

Abstracts

Risk of and Alternatives to
Homologous Blood Transfusion



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Pros and Cons with Autotransfusion Devices

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Introduction

Allogeneic blood transfusion subject patients to risks of infection and allergic reactions. It has also been suggested that patients receiving autologous blood suffer from a lower incidence of postoperative infections. The recognition of hepatitis as a serious complication of transfusion, the identification of the human immunodeficiency virus and recently BSE as transfusion transmitted diseases, has changed the attitude towards alternatives to allogeneic blood transfusions.

Although autologous blood is the safest transfusion product it represents only a small percentage of the blood transfused. Available therapies are preoperative autologous blood collection, normovolemic hemodilution, peroperative blood salvage and postoperative infusion of shed wound blood and several pharmacological treatments. Preoperative autologous blood collection is a safe and effective method for reducing allogeneic blood requirement in many surgical procedures. Preoperative autologous blood collection can be used in "high-risk" patients like cardiac, pediatric and elderly patients. Normovolemic hemodilution has been shown to save significant volumes of allogeneic blood. The techniques of perioperative autotransfusion can be subdivided depending on the extent to which the scavenged blood is processed prior to transfusion. In non-washed autotransfusion systems the blood is simply filtered whereas washed autotransfusion systems the blood is washed and centrifuged. Several pharmacological treatments have been used. The main aims with erythropoietin treatment are to minimize the requirement of allogeneic blood transfusions by increasing the amount of preoperative autologous blood collection and to maintain a proper hemoglobin value pre- and postoperatively.

The use of preoperative autologous blood collection, perioperative blood salvage, normovolemic hemodilution and pharmacological treatments lead to decreased exposure for the patients to allogeneic blood transfusions in many different surgical procedures. In order to minimize exposure to infectious agents, reduce cost, and reduce allogeneic transfusion requirements, the application of autotransfusion techniques has increased. The feasibility of operating

on Jehovah's Witnesses has also been improved with the use of intraoperative autotransfusion. Jehovah's Witnesses will not accept preoperative autologous blood collection or the use of a canister collection system if the blood is processed outside the operating room.

Techniques of autotransfusion

Non-washed autotransfusion systems

The simplest autotransfusion systems collect and reinfuse non-washed blood. Blood is collected from the surgical wound through a suction device or drain and actively aspirated to a reservoir. This reservoir has a 20-150 micrometer filter to remove large particles and cellular debris from the blood. A regulated negative pressure of no more than 100 mmHg is recommended to provide the suction necessary during blood collection. Larger negative pressures are believed to increase hemolysis. The aspirated blood may be anti-coagulated either at the point of collection or in the reservoir. Preferably, the anticoagulant is added at a rate proportional to the rate of blood collection. Clot inhibition can be accomplished either by heparin or citrate. The latter offers some advantages, as citrate-phosphate-dextrose provides a substrate for glycolysis and preserves metabolic function in red blood cells. Platelet function may also be improved due to the calcium binding effect of citrate and the negative effect of heparin and protamine is eliminated. However, since citrate is metabolized in the liver, it is best avoided in patients with hepatic insufficiency. Even without anti-coagulation, the blood collected for postoperative autotransfusion does not usually clot, as it is defibrinogenated. The blood should be reinfused within 6 hours of collection to preserve cellular viability and reduce the risk of infection.

Washed autotransfusion systems

After anticoagulation and collection as above, the blood is processed by centrifugation and the remaining blood cells are then washed with saline. This additional purification step is intended to remove activated coagulation factors, cellular stroma, free hemoglobin, anticoagulants and other contaminants that are less dense than the red blood cells. Processing of the blood is controlled by a microprocessor and there is usually an air detector. A device with a continuous washing-processing chamber has recently been developed. The salvage systems have disposable equipment packs consisting of a sterile circuit which includes a suction assembly-tubing, reservoir, centrifuge bowl, reinfusion bag and waste bag. Qualified personnel are necessary to operate the device.

