and effective at reducing allogeneic blood transfusion requirements in adult elective surgery, with stronger evidence in cardiac and orthopaedic surgery. Prolonged use of cell salvage with large-volume autotransfusion may be associated with dilution of clotting factors and thrombocytopenia, and regular laboratory or near-patient monitoring is required, along with appropriate blood product use. Cell salvage should be considered in all cases where significant blood loss (>1000 ml) is expected or possible, where patients refuse allogeneic blood products or they are anaemic. The use of cell salvage in combination with a leucocyte depletion filter appears to be safe in obstetrics and cases of malignancy; however, further trials are required before definitive guidance may be provided. The only absolute contraindication to the use of cell salvage and autologous blood transfusion is patient refusal.

Keywords: blood transfusion; care, intraoperative; surgery

The first recorded use of cell salvage and autologous transfusion was in 1818 when a gynaecologist named Blundell treated patients with post-partum haemorrhage.[1] Blood-soaked swabs were washed in saline and then the mixture was re-infused. This was unsurprisingly associated with a high mortality. Experimentation with cell salvage and autologous transfusion continued into the next century when in 1931, blood salvaged from a haemothorax was directly re-infused into the patients.[2] In 1943, Arnold Griswald developed the first cell salvage autotransfusion device.[3] Suctioned blood was collected in a bottle and then strained through a cheese cloth before being re-infused. This formed the basic principles on which modern cell salvage devices are designed today. In the 1960s, a number of commercial devices became available. The first 'modern' cell saver was produced in the 1970s; however this was associated with a number of complications, such as haemolysis, air embolism, and coagulopathy.

Principles of cell salvage

There are three phases involved in cell salvage—collection, washing, and re-infusion. Collection of red blood cells (RBCs) from the operative field requires the use of a dedicated double-lumen suction device. One lumen suctions blood from the operative field and the other lumen adds a predetermined volume of heparinized saline to the salvaged blood. The anticoagulated blood is then passed through a filter and collected in a reservoir. Separation of the components is achieved by centrifugation. The RBCs are then washed and filtered across a semi-permeable membrane, which removes free haemoglobin, plasma, platelets, white blood cells, and heparin. The salvaged RBCs are then re-suspended in normal saline with a resultant haematocrit of 50–80%. The salvaged RBCs may be transfused immediately or within 6 h.[4 5] The current accepted storage time of cell salvaged blood is 6 h, but a recent well-conducted prospective study of 101

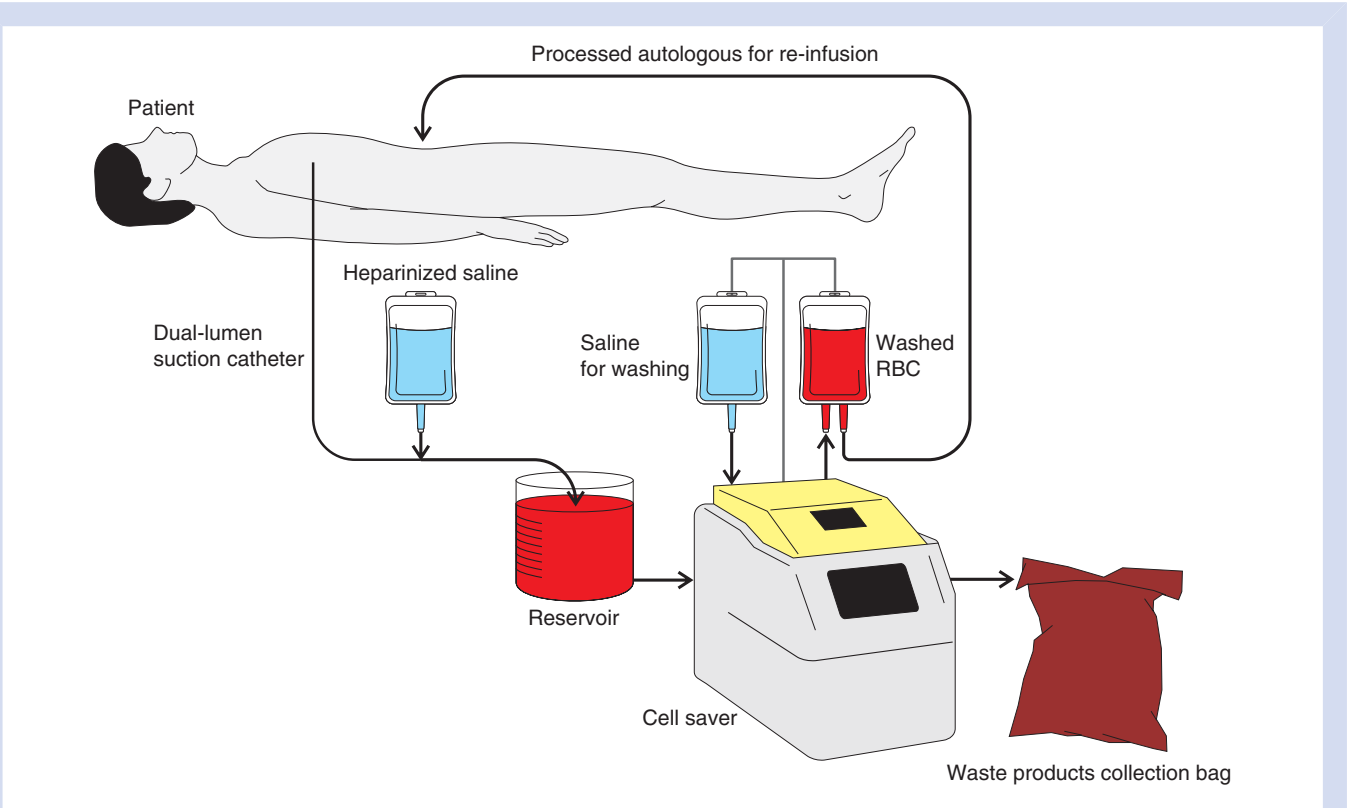

Fig 1 Diagram of the set up of a standard cell salvage circuit.

paediatric patients undergoing cardiac surgery demonstrated that extension to 18 h resulted in minimal microbiological contamination or chemical deterioration (Fig. 1).[6]

