Should Intraoperative Cell Salvage be considered for Obstetric Hemorrhage?

A literature review discussing the efficacy of Cell salvage for use in obstetrics

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Autologous Cell salvage is an intraoperative blood management modality used in various forms for 203-years with its roots in the gynecological suites of London [1]. Over the years, various protocols, indications, contraindications, and considerations arose based on the technology and research of the day. Unfortunately, as technology developed, enhancing the efficacy of cell salvage, specific procedures were still considered too dangerous to perform using intraoperative cell salvage, despite research indicating its safe use. One such procedure is that of obstetrics and the use of cell saver for treatment of hemorrhage. The purpose of this literature review is to provide an expository understanding of autotransfusion and synthesis of the contemporary research being done on cell saver for obstetric medicine.

A Brief History of Autologous Cell Salvage

Cell Salvage's beginnings in medicine started in 1818 with Dr. James Blundell, a Gynecologist practicing in London [1]. Unlike the complex centrifuge-based systems used today to process erythrocytes, Blundell's methodology relied on

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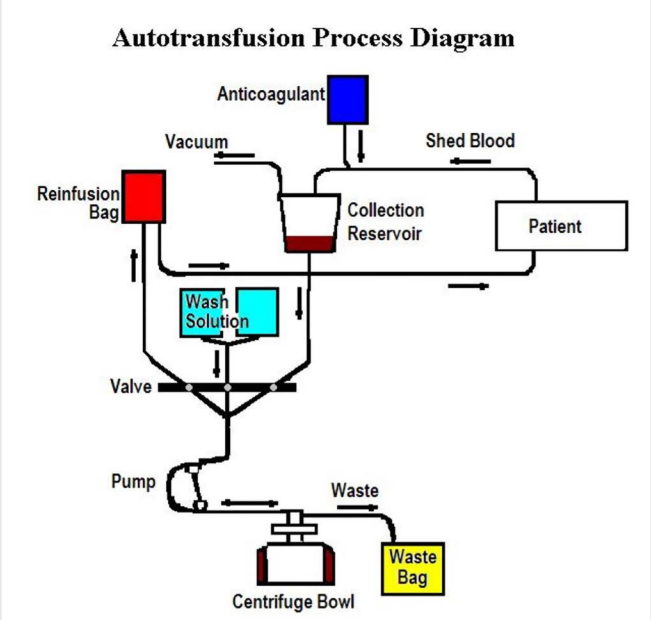
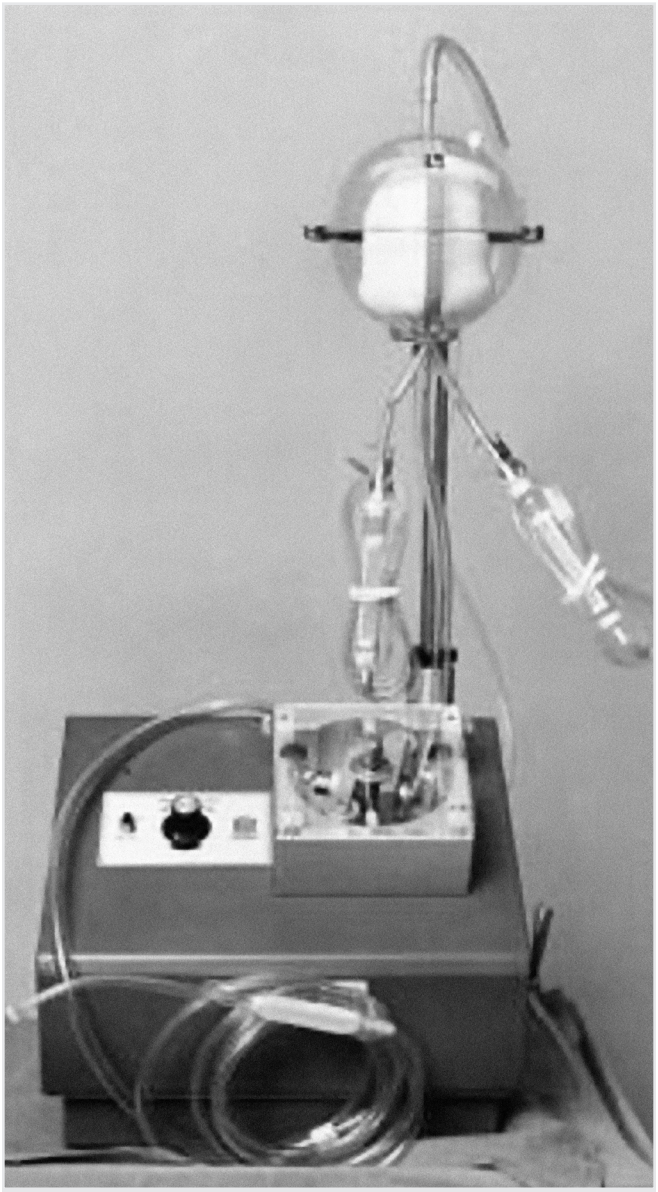
the rudimentary application of the base three domains of cell saver. Collection, washing, and reinfusion. Collection relied on gathering blood-soaked gauze mixed with a saline solution and placed in a container devoid of oxygen. The primary reason for the saline and lack of oxygen was to prevent coagulation of the cells. Then, through his patented *Impellor* device and *Gravitator*, he would rapidly insert the processed blood into a syringe and inject it back into the patient [2].

