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INTRAOPERATIVE AUTOLOGOUS BLOOD TRANSFUSION

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INTRODUCTION

Life-saving transfusion using human blood was first described by James Blundell in 1818. He performed ten transfusions, five of which were successful; of these, four were in women suffering postpartum hemorrhage. He typically used donor blood from the patient's husband, thus showing that the technique of blood injection with a syringe-infusion was safe[1]. In one account, he is credited with the re-infusion of autologous blood[2]. It is entirely appropriate, therefore, that the subject of intraoperative autologous transfusion be described in this textbook on postpartum hemorrhage. Blundell's original report described a reasonable outcome considering the crude understanding of blood transfusion techniques in existence almost a century before Landsteiner's identification of the ABO blood groups[3].

Some of the earliest reports of intraoperative blood salvage described the life-saving technique of simply collecting spilt blood from the abdominal cavity, filtering it through a gauze swab, and re-infusing what remained. In the ensuing years, techniques to collect, filter and wash blood lost at the time of surgery have become commonplace, although refinements of the method vary widely and depend not only upon the nature of the surgical procedure but also the availability of technical resources. As might be expected, expensive apheresis machines are lacking in many, if not most parts of the world, where operative obstetrics is routine. Nevertheless, the problem of postpartum hemorrhage is so common and remains such a clinical challenge that, in these circumstances, the technique as originally described is still used out of necessity. This chapter describes various methods of autologous blood salvage and, in particular, its evolving use in obstetrics with direct reference to postpartum hemorrhage.

DEFINITION

Autologous blood salvage is the collection of spilt blood resulting from surgical or traumatic bleeding that can be undertaken intraoperatively or postoperatively. The collected blood can be filtered and re-infused or filtered, washed and then re-infused.

METHODS

The quality and constitution of re-infused blood vary depending on whether unwashed or washed systems are used. In the absence of automated cell-washing devices, simple collection, filtration and re-infusion during postpartum hemorrhage have been described and continue to be used in some areas in the world. This technique is not ideal. However, the use of unwashed blood (particularly for postoperative collection and re-infusion using a sealed postoperative collection unit with a filter) has been used extensively in total knee surgery and seems safe and effective. It is interesting that a recent report suggested that the use of unwashed blood might have properties that improve the recipient's immune response[4].

The more widely applied intraoperative cell salvage is conducted with an apparatus that has the ability to collect spilt blood at the time of operation and anticoagulate it at the tip of the suction apparatus with citrated solution or heparinized saline (25 000 IU per liter of normal saline) (Figure 1). Collected blood is then transferred to a centrifugal bowl, where spinning at 5500 revolutions per second moves