Over a 1 yr period in 2007–2008, blood services in the UK issued 2 174 256 units of RBCs, 258 419 units of platelets, 295 085 units of fresh-frozen plasma, and 117 699 units of cryoprecipitate. The total number of transfused blood products has consistently decreased over the last 10 yr.[7] In 2008, there were 1049 adverse events reported to the Serious Hazards of Transfusion steering group (SHOT; Table 1). Cell salvage is an important component of blood conservation (Table 2), which aims to reduce patients' exposure to allogeneic blood transfusions. Allogeneic blood transfusions have been associated with increased risk of tumour recurrence,[8–10] post-operative infection,[11–15] acute lung injury,[16] perioperative myocardial infarction,[17] postoperative low-output cardiac failure,[18] morbidity,[19] and increased 5 yr mortality.[20] The risks of postoperative infections and tumour recurrence associated with allogeneic blood transfusion are dose-dependent[8–10] and are thought to be as a result of immunomodulation. This is supported by a study of patients undergoing renal transplantation, which demonstrated that transfusion of allogeneic blood has been found to decrease transplant rejection.[21] Exposure to multiple units of allogeneic blood increases the risk of developing abnormal antibodies, which makes future cross-matching more difficult and time-consuming.[22]

We have reviewed the current evidence for cell salvage in modern surgical practice, including the controversial issues surrounding cell salvage, such as the use of cell salvage in obstetrics, in malignancy, and in patients with intra-abdominal or systemic sepsis.

Table 1 SHOT 12th annual report[7]

Transfusion incident	Number of cases (total 1049)	Per cent
Mortality	9	0.9
Incorrect blood component transfused	262	25
ABO incompatibility	11	1.0
Inappropriate and unnecessary transfusion	76	7
Handling and storage errors	139	13
Anti-D events	137	13
Acute transfusion reactions	300	29
Haemolytic transfusion reactions	55	5
Transfusion-related acute lung injury (TRALI)	17	2
Post-transfusion purpura	1	0.1
Graft *vs* host disease (GvHD)	0	0
Transfusion transmitted infections	6	0.6
Transfusion-associated circulatory overload	18	2
Transfusion-associated dyspnoea	1	0.1
Autologous transfusion reactions	28	3

Table 2 Methods of blood conservation

Method of blood conservation	Advantages	Disadvantages
Acute normovolaemic haemodilution	Autologous blood	Haemodynamic instability during venesection
	Reduction in allogeneic blood transfusions	Additional training required
	Whole blood	
	Inexpensive	
Preoperative autologous donation (not widely used in the UK)	Autologous blood (up to 4 units)	Logistical planning
	Reduction in allogeneic blood transfusions	Perioperative anaemic
	Whole blood	Mis-transfusion due to clerical errors
		Up to 50% of predonated blood is unused
		Potential bacterial contamination of predonated blood
Preoperative erythropoietin	Optimize haemoglobin	Expensive
Education	Reduces inappropriate allogeneic blood transfusions	Time-consuming

Table 3 Scottish Intercollegiate Network Grading new system for grading recommendations in evidence-based guidelines

Level of evidence	Criteria
1++	High-quality meta-analysis, systematic reviews of RCTs, or RCT with a very low risk of bias
1+	Well-conducted meta-analysis, systematic reviews, or RCTs with a low risk of bias
1−	Meta-analysis, systematic reviews, or RCTs with a high risk of bias
2++	High-quality systematic reviews of case–control or cohort studies or high-quality case–control or cohort studies with a very low risk of confounding or bias and a high probability that the relationship is causal
2+	Well-conducted case–control or cohort studies with a low risk of confounding or bias and a moderate probability that the relationship is causal
2−	Case–control or cohort studies with a high risk of confounding or bias and a significant risk that the relationship is not causal
3	Non-analytic studies, e.g. case reports, case series
4	Expert opinion

Methods

A comprehensive literature search of MEDLINE, EMBASE, and the Cochrane Central Register of Controlled Trials using the Search 2.0 interface was undertaken. Relevant thesaurus terms were used and limits applied for language (English) and publication year (2000–9). Free-text phrases were also used to pick up any recent items yet to be indexed. The Cochrane Library, Issue 3, 2009, was also searched using the free-text phrases, blood transfusion, autologous, surgical blood loss, cell salvage, cell saver, and blood salvage. The findings were exploded for: peritonitis, neoplasms, sepsis, urologic surgery, abdominal surgery, liver surgery, and peritonitis. We also searched reports and guidelines produced by the National Institute of Clinical Excellence (NICE), the Association of Anaesthetists of Great Britain and Ireland (AAGBI), the Obstetric Anaesthetists Association (OAA), SHOT steering group, and the Confidential Enquiry of Maternal and Child Health (CEMACH).

The Library and Knowledge Services Manager performed the literature search, which identified 230 relevant abstracts. Two reviewers assessed these abstracts independently and 62 full-text articles were obtained. We also obtained the full text of articles from relevant references identified in the reviewed articles. The reviewers used the Scottish Intercollegiate Guidelines Network grading system to assign levels of evidence to all reviewed articles (Table 3).[23] The level of evidence provided by the studies reviewed in detail is summarized in Table 4.

Risks of cell salvage

There are many potential complications associated with cell salvage, such as non-immune haemolysis, air embolus, febrile non-haemolytic transfusion reactions, mis-transfusion, coagulopathy, contamination with drugs, cleansing solutions and infectious agents, and incomplete washing leading to contamination with activated leucocytes, cytokines, and other microaggregates.[24] The risks of such complications have decreased with technical advances, staff training, and growing experience with cell salvage. Processing of salvaged blood removes platelets and coagulation factors which can result in a coagulopathy. It has been demonstrated that a patient's coagulation remains normal if the blood loss is <3 litre.[25] The Cleveland Clinic carried out a 5 yr retrospective review of adverse events associated with allogeneic blood transfusion and cell-salvaged autotransfusion. They found the incidence of adverse events with autotransfusion to be 0.027% compared with 0.14% with allogeneic blood transfusion.[26]

Suctioning of RBCs may cause sheer stress injury, which can result in haemolysis and therefore reduction in return of RBCs.[27] One method of reducing RBC haemolysis is minimizing the pressure in the suction device. Variable suction