By 1943, additional experimentation into transfusion medicine and the preservation of a patient's own blood advanced into what is agreed upon as the first use of contemporary call saver technology [1]. Griswold's system relied on suction, a container, and a method for cleaving the red blood cells from particulate debris and other large molecules. Unlike the centrifuge systems used today, Griswold relied on cheesecloth to process the collected cells [3]. The use of a centrifuge and crystalloid solutions for processing would not occur until 1968 with the work of Wilson and Taswell. The work of Wilson and Taswell resulted in biomedical technology companies investing resources in developing specific systems for autotransfusion, relying on the groundwork laid from the 1940s to the 1960s [4].



The first manufactured cell saver would be developed in 1968 by Klebanoff [5]. The *Bentley Autotransfusion System* was a breakthrough in transfusion medicine occurring contemporaneously with the development of cardiopulmonary bypass devices. The device introduced advancements such as a cardiotomy, a pressure-relief valve, a 125-micron filter, and a DeBakey roller clamp. However, despite the considerable improvement, the *Bentley Autotransfusion System* was highly prone to introducing fatal air embolisms [3].



The Bentley Autotransfusion System

As micro-processing technology would advance globally, The advancement in computer technology would be utilized in Cell Saver systems [3]. Despite the increased demand for cell saver in the perioperative environment by 1975, the last significant advancements in cell saver would come with the introduction of the Latham bowl, Sorenson cardiotomy, and the standardized practice of using heparin—the primary anticoagulant for cell salvage [3].

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Despite the increasing use of cell saver in the later 20th century, primarily for cardiovascular surgery, autotransfusion was avoided in obstetrics medicine despite cell savers roots being firmly planted in the postpartum hemorrhage work of Dr. James Blundell in the 19th century.

Explaining the lack of Cell Saver Services in Obstetric Medicine

The limited use of cell saver in obstetric medicine, particularly in that of cesarean section and postpartum hemorrhage, is based on the premise that amniotic fluid (AF) could potentially pass through the processing phase of the cell saver and be introduced to the patient resulting in catastrophic events like Amniotic Fluid Embolism (AFE) and Disseminated Intravascular Coagulopathy (DIC) [3]. Unfortunately, this supposition has remained primarily a theoretical fear, despite numerous clinical studies indicating amniotic fluid is removed entirely, along with all other fluid components like fetal debris, Alpha Fetal Protein (AFP), trophoblasts, and lanugo hair, among other items [6].