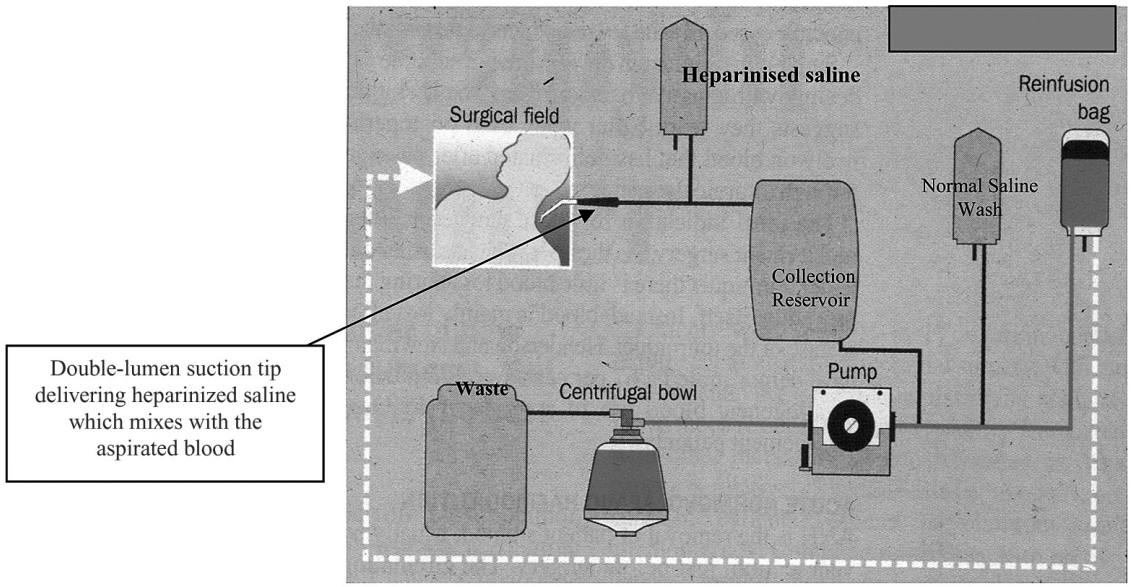

Figure 1 A diagrammatic representation of intraoperative cell salvage. (Adapted from an original drawing with the kind permission of Haemonetics Inc., Baintree). The dotted line represents infusion sent back to the patient. In the case of a Jehovah's Witness, this is primed with saline before starting to complete continuity of the circuit

the heavier red cells to the outer periphery of the bowl. As the bowl fills, the accumulation of red cells forces the plasma, platelets and other cellular debris out of a central exit, discarding waste products of the process. Special sensors identify when the bowl is full of red cells, and the fully automated machine begins to wash the collected and concentrated erythrocytes with normal saline. This process further cleanses the red blood cells. The resultant concentrate is then suspended in normal saline, producing a solution with a hematocrit of 60%. Most of the platelets and clotting factors will have been washed away at this point, however, and the fluid for re-infusion consists of autologous red cells suspended in normal saline[5].

In the presence of brisk bleeding, any of the commercially available automated cell-washing devices can produce a unit of red cell concentrate in 5–10 min. The volume of lost blood that can be processed is infinite, and reports of cell salvage in major trauma describe its successful use, the process providing approximately 50% of the required red cell transfusion[6]. Of course, in such situations, the use of cell salvage only minimizes the demand for allogeneic blood. In cases of massive hemorrhage, the cell salvage devices help to recycle transfused allogeneic blood as well as autologous blood.

As few platelets and minimal clotting factors are present in these re-infused red cells, careful assessment of coagulation parameters is required in cases of excessive bleeding where massive transfusion is required. Nowadays, this is the case in patients with massive hemorrhage anyway, as the provision of red cells suspended in a mixture of saline, adenine, glucose and mannitol (SAGM) means that only packed allogeneic red cells are being infused, and so similar provisos apply. Early consideration therefore needs to be given to platelet and fresh frozen plasma administration.

HISTORICAL COMPLICATIONS

Current machines have an extremely good safety record, but it is worthwhile dispelling some misconceptions about the technique that persist today. Air embolism is not a problem with modern equipment when it is used correctly. Free hemoglobin is almost completely removed, and the very small amounts that

remain have no significant clinical effect. Platelets are activated during salvage, but the majority are removed during the process. Leukocytes, complement and kinins are also activated during salvage, but systemic inflammatory responses have not been reported as clinically relevant.

POSSIBLE CONTRAINDICATIONS

Following a seminal report[7] supporting this technology, it now is accepted that three areas exist where the process of red cell salvage needs to be used with caution and following necessary risk–benefit analysis, depending on the clinical urgency of the situation. These involve the use of red cell salvage when spilt operative blood may contain malignant cells, or be heavily contaminated with bowel bacteria. Another area of caution is the use of red cell salvage when contaminated by amniotic fluid. It is accepted that, in the presence of any of these preconditions, cell salvage is not used unless considered necessary.

The non-availability of a safe allogeneic blood supply is clearly a situation when the use of cell salvage is justified in an attempt to preserve the patient's own blood and help oxygen carriage In the UK, current blood conservation recommendations promote the use of cell salvage[8]. The current drive for blood conservation is multifactorial, but the most topical reason is the potential decrease in the availability of donor blood resulting from the introduction of a test for the presence of abnormal prion protein. However, reduced numbers of donors is a problem that had its inception prior to the present testing concerns, as the presence of HIV and other viral pathogens have also restricted the number of potential donors.

It is against this backdrop that consideration of cell salvage in postpartum hemorrhage was made, and the remainder of this chapter examines the use of intraoperative cell salvage during postpartum hemorrhage. Fortunately, the widespread use of such devices has confirmed the safety of this process, providing there is no technical failure and the correct procedure for machine operation is practiced. The use of such devices is endorsed by national guidelines and Government directives[9,10].