Table 4 Details of studies included

Authors	Year of publication	Level of evidence	Recommendations
Carless and colleagues[36]	2006	1++	Cochrane review—'Cell salvage for minimizing perioperative allogenic blood transfusion (Review)'—51 RCTs—meta-analysis
			Cell salvage reduced allogeneic blood transfusion by 39%. 4.3 patients would have to undergo cell salvage so that one patient could avoid allogeneic blood
			A larger relative risk reduction (RRR) of allogeneic blood transfusion was observed in orthopaedic trials (58%) than in cardiac trials (23%)
			RRR in vascular surgery was not significant
			RRR of 38% when cell salvage combined with PAD/ANH/aprotinin compared with without cell salvage
			Majority of trials were poor quality
			Cell salvage did not affect morbidity or mortality. Cell salvage reduced incidence of non-fatal MI and infection
Obstetrics			
Allam and colleagues[4]	2008	2+	Systematic review
			Autotransfusion does not increase the rate of amniotic fluid embolus (AFE), infection, or DIC
			May decrease infectious and non-infectious complications of allogeneic blood transfusion
			Cell salvage is recommended in cases of expected major haemorrhage
			Cell salvage may decrease mortality
Geoghegan and colleagues[39]	2009	1−	Systematic review (only one RCT)
			Cell salvage does not increase the risk of AFE
			Cell salvage is effective at reducing the need for allogeneic blood transfusion
			Cell salvage may be cost-effective
			There are currently no recommendations for the use of cell salvage outside the emergency setting
Sullivan and colleagues[43]	2008	2−	34 patients—case–control study
			Cell salvage with LDF significantly reduced levels of amniotic fluid contaminants
			Fetal RBCs are not removed by cell salvage with LDF resulting in risk of maternal alloimmunization
			Only one suction device needs to be used
Fong and colleagues[24]	2007	2−	Retrospective cohort case–control study
			Theoretical study of potential reduction in allogeneic blood transfusion with cell salvage in Caesarean sections
			Cell salvage reduced exposure to allogeneic blood 48.6% of patients
			Cell salvage could have eliminated allogeneic blood transfusion in 14.5–25.1% of patients (depending on efficiency of RBC recovery)
Vascular			
Maarkovic and colleagues[47]	2009	2−	180 patients—prospective observational study with a historical control group
			Elective AAA repair
			Cell salvage resulted in a significant reduction in allogeneic blood transfusion (P=0.0032)
			Cell salvage more efficacious in cases of ruptures AAA repair
			Cell salvage did not increase postoperative complications
Healy and colleagues[49]	2007	2−	79 patients undergoing elective and emergency AAA repair
			Cell salvage is safe and significantly reduces allogeneic blood requirements
Alvarez and colleagues[45]	2004	1−	5 RCTs—small numbers in each RCT
			Not enough evidence to support the claim that the use of cell salvage reduces the need for allogeneic blood
Haynes and colleagues[51]	2005	3	10 patients—cohort study
			Elective AAA repair
			Swab washing increases RBC recovery by 33%

Continued

Table 4 *Continued*

Authors	Year of publication	Level of evidence	Recommendations
Serrachino-Inglott and colleagues[48]	2005		Prospective observational study
			154 patients who had undergone emergency AAA repair
			Cell salvage resulted in reduced allogeneic blood transfusions (3 units of RBCs per patient), $P<0.01$
			The use of cell salvage reduced hospital mortality ($P=0.01$)
Haynes and colleagues[108]	2002	1−	145 patients, RCT
			Autologous transfusion is cost neutral in elective aortic surgery
Takagi and colleagues[46]	2007	1−	Meta-analysis of four RCTs
			Cell salvage resulted in 37% reduction in risk of allogeneic blood transfusion ($P=0.03$)
Orthopaedics			
Bridgens and colleagues[30]	2007	3	97 patients (47 in cell salvage group)—retrospective case review with the control group
			Revision hip surgery
			Use of cell salvage resulted in median reduction of allogeneic blood transfusion of 4 units/patient ($P=0.0006$)
			59% reduction in mean volume of allogeneic blood transfused
			The average cost saving is £406.84/patient
Scannell and colleagues[58]	2009	3	186 patients—retrospective case note review study
			Patients with acetabular fractures
			Use of cell salvage did not affect rates of allogeneic blood transfusion
			The injury severity scores were much higher in the cell salvage group
Gause and colleagues[55]	2008	3	188 patients [cell salvage used in 141 (75%) cases]
			Retrospective case note review of patients undergoing posterior lumbar fusion
			Increased allogeneic blood transfusions in the cell salvage group
Shenolikar and colleagues[52]	1997	1+	100 patients—prospective randomized study
			Patients undergoing total knee replacement
			Cell salvage reduced allogeneic blood requirements from 80% to 16%
Reitman and colleagues[56]	2004	2−	102 patients—prospective review
			Patients undergoing postero-lateral spinal fusion with internal fixation
			Cell salvage did not result in a significant reduction in allogeneic blood transfusion
Sinclair and colleagues[53]	2009	2−	154 patients undergoing total knee replacement
			Retrospective review
			The use of cell salvage and PAD reduced allogeneic blood transfusion. 51.9% RRR in transfusion associated with cell salvage
Weiss and colleagues[57]	2007	2−	95 patients—retrospective review
			Patients undergoing posterior fusion for scoliosis
			Cell salvage did not reduce allogeneic blood transfusion
Innerhofer and colleagues[12]	2005	2−	Prospective observational study investigating postoperative infections
			308 consecutive patients who had opted for PAD and undergoing primary hip or knee replacement surgery
			Allogeneic blood transfusion was associated with increased incidence of postoperative infections compared with autologous transfusion ($P=0.0053$)
Cardiac surgery			
Goel and colleagues[65]	2007	1−	RCT—49 patients undergoing elective off-pump CABG
			Cell salvage resulted in reduced allogeneic blood transfusion [83% *vs* 100% ($P=0.02$)]
			The use of cell salvage did not increase postoperative bleeding