Early research into the Efficacy of Cell Saver and the presence of Amniotic Fluid

Thornhill et al. - 1991 - An in-vitro assessment of amniotic fluid removal from human blood through cell saver processing

Research into the efficacy of autotransfusion for cesarean section and postpartum hemorrhage dates back to 1991[3]. Thornhill et al. published an In-vitro study in *Anesthesiology* of six sterile amniotic fluid samples processed in mixed blood samples through a *Shiley Dideco 795 P Cell Saver*. The fluid was collected from ASA I and II patients and was subsequently divided into 12 smaller samples. First, six samples were mixed with expired red blood cells from the blood bank with a 20% amniotic fluid to 80% erythrocytes ratio. The second set of six sterile amniotic fluid samples was mixed with fresh blood derived from hemochromatosis patients. Hemochromatosis is a blood disorder that causes an overload of iron to build within the bloodstream. The amniotic fluid to fresh hemochromatosis whole blood was mixed in a 20%-33% amniotic fluid ratio to 67%-80% whole fresh hemochromatosis blood[6].

The study results indicated no amniotic fluid or AFP could be detected in the post-wash sample and no gross particulates in all twelve samples. Despite the low *n-value*, the study revealed that technology from the late 1980s and early 1990s could produce cell saver products with no containments that would induce AFE or DIC. The authors did not make any declarative statements on the study, and the resulting conclusions did not change the supposition that cell saver was dangerous for cesarean section and postpartum hemorrhage.

Rebarber et al. - 1998 - The safety of intraoperative autologous blood collection and autotransfusion during cesarean section.

In 1998, clinicians and researchers at Yale University School of Medicine conducted a study evaluating the safety of cell saver with 139 participants [3]. Of the 139, 52 patients underwent cesarean section with the use of intraoperative cell salvage (ICS), with the remaining 87 undergoing cesarean sections receiving allogeneic blood transfusions (ABT) only [7]. There were other studies into the efficacy of cell savers for obstetric medicine between 1991 and 1998; however, this study was the most significant and most conclusive to date.

For this study, cell saver services were performed at three medical centers affiliated with Yale University School of Medicine, Yale-New Haven Hospital, Good Samaritan Hospital, and Hinsdale Hospital. The experimental group processing volumes had wide ranges of return volumes across the three facilities, with a total processing range of 125-4750mL [7]. Results from the three facilities were insignificant, and when compared to the control group, the authors could not indicate any "*increased risk of complications in patients receiving autologous blood collection autotransfusion during cesarean section* (Rebarber, 1998)."

> **"[no] increased risk of complications in patients receiving autologous blood collection autotransfusion during cesarean section"**
> *~ Rebarber, 1998 ~*

Despite the growing body of evidence during the 1990s, the use of cell saver was still contraindicated, as evidenced by the AABB in their 1997 *AABB Guidelines for Blood*

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Recovery and Reinfusion in Surgery. The guidelines asserted by the AABB indicated that aspiration in the presence of amniotic fluid should be avoided as it "*Contains proteolytic enzymes that may activate clotting* (AABB, 1997)[8]." In addition, the AABB considers the use of cell saver a relative contraindication if the services are provided after the fetus is delivered and confirmation that all amniotic fluid has been removed via "*...copious irrigation with 0.9% sodium chloride solution to an alternate suction source* (AABB, 1997) [8]." While this paper's goals are not to question the 1997 guidelines directly, it seeks to highlight almost decades' worth of research indicating the centrifuges' ability to remove AF and AFE in the wash cycle producing a safe cell saver product.

Turn of the Century Research into the Efficacy of Cell Saver for Obstetric Medicine

Waters et al. - 2000 - Amniotic Fluid Removal during Cell Salvage in the Cesarean Section Patient

Despite guidelines suggesting the safe use of cell saver during cesarean section and that the risks of fatal coagulopathies and embolisms were low, research continued to provide more validation for using cell saver in obstetrics. Finally, in 2000, a study was published which directly contradicted the aforementioned theoretical catastrophes [3]. Principal researcher Waters and his team at Cleveland Clinic Foundation decided to undertake an exhaustive investigation to evaluate—at the cellular level—what occurs in the Latham bowl when amniotic fluid is present. Measurements included quantification of "*...squamous cell concentration, lamellar body count, quantitative bacterial colonization, potassium level, and fetal hemoglobin* (Waters et al., 2000) [9]." What made this study so important rested on the methods used. Previous studies into the efficacy of cell saver relied on a two-step process to evaluate effectiveness. The study sampling would be sequential, taking four samples from fifteen patients at different intraoperative periods. The first sample was "*unwashed blood from the surgical field.*" The second sample was derived from the washed product, and the third sample was derived during post-filtration before patient administration. The final sample drawn was a venous ABG drawn from a femoral catheter.