SAFETY OF CELL SALVAGE IN OBSTETRICS

Two theoretical problems attend the use of cell salvage at the time of Cesarean section. First, in a Rh-negative mother, there is a risk of Rh immunization if the fetus is Rh-positive. As the cell saver cannot distinguish fetal from adult red cells, any fetal red cells suctioned from the operative field will be processed and re-infused with the maternal red cells. In practice, studies show that the degree of contamination with fetal red cells during cell salvage at Cesarean section is between 1 and 19 ml[11–13]. Applying the standard Kleihauer calculation, this would require between 500 and 2500 units (1–5 ampules) of Anti-D to avoid Rh immunization. As all Rh-negative patients require Anti-D after Cesarean section, patients receiving salvaged blood may simply require an increased dose.

The second theoretical problem is contamination with amniotic fluid, raising the specter of iatrogenic amniotic fluid embolus (AFE). This theoretical complication has been investigated by several workers, and has not been found to be a problem in practice[12–16]. The difficulty is that the precise elements of amniotic fluid, which cause the rare, and unpredictable 'anaphylactoid syndrome of pregnancy' (as AFE is more correctly called), remain unknown. To conduct a prospective, randomized, controlled trial with an 80% power to demonstrate that cell salvage does not increase the incidence of AFE by five-fold would require up to 275 000 patients, a number so enormous that the effort is unlikely ever to be undertaken. To demonstrate the absolute safety of a technique without randomized, controlled trials requires careful clinical audit of a large number of cases, supported by robust *in vitro* evidence.

IN VITRO STUDIES OF AMNIOTIC FLUID CLEARANCE:

In vitro studies have examined the clearance of α-fetoprotein[14], tissue factor[15], trophoblastic tissue[12], fetal squames and lamellar bodies[13] from maternal blood by the cell salvage process. Small molecules are removed in the plasma fraction by the centrifuge and wash process alone, and particulate material is removed by the use

of specialized leukodepletion filters. Using the combination of cell salvage and these specialized filters, every element of amniotic fluid that has been studied so far has been effectively removed from salvaged blood prior to re-transfusion[12–16].

CLINICAL CASES

Prior to 1999, approximately 300 cases in which cell-salvaged blood was administered to patients had been reported world-wide[16]. No obstetric clinical or physiological problems were encountered, despite the fact that filters were not used at this time. This means that each of these patients had some exposure to amniotic fluid, and with no ill effects. Waters and colleagues shed some light on this topic[13] by describing not only the complete clearance of squamous cells and phospholipid lamellar bodies from filtered, cell-salvaged blood, but also by clearly demonstrating the presence of both these amniotic fluid markers circulating in the maternal central venous blood at the time of placental separation. In 100% of patients in this trial, amniotic fluid was demonstrated in the circulation of healthy parturients undergoing elective Cesarean section. It is therefore probable that amniotic fluid routinely enters the maternal circulation and does no harm in the vast majority of cases. This exposure may trigger the syndrome of AFE due to an anaphylactoid reaction to an as-yet unidentified endogenous mediator in a very small number of women, the incidence of which varies between 1 in 8000 and 1 in 80 000 patients[17]. [Editor's note: since it has never been studied, there is no evidence to state that entry does not occur in an unknown number of cases of vaginal parturition.] Clearly, re-infusion of cell-salvaged blood, even if contaminated with traces of amniotic fluid, presents no extra risk to the woman from whom that blood has come, as she has already been exposed to it.

In 1999, a single report appeared describing a seriously ill Jehovah's Witness woman with severe pre-eclampsia complicated by HELLP syndrome (hemolysis, elevated liver enzymes, low platelets) who died in Holland, after having received cell-salvaged blood[18]. It has been quoted as a 'death due to obstetric cell salvage'[19]. It should be noted, however, that a patient who is seriously ill with HELLP syndrome and who refuses platelet and coagulation factor transfusion is unlikely to survive, and that, under such circumstances, her death should logically not be related to the use of cell salvage, but rather to her refusal to accept blood component therapy.