Continued

Table 4 *Continued*

Authors	Year of publication	Level of evidence	Recommendations
Golab and colleagues[59]	2008	2−	Prospective study—122 infants (<10 kg) undergoing cardiac surgery
			The use of cell salvage resulted in reduced allogeneic blood transfusion in the first 6 h after operation (27% *vs* 59%, $P<0.001$)
Wang and colleagues[70]	2009	1+	Meta-analysis of 31 RCTs of patients undergoing cardiac surgery
			Cell salvage reduced exposure to allogeneic blood products by up to 37% and RBCs by 40%
			The use of cell salvage did not increase the incidence of FFP/platelet transfusion
			Cell salvage did not increase postoperative complications
			Cell salvage of only cardiotomy blood on CPB did not reduce allogeneic blood transfusion
Djaiani and colleagues[66]	2007	1−	RCT of 226 patients >60 yr old undergoing primary CABG
			Postoperative cognitive dysfunction 6% in the cell salvage group and 15% in the control group ($P=0.038$). No difference at 1 yr
			Higher embolic load (transcranial Doppler) in the control group
			The use of cell salvage did not reduce allogeneic blood requirements
			Cell salvage group received more FFP (25% *vs* 12%, $P=0.018$). The more cell saved blood re-infused resulted in increased FFP transfusion ($P<0.001$)
Niranjan and colleagues[71]	2006	1−	RCT of 80 patients undergoing primary CABG—on and off pump
			Four groups. Allogeneic blood transfusion use significantly greater in on-pump CABG without cell salvage. Off-pump CABG and the use of cell salvage both reduce allogenic blood transfusion
			The use of cell salvage does not cause a clinically significant coagulopathy
			Small study groups
Klein and colleagues[37]	2008	1+	RCT of 213 patients undergoing primary CABG single valve or combined procedure
			The use of cell salvage did not reduce allogeneic blood transfusion
			No difference of blood loss in first 6 h
Gu and colleagues[67]	2008	1−	RCT of 40 patients undergoing cardiac surgery with CPB
			Cell salvage processing does not affect *in vitro* RBC aggregation, but significantly reduced RBC deformability and 2,3-DPG levels
Jonsson and colleagues[72]	2009	1−	Systematic review of patients undergoing cardiac surgery—management of cardiotomy blood intraoperatively
			LDF reduces embolic load by 50%. Washing cardiotomy blood reduces postoperative neurocognitive dysfunction
			No conclusions regarding the best methods of dealing with cardiotomy blood
Murphy and colleagues[73]	2005	1−	RCT of 61 patients undergoing off-pump CABG
			Cell salvage resulted in 19% reduction in allogenic blood transfusion ($P=0.095$)
			Higher postoperative Hb in the cell salvage group
Takayama and colleagues[68]	2007	2−	Prospective observational study of 13 patients undergoing primary CABG
			Cell salvage removes all heparin, 89% of platelets and 31% of leucocytes
Malignancy			
Connor and colleagues[83]	1995	2−	Prospective study with historical control—71 cell salvage group, 231 historical control
			Patients undergoing radical hysterectomy
			Cell salvage reduced the need for allogeneic blood transfusion (19% *vs* 79%
			Cell salvage did not influence survival rates or disease recurrence
Catling and colleagues[84]	2008	2−	Prospective observational study of 50 patients undergoing major pelvic surgery for gynaecological malignancy
			Investigating ability of LDF and cell salvage processing at removing tumour cells from salvaged blood
			Tumour cells found in 68% of cell saver reservoirs. No viable tumour cells were found post-LDF
Laing and colleagues[85]	2008	2−	Prospective observational study of 32 patients undergoing orthotopic liver transplantation for hepatocellular carcinoma

Continued

Table 4 *Continued*

Authors	Year of publication	Level of evidence	Recommendations
			62.5% of patients had tumour cells in shed blood. In 75% of these tumour cells were present after processing
			LDF removed all tumour cells except in cases were the tumour had ruptured
Davis and colleagues[11]	2002	2−	Retrospective case review of 769 consecutive patients who had undergone radical retropubic prostatectomy
			Cell salvage does not influence recurrence rates of prostate carcinoma (mean follow-up 40.2 months)
Nieder and colleagues[80]	2007	2−	The use of cell salvage in patients undergoing radical cystectomy was not associated with increased recurrence of disease
Stoffel and colleagues[79]	2005	2−	Prospective observational study of 112 patients undergoing radical prostatectomy
			Cell salvage was associated with increased number of PSA cells (16% *vs* 4%) in peripheral blood after operation. There were no PSA cells in peripheral blood 3–5 weeks after operation
			The use of cell salvage was not associated with recurrence of disease (mean follow-up 44.5 months)
Nieder and colleagues[78]	2004	2−	Retrospective case review of 1038 patients undergoing radical retropubic prostatectomy
			Cell salvage reduced the need for allogenic blood
			Cell salvage was not associated with increased risk of biochemical recurrence of prostatic carcinoma
Others			
Bowley and colleagues[93]	2006	1+	RCT of 44 patients who had penetrating abdominal trauma
			Salvaged blood positive for microorganisms in 91.7% of cases
			Cell salvage significantly reduced exposure to allogenic blood transfusion (6.5 *vs* 11.7 units allogeneic blood, $P=0.008$)
Duffy and colleagues[13]	1996	1+	Meta-analysis—7 RCTs with a total of 1060 patients
			Allogeneic blood transfusion was associated with increased risk of postoperative infections ($P<0.0001$)

devices, where the suction pressure varies automatically in response to the amount of air being aspirated, have been demonstrated to minimize RBC haemolysis.[28] Shear stress injury also results in 'sublethal' damage, shortening the life span of the RBC.[28] Diluting blood with normal saline has been shown to reduce mechanical stress during suctioning, leading to a 60% reduction in RBC haemolysis.[27]

Benefits of cell salvage

The aim of cell salvage is to reduce or eliminate the need for allogeneic blood transfusion and the associated risks of infectious and non-infectious complications. The 2009 AAGBI guidelines identified indications for the use of intraoperative cell salvage: anticipated blood loss of >1000 ml or >20% estimated blood volume, patients with a low haemoglobin or at increased risk of bleeding, patients with multiple antibodies or rare blood types, and patients with objections to receiving allogeneic blood.[29]

Studies comparing cell salvaged with allogeneic blood have demonstrated increased mean erythrocyte viability[22 30] and increased 2,3-disphosphoglycerate (2,3-DPG)[31 32] and adenosine triphosphate (ATP) levels[4] in salvaged blood. The mean erythrocyte viability has been reported to be as high as 88% with cell salvage.[33] Salvaged RBCs maintain their normal biconcave disc shape, but allogeneic blood assumes an echinocyte shape (after 14 days), which is thought to impair its ability to cross the capillary beds.[34] Therefore, patients who have had autologous transfusion should have improved oxygen-carrying capacity and tissue oxygen delivery.