Hemofiltration systems

The salvaged blood from a canister collection system is normally reinfused after filtration only, but may be concentrated and washed with standard blood bank washing instruments. Another possibility is washing through hemofiltration. Apart from filtration through the membrane pores, molecules can be eliminated by adsorption to the membrane. This technique enables the operator to concentrate the blood intraoperatively while preserving the plasma proteins and platelets. The ultrafiltrate does not contain free hemoglobin, as the filter pores are too small for molecules of this size to pass through.

Indications

The use of intraoperative autotransfusion has been evaluated in total hip arthroplasty, knee arthroplasty and spinal surgical procedures. In studies of different orthopedic procedures, the over-all rate of blood salvage using an autotransfuser is estimated to be about 50% intraoperatively. Major anticipated bleeding suitable for the use of red cell salvage are revision hip arthroplasty, selected cases of primary hip revision such as congenitally dislocated hips, and extensive spinal procedures such as insertion of Harrington rods. Postoperative scavenging is often accomplished with simple non-washed autotransfusion systems in suitable cases such as patients who have been subjected to major spinal surgery, or joint arthroplasty. There are few clinical side effects reported. However, the blood aspirated during orthopedic procedures may be contaminated with bone fragments, fat, bone cement and metal fragments from saws and drills. The filters in many autotransfusion reservoirs fail to remove the smaller particulate contaminants. For this reason, washed autotransfusion systems for red blood cell scavenging are generally preferred to unwashed systems. In joint arthroplasty patients, the volume of blood collected during open-heart surgery there is often a significant blood loss due to postoperatively may be too small to motivate the technology and expense extensive surgical interventions and the derangement of hemostasis, which accompanies cardiopulmonary bypass techniques. Autotransfusion is particularly attractive as blood loss occurs in a confined area and is recoverable. The patient is fully anti-coagulated during part of the procedure and shed blood can be returned to the patient through the cardiectomy suction of the extracorporeal circuit. Aortic surgery may be suited for both washed and, since pools of blood are formed, unwashed autotransfusion. A 75% reduction in allogeneic blood products was achieved with intraoperative autotransfusion in elective aortic surgery. Massive blood loss may occur during liver transplantation due to coagulopathy and surgical bleeding. Autotransfusion devices with short processing time permitting fast transfusion are required. In the trauma situation, blood salvage can be rapidly provided in a large volume without the delays in obtaining allogeneic blood,

or limits to its availability. Both washed and non-washed systems may provide rapid transfusion.

Characteristics of recovered blood

The collected blood from the operating field is exposed to tissue factors at the operation site, to air, and to synthetic material of the collection circuit. These factors may contribute to the activation of plasma and cellular system thereby affecting the quality of the salvaged blood. In evaluating the benefits of salvaged blood, consideration must be taken whether the risk for the patient is smaller than with allogeneic blood. Mortality after allogeneic transfusion with red cell concentrates has been estimated to be as low as 1/250 000 units.

In case of large intraoperative bleeding, the use of donor blood components may be required in spite of the use of an autotransfusion device. Some red blood cells are lost due to hemolysis and washout during processing. Each time a volume of red blood cells is shed, only a fraction is returned. Because the hematocrit of packed red blood cells from autotransfusion machines usually are higher than normal patient values, clinicians may believe that reinfusing the recovered blood will maintain the patients hematocrit. Moreover, patients receiving large volumes of processed red blood cells may suffer from coagulopathies as a result of platelet and coagulation protein depletion during processing.

Intraoperatively up to 3/4 and in exceptional cases such as in vascular surgery even more, of the blood loss can be collected. Almost 1/3 of the red cell volume may be lost in the processing with a red blood cell scavenging device. In major orthopedic procedures 50-60% of the red blood cells are salvageable. With hemofiltration technique, it is possible to obtain a desired hematocrit, but a higher hematocrit requires a longer processing time.