"It is rational to assert that the study provided validation for using cell saver during cesarean section and hemorrhage."

The methods used by the team at the Cleveland Clinic Foundation revealed progressive and significant reductions of squamous cell concentration, lamellar body count, quantitative bacterial colonization, potassium level, and fetal hemoglobin. In addition, the authors concluded that the blood produced from the cell saver post-filtration almost matched the patient's venous ABG samples. Thus, the study indicates cell saver as a viable option for obstetrics patients during the cesarean section. It is important to note that while amniotic fluid was not a significant threat of DIC or embolism, the researchers did indicate that the exact cause of amniotic fluid embolism (AFE) is still unknown, a fact that remains in effect today [10].

At the time of the study, the authors indicated 390 case reports of intraoperative cell salvage being used in cesarean section with postpartum hemorrhage without filtration, a standard used in this study. In the 390 case studies, there were no incidences of AFE. This is important because Waters et al. sampled the processed blood post-filtration (the product which would be reinfused in the patient) and found no squamous cells present in addition to the absence of leukocytes and potassium. Why is this important? Amniotic fluid is primarily an electrolyte-based solution surrounding the fetus, and then in later pregnancy, squamous cells populate primarily from lung development. Based on this understanding of maternal and fetal physiology, it is rational to assert that the study provided validation for using cell saver during cesarean section and hemorrhage.

Malik et al. - 2010 – Cell saver use in obstetrics

As the technology advanced into the 21st century, so did research into autotransfusions efficacy in obstetrics. In 2010, physicians scientists from the Leicester General Hospital in Leicester, United Kingdom, conducted a retrospective study on 147 patients. Participants were selected on two factors, those who had confirmed Placenta Previa and individuals who self-disclosed as Jehovah's Witness. Of the 147 patients identified for the study, intraoperative cell salvage (ICS) was used in 52% of cases [11]. The importance of this study is multifaceted. One, it did not identify any adverse events for those who received ICS. Two, there was no marked recovery difference between those who received ICS and those who relied on homologous transfusion alone. Three, it identified

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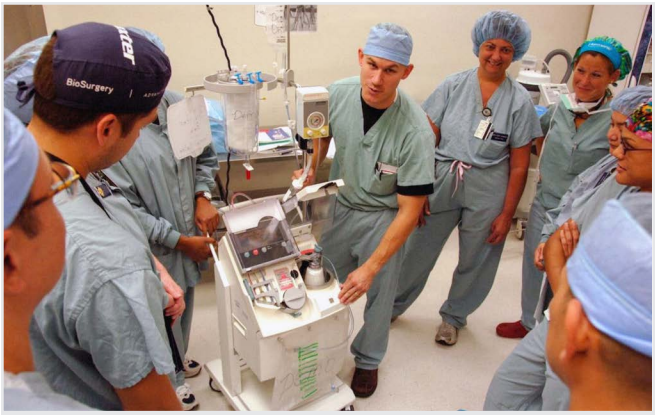

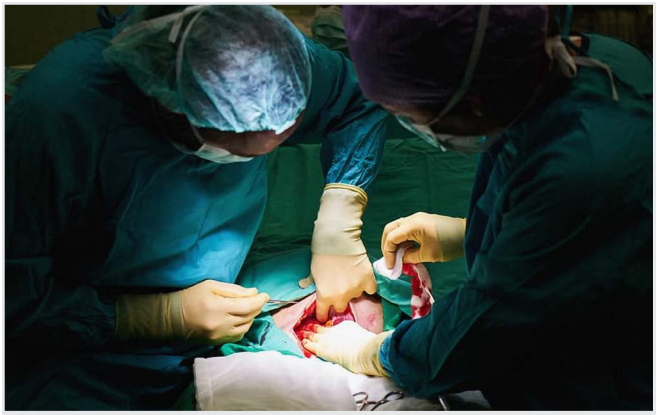

process issues with the adoption of efficient cell saver use in the operating suite.