There is evidence that autologous transfusion results in increased survival after oesophagectomy when compared with allogenic blood transfusion.[35] This may be due to the lack of immunomodulatory effects of salvaged blood compared with allogeneic blood. It has also been postulated that cell salvage may have immunostimulatory effects, which may reduce postoperative infection.[30]

In 2006, a Cochrane Collaboration meta-analysis of studies published up to 2003 of the use of cell salvage for minimizing allogeneic blood transfusion[36] found that cell salvage was efficacious in reducing the need for allogeneic blood transfusion in adult elective surgery. Overall, the use of cell salvage reduced exposure to allogeneic blood transfusion by 39%, with an average saving of 0.67 units per patient. Cell salvage was found to be the most effective in orthopaedic surgery and had no negative impact on morbidity or mortality. In patients who had received salvaged

blood, there was a decreased incidence of non-fatal myocardial infarction and reduced postoperative infections. The authors commented that the methodology and quality of the trials were poor and that bias may be present as they were unblinded.[36] The use of cell salvage has increased, and there have been a good number of studies published since 2003 which have been included in this review.

Complications of cell salvage

Complications associated with the use of cell salvage are rare and studies have shown no increase in complications in patients receiving cell salvage.[26 36] However, when patients are autotransfused large volumes, this is often accompanied by coagulopathy, as the washing process discards all platelets and clotting factors, leaving only the red cells re-suspended in normal saline. Near patient (including thromboelastography), laboratory testing (including prothrombin time, fibrinogen, and platelet count), or both should be carried out and blood product replacement considered according to local protocols. A randomized trial of 213 cardiac surgery patients showed no increase in bleeding or coagulopathy in the treatment group where the volume of blood processed by the cell saver was relatively small [342 (194) ml].[37]

Obstetrics

In the 2003–5 CEMACH report, haemorrhage was the fifth largest cause of death, with an incidence of one in 200–250 deliveries and a fatality rate of one in 600–800 cases.[38] It has been estimated that obstetric haemorrhage accounts for 3–4% of all allogeneic blood transfusion in the UK.[4] With over 2 million deliveries in 2008, about 38 000 women received allogeneic blood transfusions. Methods to conserve blood in the obstetric setting could result in a significant reduction in the use of allogeneic blood. However, the use of cell salvage in obstetrics may be limited due to the high incidence of haemorrhagic episodes requiring blood transfusions that occur out of the operative setting.[24]

A retrospective cohort, case–control study of almost 12 000 patients analysed transfusion practice and the theoretical use of cell salvage as a method of reducing allogeneic blood transfusion during Caesarean sections.[24] The overall incidence of allogeneic blood transfusion was low at 1.8%. No power analysis was carried out, but it was a large retrospective study. Cell salvage could have reduced exposure to allogeneic blood in 48.6% of patients and even eliminated it in 14.5–25.1%. Potential inaccuracy in this theoretical use was accounted for by calculating the best and worst RBC recovery rates for cell salvage. The authors concluded that the use of cell salvage in obstetrics can be effective in reducing the need for allogeneic blood transfusion.[24] These findings were confirmed by a recently published systematic review of the use of cell salvage in obstetrics.[39] Overall, the quality of evidence available is poor as there was only one randomized trial in the systematic review.

Cell salvage in obstetrics has been controversial because of the theoretical risk of precipitating amniotic fluid embolus (AFE)[24] based on the concern that amniotic fluid mixed with the salvaged RBCs may not be completely removed by the washing process and subsequently re-infused. It is now widely accepted that the risk of AFE has been overestimated. A review of 46 cases of AFE found that the clinical and haemodynamic findings were similar to those of anaphylactic and septic shock.[40] The authors suggested that a common pathophysiological mechanism may be responsible and that the term ‘amniotic fluid embolism’ may be a misnomer and ‘anaphylactoid syndrome of pregnancy’ may be more appropriate. However, it is still unclear which component, if any, of the amniotic fluid is the precipitant.[40–42] The presence of fetal squames in maternal blood was regarded as a marker of AFE, but they have been found in blood samples from pulmonary artery catheters in otherwise normal parturients.[41] There have been no proven cases of AFE caused by re-infusion of salvaged blood.[29] Two recent systematic reviews published concluded that the re-infusion of RBCs salvaged during Caesarean section is not associated with an increase in the incidence of AFE.[4 39] This supports the safety of cell salvage in obstetrics but must be interpreted with caution because the quality of evidence is poor and also AFE is rare and difficult to diagnose.

It has been demonstrated that cell savers used in combination with a leucocyte depletion filter (LDF) can significantly reduce the levels of amniotic fluid,[4 43] but not fetal RBCs,[4] in salvaged blood. Cell savers are unable to differentiate fetal from maternal RBCs. The presence of fetal RBCs in the salvaged blood for re-infusion increases the risk of maternal alloimmunization if there is any incompatibility between maternal and fetal antigens. The risk of alloimmunization is unlikely to be greater than that incurred in a normal vaginal delivery.[4]

In the past, manufacturers recommended that two suction devices should be used, one to aspirate as much of the amniotic fluid as possible before suctioning blood from the operative field using a new device. A prospective randomized study compared the efficiency of amniotic fluid removal in two groups using either one or two suction devices.[43] The study was small (34 patients) but well conducted with low risk of bias because testing of cell salvaged blood was carried out by independent laboratory technicians. There was no statistically significant difference between the two groups; therefore, the use of only one suction device may be as safe and should in theory increase the efficiency of RBC recovery.[43]

In 2005, NICE produced guidelines that concluded that the use of intraoperative cell salvage in obstetrics was safe if used in combination with an LDF.[44] CEMACH,[38] the AABGI, and OAA[29] have also endorsed cell salvage.

Vascular

Cell salvage has been used for many years in elective and emergency vascular surgery. It has been demonstrated to

be safe, but its efficiency at reducing the need for allogeneic blood transfusion and cost-effectiveness has not yet been proven. A systematic review of five randomized controlled trials (RCTs) in 2004 concluded that there was not enough evidence to recommend the routine use of cell salvage during elective abdominal aortic aneurysm (AAA) or aorto-femoral bypass surgery.[45] The authors commented that a large RCT should be carried out. These findings were contradicted by a meta-analysis of five RCTs in 2007, which found that cell salvage reduced the risk of exposure to allogeneic blood transfusion by 37% ($P=0.03$) in patients undergoing elective AAA repair.[46] The results of this meta-analysis have been confirmed by two prospective observational studies and one retrospective review which demonstrated that the use of cell salvage resulted in a statistically significant reduction in exposure to allogeneic blood in patients undergoing abdominal aortic surgery.[47–49] These studies were not randomized, and enrolled small numbers of patients (180, 154, and 79 patients, respectively) which increased the risk of bias and of being underpowered. One of the prospective studies investigating the use of cell salvage in ruptured AAA surgery found that the use of cell salvage reduced the exposure to allogeneic blood by 3 units per patient. The study was not powered for subgroup analysis, but there was a trend towards reduced hospital mortality in the cell saver group.[48]