Red cells salvaged with either a canister collection system or with a red blood cell processor do not have significantly shorter 24-hour post-transfusion survival, compared with cells that have not undergone the trauma of salvage. Washed autologous erythrocytes show, in contrast to allogeneic donor blood, normal morphology. Hemolysis secondary to the surgical trauma, suctioning techniques and to the vacuum aspiration is significant. The free hemoglobin level in salvaged blood is sometimes as high as 20.000 mg/l. Following autotransfusion of a unit of unwashed salvaged blood, the patients plasma concentration of free hemoglobin increases substantially. Washing and centrifugation removes more than 90% of the free hemoglobin. The leukocyte count in salvaged blood is often close to that of normal blood or $4-12 \cdot 10^9/l$.

The potassium concentration in salvaged blood is dependent on many factors such as degree of red cell hemolysis and time elapsed before reinfusion. Intraoperatively salvaged blood has a low concentration of fibrinogen, about

1 g/l and of factors V, VIII, and X. Washed and processed blood from a red cell autotransfusion device has also a fibrinogen concentration of about 1 g/l. Processing autotransfusion systems should be able to remove 90% of the heparin added for anticoagulation to be safe even for massive reinfusions. Most red cell salvage devices fulfill this requirement. During massive infusions hypocalcaemia may develop if citrate is used as anticoagulant. As a result of complement system activation, the anaphylatoxins C3a and C5a are formed during collection of drainage blood. Plasma levels of the white cell enzyme elastase are raised in collected blood. Retransfusion of small volumes, about 400 ml, after hip replacement surgery resulted in increased patient concentration but was not associated with any clinical complications. Whole blood collected from the wound during hip replacement surgery contains large amounts of cytokines. There were increased concentrations of interleukines IL-1, IL-1 β , IL-6 and IL-8 in collected blood. The patient plasma IL-6 concentrations increased after retransfusion.

Risks

Most contraindications to blood salvage are relative and only limited data substantiate the associated complications. Contraindications to blood salvage include infection and malignant disease. Washing of contaminated blood reduces but does not eliminate microorganisms. Several studies have found that allogeneic transfusion is an independent risk factor for postoperative infection and autologous blood recipients have a low rate of infection similar to that seen in non transfused patients. Malignant cells are also known to survive the processing and filtration of salvaged blood. Leukocyte filters may eliminate tumour cells when they are used both up-stream and down-stream from a conventional washed autotransfusion system. The potential risk of reinfusing tumour cells should be weighed against the immunosuppressive effect of allogeneic blood transfusion, which in turn may increase the incidence of cancer recurrence. Leukocyte-depleted blood and autologous transfusion are strategies to minimize this immunosuppression. Despite widespread experience with blood salvage and intraoperative autotransfusion, the reported complications are scarce. As the risks of autologous transfusion are less than those of allogeneic transfusion, there might even be a tendency to use less restrictive transfusion criteria. However, no transfusion is ever totally without risk. Salvaged blood contains increased free hemoglobin levels, decreased coagulation factors, increased fibrin degradation products and substantial amounts of anticoagulant. Reports on autotransfusion of large volumes using unwashed blood are rare. It is generally accepted to observe a limit in transfusing this blood. A recommendation for this limit is 500-1500 ml. The safety of salvage procedures that involve