Cell salvage in obstetrics was introduced in the UK in 1999, and its use is growing rapidly, with most major obstetric units now advocating the technique in selected circumstances. The Confidential Enquiry into Maternal and Child Health 2000–2002 (CEMACH)[20] stated that *'. . . (cell salvage) may be used in any case of obstetric haemorrhage, not just women who refuse blood transfusion'* and described the technique as *'a new development which will prove helpful in the future'*. It further stated that 'the risk of causing coagulopathy by returning amniotic fluid to the circulation is thought to be small'. Subsequent to this, the 2005 revised Guidelines for Obstetric Anaesthetic Services were published jointly by the UK Obstetric Anaesthetists Association (OAA) and the Association of Anaesthetists of Great Britain and Ireland (AAGBI)[21], stating that *'an increasing shortage of blood and blood products and growing anxiety about the use of donor blood are leading to an increasing interest in the use of cell salvage in obstetrics. Staff will have to be suitably trained, and equipment obtained and maintained. . .'*

In November 2005, the UK National Institute for Clinical Excellence (NICE) reported on Cell Salvage in Obstetrics[22], describing cell salvage as 'an efficacious technique for blood replacement, well established in other areas of medicine' and pointing out the *theoretical* concerns when used in obstetrics. NICE goes on to recommend that clinicians using it in the UK should report any side-effects to the UK Department of Health Regulatory Authority (MHRA), that patients should be fully informed prior to its use, and that cell salvage in obstetrics should be performed by multidisciplinary teams that have developed regular experience in its use.

PRACTICAL USE OF CELL SALVAGE IN OBSTETRICS

There presently exists a substantial experience with the use of cell salvage in obstetrics in the

UK; cases include major hemorrhage due to placenta previa, placenta accreta, ruptured uterus, extrauterine placentation, massive fibroids and placental abruption, as well as routine use in Jehovah's Witnesses to avoid postoperative anemia[14].

The following guidelines are in use for cell salvage in obstetric use in the Swansea NHS Trust Hospitals, UK:

(1) It may be used for any situation in which allogeneic blood is used, but in practice this has so far been confined to Cesarean sections and uterine re-exploration or laparotomy following postpartum hemorrhage. There is no reason why vaginal blood loss could not be collected and cell-salvaged, as fears about infection have proved unfounded in abdominal gunshot wounds as long as the patients are on antibiotics – but the technical problem with physically collecting vaginal blood loss has yet to be solved! [Editor's note: the routine and planned use of the BRASSS technique described in Chapter 4 would be useful to overcome this problem as well as underestimation of loss.]

(2) The machine is set up and operated according to standard operating procedure, with an 'in-continuity' set-up for Jehovah's Witnesses (this means that the whole circuit is run through with saline and the re-transfusion bag connected to the intravenous cannula before starting the salvage suction, thereby establishing a continuous circuit between the blood lost and the recipient vein).

(3) In cases where there is doubt about the extent of expected blood loss, it is economical to set up the aspiration and reservoir kit only – the decision to process and re-transfuse can be made when the degree of hemorrhage has become clear (e.g. 'expected' bleeding from placenta previa).

(4) Where practicable, amniotic fluid should be removed by separate suction prior to starting cell salvage.

(5) Suction should be via the wide-bore suction nozzle in the kit, and the surgeon should try to suction blood from 'pools' rather than 'dabbing' tissue surfaces with the suction tip, as this minimizes erythrocyte damage.

(6) Blood from swabs can be gently washed with saline and salvaged from a sterile bowl into the main reservoir.

(7) Suction pressure should be kept as low as practicable (< 300 mmHg) to avoid red cell damage, although higher vacuum can be safely used if necessary with only a minimum increase in red cell damage.

(8) It is advisable to use a leukocyte depletion filter (Leukoguard RS Pall) in the re-transfusion circuit if there is any risk of amniotic fluid contamination. This is currently the only filter that has been shown to remove all particulate elements of amniotic fluid (fetal squames, lamellar bodies). This filtration process will necessarily slow down the rate at which blood can be infused, but it is permissible to pressurize the bag of salvaged red cells up to 200 mmHg after having ensured there is no air in the bag (otherwise it may burst!), or to use a large-volume syringe and three-way tap. In situations when hemorrhage is rapid, it is possible to connect more than one suction nozzle to the reservoir, and two filters and a dual giving-set to the re-infusion bag.