In vascular surgery, the use of a combination of methods of blood conservation has been demonstrated to be effective. A small multicentre, prospective, randomized study found that cell salvage in combination with acute normovolaemic haemodilution (ANH) decreased the exposure to allogeneic blood transfusion from 80.0% to 33.7%.[50] It is difficult to draw conclusions regarding benefits from this study because it was underpowered and cell salvage was combined with ANH. RBC loss in swabs has been shown to account for 30–50% of intraoperative blood loss. A small prospective study of patients undergoing elective AAA surgery found that washing swabs increased RBC recovery by 33%.[51]

Orthopaedics

Cell salvage has a better evidence base of safety and efficacy in orthopaedic surgery. It has been demonstrated that cell salvage reduces the need for allogeneic blood transfusion in revision hip[30] and knee replacement surgery.[52–54] The hip revision study was a retrospective database review which increases the risk of bias as it was not randomized. Only 94 cases were reviewed and no power analysis was made, but the authors suggest that the use of cell salvage resulted in a median reduction in allogeneic blood transfusion of 4 units and an average cost saving of £406.84 per patient.[30] The evidence supporting the use of cell salvage in knee replacement surgery is more robust and includes two RCTs and a larger (154 patients) retrospective review. One of the RCTs enrolled 100 patients, who had undergone total knee replacements and demonstrated that the use of intraoperative cell salvage reduced the requirement for allogeneic blood transfusion from 80% to 16%.[52] There is, however, no evidence that intraoperative cell salvage reduces allogeneic blood transfusion requirements or cost in adult posterior lumbar fusion surgery,[55 56] scoliosis surgery,[57] or operative treatment of acetabular fractures.[58] The majority of available evidence is grade 2/3 and consists of non-randomized, retrospective studies where the use of cell salvage is at the surgeon's discretion.

In addition to the benefits of avoiding allogeneic blood as discussed earlier, there may be other benefits in orthopaedic surgery. A prospective observational study of 308 patients found that allogeneic blood transfusion was associated with increased incidence of postoperative infections when compared with autologous transfusion ($P=0.0053$).[12]

Paediatrics

There is very little evidence for the use of cell salvage in paediatric patients. This has been largely due to the size of the blood collection bowl and therefore the volume of blood that has to be collected before processing. Most manufacturers now produce paediatric sized bowls.[59] In addition, modern cell salvage machines that do not use bowl centrifugation can process any volume of blood, such as the CATS device (Fresenius Kabi, Warrington, UK). A prospective study of 79 paediatric patients undergoing craniosynostotic correction compared preoperative erythropoietin and intraoperative cell salvage with a control group.[22] The combination of preoperative erythropoietin and intraoperative cell salvage resulted in a 95% reduction in the use of allogeneic blood and a 95.5% reduction in the use of other blood products. The impact of cell salvage on allogeneic blood use was difficult to interpret as the preoperative erythropoietin resulted in significantly higher haemoglobin concentrations and the patient numbers were small.[22] Cell salvage has also been demonstrated to reduce allogeneic blood requirements in infants (<10 kg) undergoing cardiac surgery.[59] These studies have demonstrated that the use of cell salvage in paediatric patients is efficient at reducing allogeneic blood transfusion in certain types of surgery.

Neurosurgery

There is limited evidence available to support the use of cell salvage in neurosurgery. A prospective observational study of 472 patients undergoing intracranial surgery found that the use of cell salvage resulted in a reduction in the use of allogeneic blood transfusion by 74%. In 25% of patients who required blood transfusions, the use of allogeneic blood was avoided altogether.[60] Although the evidence for the use of cell salvage in neurosurgery is limited, it should be considered if blood loss >1000 ml is anticipated or there is the potential for sudden blood loss.

Cardiac

The need for blood transfusion in cardiac surgery has remained high, despite advances in surgical techniques and

pharmacological methods used to reduce blood loss. Allogeneic blood transfusion in cardiac surgery accounts for ~10% of all blood supplied by the national blood service in the UK.[61] Blood transfusion in cardiac surgery has been shown to result in a dose-dependent depression of immune function and increased risk of postoperative infection.[13–15] It has also been associated with higher hospital mortality,[62] renal dysfunction,[63] pneumonia,[64] wound infection,[15] and sepsis.[62 65]

Cardiotomy suction has been used in cardiac surgery for many years to reduce blood loss and allogeneic transfusion requirements. It involves suction of pericardial blood intraoperatively which is then returned to the CPB circuit. The re-transfusion of cardiotomy blood has been implicated with the development of a coagulopathy and increased blood loss,[66] increased incidence of postoperative neurocognitive dysfunction,[67] and systemic inflammatory response syndrome.[68 69]

The use of intraoperative cell salvage in cardiac surgery has been extensively studied. A meta-analysis of 31 RCTs published in 2009 found that the use of cell salvage significantly reduced exposure to any allogeneic blood products by up to 37% and RBCs by 40%.[70] It was not associated with any increased risk of hospital mortality, postoperative stroke, acute myocardial infarction, postoperative atrial fibrillation, renal dysfunction, infection, or reoperation for bleeding.[70] The use of cell salvage pre- and post-cardiopulmonary bypass (CPB) was found to be the most effective in reducing allogeneic blood transfusions, compared with cell salvage of cardiotomy blood during CPB.[70] These results have been confirmed[65 71–73] and contradicted by recent RCTs.[37] Three of the RCTs[65 71 73] supporting the efficacy of cell salvage in cardiac surgery are underpowered, but overall the current evidence supports the routine use of cell salvage in cardiac surgery, although it may not be cost-effective in low-risk cases, such as primary coronary surgery or isolated valve replacement or repair.