reinfusion of unwashed blood does not appear to be established. When a small volume of unwashed blood is retransfused, there are few side effects but the benefit is at best limited. On the other hand, if a large volume of blood is needed, there is substantial biochemical evidence that unwashed salvaged blood is potentially dangerous. Febrile reactions and hypotension may occur after even small transfusion volumes of unwashed shed blood. The incidence of febrile reactions was 2% when shed blood was retransfused within the first 6 postoperative hours. There has also been a case report on acute respiratory failure due to upper airway oedema after transfusion of unwashed salvage blood. Hemolysis occurs if the suction level is too high or if air is mixed with blood during aspiration. Reinfusion of salvaged blood containing large quantities of free hemoglobin and red cell stroma is occasionally associated with renal damage. Air embolism can occur if the reinfusion bag of the cell salvage circuit is directly connected to the patients vascular system, particularly if the infusion is done under pressure. By transferring the red cell suspension into a separate bag before administration, air embolism is prevented. Coagulopathy can result from dilution of coagulation factors, activation of inflammatory mediators, platelets and leukocytes or from infusion of residual anticoagulant. During collection and reinfusion of whole blood, a larger contact filter area may induce more activation of intrinsic coagulation, fibrinolytic and complement pathways. Coagulopathy may occur particularly if unwashed blood is reinfused. Cost-benefit analysis of autotransfusion is an active area of investigation. In the short term, autologous blood techniques are often more expensive than conventional therapy. The costs of blood collection have been compared with the savings in allogeneic blood that was needed. The prices of the devices are relatively high.

Effects of Blood Management in Clinical Practice

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Introduction

For many years now, Sint Maartenskliniek in Nijmegen – a clinic where purely elective orthopaedic procedures take place – has been particularly interested in active blood management. A number of studies show that transfusion of allogeneic blood can involve risks, especially in orthopaedic surgery. Allogeneic blood transfusion increases hospital stay, increases the incidence of postoperative wound disturbances and infections. This was a good reason to pursue an even more active blood management policy. Four major steps to achieve this goal have recently been made.

1. Transfusion policy

In applying transfusion policy, it is vitally important for consensus to exist between the different medical specialists. In addition, it is essential to determine the Hb-level before deciding to give a transfusion of allogeneic blood. As a result of compliance with these two basic conditions, Sint Maartenskliniek has succeeded in halving its use of homologous packed cells. Our transfusion policy – based on the Hb-level as transfusion trigger – is shown in the tables below. The most recent national transfusion guideline has been incorporated.

Patients below the age of 60 years

<i>Within 4 hours of surgery</i>	<i>More than 4 hours after surgery</i>
Hb > 6.4 g/dl = 0 packed cells	Hb > 6.4 g/dl = 0 packed cells
Hb < 6.4 g/dl = 1 packed cells	Hb < 6.4 g/dl = 1 packed cells
Hb < 4.8 g/dl = 2 packed cells	Hb < 5.6 g/dl = 2 packed cells

Patients over the age of 60 years

<i>Within 4 hours of surgery</i>	<i>More than 4 hours after surgery</i>
Hb > 7.2 g/dl = 0 packed cells	Hb > 8.0 g/dl = 0 packed cells
Hb < 7.2 g/dl = 1 packed cells	Hb < 8.0 g/dl = 1 packed cells
Hb < 6.4 g/dl = 2 packed cells	Hb < 7.2 g/dl = 2 packed cells

Patients with cardiac diseases

<i>Within 4 hours of surgery</i>	<i>More than 4 hours after surgery</i>
Hb < 8.8 g/dl = 0 packed cells	Hb < 8.8 g/dl = 1 packed cells
Hb < 8.0 g/dl = 1 packed cells	Hb < 8.0 g/dl = 2 packed cells
Hb < 7.2 g/dl = 2 packed cells	Hb < 7.2 g/dl = 2 packed cells

2. Use of Epoetin alpha (Eprex® - Hb < 13 g/dl)

All patients who have to undergo a planned major orthopaedic intervention and who have a preoperative Hb-level of 13 g/dl are suitable candidates for this. It is this group of patients that receives 50% of all blood transfusions in orthopaedic surgery. Administration of a total of four subcutaneous injections of 40,000 I.U. erythropoëtine (Eprex®) corrects the pre- and postoperative Hb-levels. The injections are given weekly, starting three weeks before the planned operation. At Sint Maartenskliniek, an average preoperative increase in Hb of 1.9 g/dl has been achieved. In this patient population (lower Hb-level and bigger orthopaedic intervention), it was possible to reduce the number of blood transfusions by 82%.