The study noted that while cell saver proved effective without any adverse events occurring, the study did note that processing volumes varied widely with a reprocessing range between 0 and 1,800mL and a mean volume of 95.5mL per case [11]. During the discussion, the researchers noted that the vast range was attributed to the avoidance of cell saver in high volume bleeds. The reason for this avoidance harkens back to the theoretical concern of amniotic fluid embolism, a risk that is anomalous with research indicating incidences between "1 in 8000 and 1 in 80000 deliveries [12]". Secondary reasons for the low processing volumes include lack of enough equipment and properly trained and credentialed staff needed to improve efficiency in processing and performing procedures [11].

Closing Thoughts With Considerations From Contemorary Research

With research into the use of cell salvage dating back more than three decades, it would seem that there is a cause for the inclusion of cell salvage into the obstetric operating suite as a standard practice. The most significant barrier to inclusion is the theoretical fear of an AME and a belief that a large enough study has not been conducted to validate its use [14]. Arguably, yes, n=values in studies conducted over the years have been low. However, it is essential to note that AME is an already rare event. With its unknown mechanism of action, researchers may likely never allocate a large enough sample size. Despite the barriers to overcome, the use of cell salvage in the cesarean section is gaining momentum. In 2017, the most extensive randomized controlled study was conducted on the efficacy of cell salvage in cesarean section and postpartum hemorrhage, with 1,498 patients receiving cell salvage during the cesarean section. The research noted that fetal blood mixing was occurring but noted that amniotic fluid embolism should not be treated as a barrier to use.

Additionally, they noted that due to leukocyte depletion, filters should be avoided [13]. In the end, the only significant conclusions that can be drawn are the fact that the AFE is a theoretical fear but that more research needs to be conducted into fetal blood interactions and leukocyte depletion. While these results cannot prove the use of cell salvage in the cesarean section, and policymakers will ultimately decide its use in operating rooms, the continued research into cell salvage for cesarean section and hemorrhage is pointing toward a future where it could be regularly used for emergency events.

References

1. A. Ashworth, A. A. Klein, Cell salvage as part of a blood conservation strategy in anaesthesia, BJA: British Journal of Anaesthesia, Volume 105, Issue 4, October 2010, Pages 401–416, https://doi.org/10.1093/bja/aeq244
2. Adams, S. (2009, February 25). *James Blundell: pioneer of blood transfusion.* Healio. https://www.healio.com/news/hematology-oncology/20120325/james-blundell-pioneer-of-blood-transfusion.
3. Roets, M., Sturgess, D. J., Wyssusek, K., & van Zundert, A. A. (2019). Intraoperative cell salvage: A technology built upon the failures, fads and fashions of blood transfusion. *Anaesthesia and Intensive Care, 47*(3_suppl), 17–30. https://doi.org/10.1177/0310057x19860161.
4. Wilson, J, Utz, D, Taswell, H. Autotransfusion during transurethral resection of the prostate: technique and preliminary clinical evaluation. Mayo Clin Proc 1969; 44: 374–386.