Neurocognitive dysfunction is a common complication after cardiac surgery, with an incidence of 15–36%,[66 72] with cerebral microembolization the most likely.[70] Blood collected from cardiotomy suction contains high levels of cellular debris and lipid microparticles, which contributes to the microembolic load. It has been demonstrated that processing of salvaged blood reduces lipid and other microparticles.[74] This was confirmed by an RCT of 162 patients, which demonstrated that cell salvage used in combination with an LDF reduced the embolic load by 50%.[75] An RCT of 226 patients undergoing primary coronary surgery which compared standard cardiotomy suction with cell salvage reported the incidence of postoperative neurocognitive dysfunction to be 6% in the cell salvage group compared with 15% (P=0.038) in the control group 6 weeks after surgery. There was an increased embolic load on transcranial Doppler in the control group. The differences between the two groups were not sustained at 1 yr follow-up.[66] A recent systematic review found that processing cardiotomy blood through the cell saver reduced neurocognitive dysfunction after operation.[72] The use of an LDF and the associated reduction in lipid and microembolic load has other benefits, such as improvements in postoperative lung function and shunt fractions and lower pulmonary vascular resistance.[76] The improvements in lung function have not translated into improvements in mortality or hospital length of stay.

Malignancy

The use of cell salvage and autologous blood transfusion has previously been contraindicated in cases of malignancy due to the theoretical risk of disseminating the tumour. In 1986, the American Medical Councils report on 'Autologous Blood Transfusions' concluded that cell salvage was contraindicated in cases of malignancy.[77] However, there is evidence from different surgical specialities for the use of cell salvage in cases of malignancy. Owing to practical and ethical constraints, it is difficult to conduct RCTs in this area. Most of the current evidence takes the form of small prospective studies or large case note reviews.

The use of cell salvage and autologous transfusion has been extensively investigated in patients with urological malignancies. Prostate cancer is well suited for investigation of tumour recurrence using prostate-specific antigen (PSA).[78] In a retrospective case note review of recurrence (median follow-up 40.2 months) in more than 1000 patients after radical retropubic prostatectomy during which 25.5% of patients received cell salvaged blood, the use of cell salvage and autologous transfusion did not increase recurrence rates and was effective at reducing allogeneic blood transfusion requirements.[78] These findings have been confirmed by similar retrospective reviews of patients who had undergone radical prostatectomy,[11 79] radical cystectomy,[80] and radical nephrectomy.[81] There is only one prospective study, but the other retrospective reviews are large and consistent in their findings. In 2008, NICE published guidelines endorsing the use of intraoperative cell salvage in combination with an LDF for radical prostatectomy and cystectomy.[82]

The use of cell salvage has also been investigated in gynae-oncology surgery. In a prospective study with a large historical control group, the use of cell salvage in patients undergoing radical hysterectomy for cervical cancer reduced allogeneic blood transfusion requirements from 79% to 19%.[83] Both groups were well matched for clinical and pathological indices. Autologous blood transfusion had no influence on survival rates or disease recurrence (mean follow-up 24 months).

An observational study of 50 patients undergoing major gynae-oncology surgery investigated the ability of LDFs to remove tumour cells from salvaged blood.[84] Blood samples were obtained before operation, from the cell saver before and after processing and after passing through an LDF. Viable tumour cells were found in 4% of preoperative samples, in 68% of cell saver reservoirs before processing, and in 62% after processing. After the salvaged blood was passed through an LDF, they found no tumour cells, but they did find tumour cell fragments, which were unable to cause metastases.

Orthotopic liver transplantation is the therapeutic option of choice for many end-stage liver diseases.[85] It is associated with potential massive blood loss, so cell salvage has great potential for reducing exposure to allogeneic blood. During these cases, the presence of tumour cells in shed blood can be as high as 91–100%, which raises concerns regarding the use of cell salvage and the potential dissemination of malignancy.[85] A prospective observational study of 32 patients undergoing orthotopic liver transplantation for hepatocellular carcinoma investigated the presence of tumour cells in shed blood and the efficiency of cell salvage in combination with an LDF at removing them.[85] Tumour cells were present in the cell saver reservoir in 62.5% of patients and after processing tumour cells were still detected in 75% of those. After passing through an LDF, tumour cells were only detected in 10% of samples where the tumour had ruptured intraoperatively. They demonstrated that processing of salvaged blood in combination with an LDF significantly reduced the presence of tumour cells in the autologous blood for re-infusion. Their findings suggest that in cases where the tumours rupture the use of cell salvage may be contraindicated due to the persistence of tumour cells in salvaged blood.[85] The use of cell salvage during liver transplantation for hepatocellular carcinoma has been found to reduce the exposure to allogeneic blood and to be cost-effective.[25 86 87]

Microbiological contamination

The use of cell salvage is contraindicated by the manufacturers in cases where there is potential contamination of salvaged blood with enteric contents.[88] In 1986, the American Medical Councils report on 'Autologous Blood Transfusions' stated that cell salvage was contraindicated where the blood has come into contact with bacteria.[77] Since then many studies have investigated the incidence and clinical effects of microbiological contamination of salvaged blood. During 'sterile' procedures, the incidence of microbiological contamination of salvaged blood ranges from 12.7%[89] to 33.3%.[90] The most common source of contamination is thought to be skin and environmental contamination. A prospective study of cell salvage in combination with an LDF to reduce bacteriological contamination of salvaged blood used expired packs of erythrocytes inoculated with *Escherichia coli, Pseudomonas aeruginosa, Staphylococcus aureus*, and *Bacteroides fragilis*.[91] The blood was then washed, processed by a cell saver, passed through an LDF, and then collected for culture. They demonstrated that the use of cell salvage in combination with an LDF removed 99.0% of *E. coli*, 99.9% of *S. aureus*, 100% of *P. aeruginosa*, and 97.6% of *B. fragilis*. The results demonstrated that cell salvage and an LDF resulted in significant reductions in bacterial contamination. The authors continued the study with increasing levels of bacterial contamination to simulate enteric content contamination, and found that processing salvaged blood mixed with faeces resulted in significant residual bacterial contamination.[91]

The relationship between the transfusion of contaminated cell-salvaged blood and adverse clinical outcomes is not clear. A prospective observational study of 38 patients undergoing orthotopic liver transplantation, who were chronically immunosuppressed and therefore at high risk of infectious complications, found samples of processed salvaged blood were positive for microorganisms in 68.4% cases.[92] A variety of microorganisms were cultured—*Staphylococcus* (73%), *E. coli* (4%), *Propionibacter* (4%), and *Candida* (8%). All the patients in this study had blood cultures obtained on postoperative days 1 and 3, and none was positive for the organisms previously cultured from the salvaged blood.[92] The use of cell salvage in cases of major penetrating abdominal trauma is contraindicated due to potential enteric content contamination. An RCT of 44 patients with penetrating abdominal trauma found that salvaged blood was positive for microorganisms in 91.7% of cases.[93] The organisms cultured were polymicrobial (36%), *Staphylococcus* (36%), coliforms (9%), and yeasts (18%). There was no association between positive microbiology of the salvaged blood and postoperative infectious complications.[93] Case series have also reported the use of cell salvage in excisional burn surgery[94] and in more than 150 patients with intestinal injury secondary to abdominal trauma with no increase in infectious complications.[95 96]