(9) As with any transfusion, the patient should be carefully monitored, preferably in an obstetric 'critical care' facility for 24 h. Coagulation tests should be obtained post-transfusion, and repeated if abnormal or if clinically indicated.

(10) If the patient is Rh-negative, a Kleihauer–Braun–Betke test should be performed and Anti-D administered as appropriate within 72 h.

Units that use obstetric cell salvage should keep careful records for Audit reporting in due course – with any problems also being reported to the MHRA as per NICE Guidelines.

SUMMARY

The use of intraoperative cell salvage is a safe method of conserving operative blood loss and minimizing the need for allogeneic transfusion. In an environment where allogeneic blood is in limited supply or the demands for blood transfusion are so great, as in the case of massive postpartum hemorrhage, the use of intraoperative cell salvage may be life-saving and its use in this area is gaining clinical acceptance.

References

1. Blundell J. Experiments on the transfusion of blood by the syringe. *Med Chirg Trans* 1818;9: 57–92
2. Allen JG. Discussion. *Ann Surg* 1963;158:137
3. Landsteiner K. Ueber Agglutinationserscheinungen normalen menschlichen Blutes. *Wien Klin Wochenschr* 1901;14:1132–4
4. Gharehbaghian A, Haque KM, Truman C, *et al*. Effect of autologous blood on postoperative natural killer cell precursor frequency. *Lancet* 2004;363: 1025–30
5. Tawes RL, Duvall TB. The basic concepts of an autotransfusor: the cell saver. In Tawes RL, ed. *Autotransfusion*. Michigan: Gregory Appleton, 1997
6. Hughes LG, Thomas DW, Wareham K, *et al*. Intra-operative blood salvage in abdominal trauma: a review of 5 years' experience. *Anaesthesia* 2001;56:217–20
7. Council on Scientific Affairs. Autologous blood transfusions. *JAMA* 1986;256:2378–80
8. A National Blood Conservation Strategy for NBTC and NBS. Compiled by Virge James on behalf of the NBS Sub-Group 'Appropriate Use of Blood', January 2004
9. NHS Executive. *Better Blood Transfusion: Appropriate Use of Blood*. London: Department of Health, 2002 (Health Service Circular 2002/009)
10. Peri-operative Blood Transfusion for Elective Surgery. http://www.sign.ac.uk
11. Fong J, Gurewitsch ED, Kump L, Klein R. Clearance of fetal products andsubsequent immunoreactivity of blood salvaged at Cesarean delivery. *Obstet Gynecol* 1999;93:968–72
12. Catling SJ, Williams S, Fielding AM. Cell salvage in obstetrics: an evaluation of the ability of cell salvage combined with leucocyte depletion filtration to remove amniotic fluid from operative blood loss at caesarean section. *Int J Obstet Anesth* 1999;8:79–84
13. Waters JH, Biscotti C, Potter PS, Phillipson E. Amniotic fluid removal during cell salvage in the Cesarean section patient. *Anaesthesiology* 2000; 92:1531–6
14. Thornhill MI, O'Leary AJ, Lussos SA, Rutherford C, Johnson MD. An in vitro assessment of amniotic fluid removal from human blood through cell saver processing. *Anaesthesiology* 1991;75:A830
15. Bernstein HH, Rosenblatt MA, Gettes M, Lockwood C. The ability of the Haemonetics 4 cell saver to remove tissue factor from blood contaminated with amniotic fluid. *Anesth Analgesia* 1997;85:831–3
16. Catling SJ, Freites O, Krishnan S, Gibbs R. Clinical experience with cell salvage in obstetrics: 4 cases from one UK centre. *Int J Obstet Anesthes* 2002;11:128–34
17. Morgan M. Amniotic fluid embolism. *Anaesthesia* 1979;34:20–32
18. Oei SG, Wingen CBM, Kerkkamp HEM (letter). *Int J Obstet Anesth* 2000;9:143
19. Controversies in Obstetric Anaesthesia Meeting, London UK, March 2004
20. Confidential Enquiry into Maternal and Child Health (CEMACH) 2000–2002. The 6th report of the Confidential Enquiries into Maternal Deaths in the UK
21. AAGBI Guidelines for Obstetric Anaesthetic Services, Revised Edition 2005
22. Intra-operative blood cell salvage in obstetrics. National Institute for Health and Clinical Excellence, November 2005