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5. Klebanoff, G. (1970). Early Clinical Experience with a Disposable Unit for the Intraoperative Salvage and Reinfusion of Blood Loss (Intraoperative Autotransfusion). *The American Journal of Surgery, 120*(6), 718–722. **https://doi.org/10.1016/s0002-9610(70)90066-8**.
6. Johnson, Thornhill, M. L., O'Leary, A. J., Lussos, S. A., & Rutherford, C. (1991). AN IN-VITRO ASSESSMENT OF AMNIOTIC FLUID REMOVAL FROM HUMAN BLOOD THROUGH CELL SAVER PROCESSING. *Anesthesiology, 75*(3). **https://doi.org/10.1097/00000542-199109001-00829**.
7. Rebarber, A., Lonser, R., Jackson, S., Copel, J. A., & Sipes, S. (1998). The safety of intraoperative autologous blood collection and autotransfusion during cesarean section. *American Journal of Obstetrics and Gynecology, 179*(3 Pt 1), 715–720. **https://doi-org.occc.idm.oclc.org/10.1016/s0002-9378(98)70070-5**.
8. AABB (1997). *Guidelines for blood recovery and reinfusion in surgery and trauma*
9. Waters, J. H., Biscotti, C., Potter, P. S., & Phillipson, E. (2000). Amniotic fluid removal during cell salvage in the cesarean section patient. *Anesthesiology, 92*(6), 1531–1536. **https://doi-org.occc.idm.oclc.org/10.1097/00000542-200006000-00008**.
10. Haftel A, Chowdhury YS. Amniotic Fluid Embolism. [Updated 2020 Nov 29]. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2021 Jan-. Available from: **https://www.ncbi.nlm.nih.gov/books/NBK559107/**.
11. S. Malik, H. Brooks & T. Singhal (2010) Cell saver use in obstetrics, Journal of Obstetrics and Gynaecology, 30:8, 826-828, DOI: 10.3109/01443615.2010.511727
12. Kaur, K., Bhardwaj, M., Kumar, P., Singhal, S., Singh, T., & Hooda, S. (2016). Amniotic fluid embolism. *Journal of anaesthesiology, clinical pharmacology, 32*(2), 153–159. **https://doi.org/10.4103/0970-9185.173356**.
13. Khan, K. S., Moore, P., Wilson, M. J., Hooper, R., Allard, S., Wrench, I., Beresford, L., Roberts, T. E., McLoughlin, C., Geoghegan, J., Daniels, J. P., Catling, S., Clark, V. A., Ayuk, P., Robson, S., Gao-Smith, F., Hogg, M., Lanz, D., Dodds, J., & SALVO study group (2017). Cell salvage and donor blood transfusion during cesarean section: A pragmatic, multicentre randomised controlled trial (SALVO). *PLoS medicine, 14*(12), e1002471. **https://doi.org/10.1371/journal.pmed.1002471**
14. Arendt, K. (2019, October 19). *Is it appropriate to use cell savers to collect and re-infuse blood during a c-section?* Anesthesia Patient Safety Foundation. **https://www.apsf.org/article/is-it-appropriate-to-use-cell-savers-to-collect-and-re-infuse-blood-during-a-c-section/**.

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Continuing Education Quiz

To test your knowledge on this issue's article, provide correct answers to the following questions on the form below. Follow the instructions carefully.

1. What are the three domains of cell salvage
a. Collection, Washing, Reinfusion
b. Collection, Retention, Washing
c. Vacuuming, Purging, Reinfusion
d. Heparin, Normal Saline, Filtration

2. Griswold's early cell saver system relied on cheesecloth for cleaving.
a. True
b. False

3. The AABB considers cesarean section to be a relative contraindication and recommends copious irrigation of the surgical site prior to using/ resuming cell saver.
a. True
b. False

4. Malik et al.'s research excluded Jehovah's Witness from research.
a. True
b. False

5. Amniotic Fluid Embolism occurs between
a. 1:8,000 and 1:80,000 deliveries
b. 1:800 and 1:8,000 deliveries
c. 1:80 and 1:800 deliveries
d. 1:100,000 and 1:1,000,000 deliveries

6. Waters et al. noted that AFE occurred in 10 patients evaluated.
a. True
b. False

7. What size filter did the Bentley Autotransfusion system utilize?
a. 125-micron
b. 140-micron
c. 170-micron
d. 200-micron

8. Latham Bowls were introduced for Cell saver in 1975.
a. True
b. False

9. Researchers have determined the mechanism of action for AFE.
a. True
b. False

10. Malik et al. noted that a barrier to higher use of cell saver was not enough trained personnel.
a. True
b. False

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1:	A B C D	**6:**	A B
2:	A B	**7:**	A B C D
3:	A B	**8:**	A B
4:	A B	**9:**	A B
5:	A B C D	**10:**	A B

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