Studies of autologous transfusion of microbiologically contaminated salvaged blood have demonstrated no adverse outcomes or increase in postoperative infectious complications.[92 93 95 96] Therefore, enteric content contamination or systemic sepsis should no longer be considered an absolute contraindication to the use of intraoperative cell salvage. In cases where there is gross enteric content contamination, the surgeons should avoid suctioning faecal matter, broad-spectrum antibiotics should be administered, and the volume of saline wash can be increased.[29] In an animal study where dogs were transfused contaminated blood, the administration of broad-spectrum antibiotics reduced mortality from 70% to 10%.[97]

Special circumstances

The use of cell salvage has become an important part of intraoperative management of Jehovah's Witnesses who refuse allogeneic blood or blood product transfusions on religious grounds. Cell salvage is usually acceptable to Jehovah's Witnesses, but consent needs to be obtained on an individual basis. The AAGBI guidelines recommend the use of cell salvage in cases where patients have objections to receiving allogeneic blood transfusions.[29] There are many case reports of the successful use of cell salvage in Jehovah's Witness patients undergoing major surgery, including radical prostatectomy,[98] living donor liver transplants,[99] renal cell carcinoma extending into the right atrium,[100] and gynae-oncology surgery.[101] There is limited evidence for the use of cell salvage in patients with haematological diseases. The use of cell salvage in patients with sickle-cell disease has generally been avoided because the hypoxic

environment of the reservoir was thought to result in RBC sickling and re-infusion of this blood may precipitate a sickle-cell crisis.[102] A brief report described the use of cell salvage in two patients with sickle-cell trait undergoing elective Caesarean section.[102] Blood films of the salvaged blood showed 15–20% sickled RBCs in Case 1 and 20% altered, but not sickled, in Case 2. Both patients received autologous blood transfusions and had an uneventful recovery. The authors concluded that cell salvage can be used in patients with sickle-cell trait if the clinical circumstances justify it, but should be avoided in patients with sickle-cell disease.[102] β-Thalassaemia results in increased RBC rigidity and reduced membrane stability, which is thought to make them more susceptible to damage from the shear forces they encounter during cell salvage. There is a case report of the successful use of cell salvage in an obstetric patient with β-thalassaemia, with no evidence of increased RBC haemolysis.[103]

Training

The UK Cell Salvage Action Group has developed online resources to assist training in the use of cell salvage. They state that training and education should be competency-based. An 'Intraoperative Cell Salvage Competency (ICS) Assessment Workbook' can be downloaded from www.transfusionguidelines.org.uk. Initial training can be provided by the manufacturers, which can be negotiated at the time of purchase. Further training can be delivered in-house or via e-learning, the ICS workbook, or the ICS competency assessment workbook.[104]

Cost of cell salvage

The cost of cell salvage is an important consideration, and must take into account the financial benefits of autologous transfusion such as reduction in allogeneic blood transfusion, reduced blood transfusion reactions, reduced postoperative infection rates, and shorter hospital length of stay.[105] A prospective study of the cost-effectiveness of cell salvage in a large teaching hospital found cell salvage to be cost-effective.[105] An American review of costs associated with allogeneic blood transfusion and cell salvage in a large teaching hospital compared the average cost of a unit of allogeneic blood with an equivalent processed by cell salvage and found that cell salvage resulted in an average saving of $110.54 per unit.[106] A systematic review analysed the cost-effectiveness of cell salvage in the different surgical specialities.[107] The authors commented that the quality of economic evaluations was poor due to insufficient data for analysis or lack of relevance to UK practice. They found that cell salvage was more cost-effective in cardiac and orthopaedic surgery than in vascular surgery. Washed intraoperative cell salvage was found to be more cost-effective than unwashed postoperative cell salvage in cardiac surgery, but in orthopaedic surgery, unwashed postoperative cell salvage was more cost-effective than intraoperative cell salvage.[107]

An RCT compared the cost of allogeneic blood transfusion with cell salvage and ANH in patients undergoing elective AAA repair. It found that the cost of allogeneic blood was the same as cell salvage combined with ANH. This review, however, did not take into account the use of cell salvage in emergency AAA repairs, where it is more cost-effective[108] and has been demonstrated to reduce hospital mortality,[48] or the cost benefits of reducing complications associated with allogeneic blood transfusions.

The cost of cell salvage can be reduced through the use of a standby system, which collects blood in a specifically designed reservoir. Anti-coagulant (usually heparin) is added to the collected blood, which is only processed if a sufficient volume is recovered. The disposables necessary for washing need only be set up when a decision to process the blood is made, thus reducing the disposables cost of cell salvage by two-thirds if no blood is processed.[106]

Leucocyte depletion filters

LDFs are used during the processing of donated blood to remove white blood cells. Leucodepletion is thought to improve cell salvage safety and reduce the side-effects.[13] LDF consist of a sieve with a negative surface charge, which have been demonstrated to be efficient at removing white blood cells, tumour cells,[12 84 85] amniotic fluid,[43] and microorganisms.[92] In 1998, an update consensus conference on autologous transfusion endorsed the use of cell salvage with an LDF.[109]

Conclusions

Cell salvage and autologous transfusion is safe and effective at reducing allogeneic blood transfusion requirements, and also being cost-effective in cardiac and orthopaedic surgery. Cell salvage should be considered in all cases where significant blood loss is expected or possible, in patients with preoperative anaemia, and who refuse allogeneic blood products. The standby system allows cell salvage to be used in cases where the anticipated blood loss is $<$1000 ml, but significant bleeding is a possibility. This will result in further reduction in allogeneic blood transfusion requirements.

Recent evidence has shown that cell salvage may be used in obstetrics or malignancy. LDFs may provide an additional element of safety, and should be used unless rapid re-transfusion is required. In addition, enteric contamination or systemic sepsis does not preclude the use of cell salvage if adequate precautions are taken. Therefore, the only absolute contraindication to the use of cell salvage should be patient refusal.

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