3. Use of (or switch to) COX-2 selective NSAIDs

The use of non-selective NSAIDs no longer seems justifiable in the perioperative stage if the aim is to limit blood transfusions. In a recent study, an 18% reduction in blood loss during one type of operation was shown to be feasible when using COX-2 selective NSAID's. The overall results at our clinic indicate a 28% reduction in preoperative blood loss. Patients at our clinic who use a non-selective NSAID preoperatively are actively switched to the COX-2 selective NSAID meloxicam (Movicox®) in the perioperative phase.

4. Postoperative cell saving (Bellovac® A.B.T)

The Bellovac® A.B.T system (A.B.T = autologous blood transfusion) concerns a form of postoperative cell saving where blood from the operation wound is collected and filtered and then returned to the patient. This blood salvaging system helped to reduce the number of blood transfusions at our clinic to zero in total knee - and revision knee replacement surgery.

rHuEPO Alone and in Combination with Predonation

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The requirement for blood transfusion in surgical patients (Pts) depends on 2 major variables: 1) the volume of perioperative blood loss; and 2) the volume of blood that the patient can tolerate to lose before blood transfusion support is indicated.

This second parameter is mainly affected by the clinical conditions of the Pt, particularly by the cardiopulmonary condition and the haematological status, i.e. the total circulating RBCs mass. Low baseline hematocrit has been shown to be a critical parameter in affecting transfusion requirement. The incidence of preoperative anemia is relevant in many categories of Pts but particularly in Pts with anemia of chronic diseases. The Pts more interested by this type of anemia are those with cancer and rheumatoid arthritis.

In a study carried out at the G. Pini Orthopedic Institute, it has been observed that out of 2.183 evaluated Pts, 18% of the Pts had a baseline Hct < 34%, value that prevents the use of PABD, method of proven efficacy to reduce the use of allogeneic blood in surgical Pts. Moreover a further 46% of the Pts had baseline Hct values between 34% and 40% and is at high risk of allogeneic transfusions when undergoing to surgical procedures with expected transfusion need of 2-3 units. Only 36% of the Pts had optimal baseline values.

Accordingly to the analysis a consistent proportion of Pts undergoing major surgical procedures can be expected to require allogeneic blood transfusion to face perioperative blood loss induced anemia. In these Pts the administration of rHuEPO may be a valuable adjunct to stimulate erythropoiesis and to expand their RBCs mass thus allowing the Pt to tolerate higher volume of blood losses or to increase the volume of autologous blood that they can predeposit before surgery.

Several studies have evaluated, in different group of Pts, the efficacy of rHuEPO in enhancing the collection of autologous blood in Pts candidate to elective surgery, in correcting anemia before surgery and in accelerating postoperative erythropoietic response thus reducing the use allogeneic blood. In these clinical studies, rHuEPO was found to be effective in stimulating erythropoiesis and increasing new RBC production and the number of units predeposited. It was also effective in correcting anemia induced by blood collection.

Currently, dosage of 100 to 300 IU/kg SC twice weekly for 3 weeks plus an optional initial IV administration of 150 to 200 IU/kg at the time of enrolment is

recommended. Moreover, iron supplementation in combination with rHuEPO should be administered intravenously as iron sucrose (200mg of elemental iron at each donation visit). If this or any other safe preparation of IV iron is not available oral supplementation should be provided by administering at least 200mg of elemental iron daily.

Recently, some studies have also evaluated the role of rHuEPO in those subgroups of Pts for whom preoperative autologous blood donation is not feasible. These include

Pts with anemia or other disorders precluding donation, Pts with limited time to surgery, and individuals who are unwilling to participate in an autologous blood donation program because of logistical problems or religious beliefs. For example, postponing the operation in cancer Pts or candidates to heart surgery might be more detrimental than receiving allogeneic blood transfusion.

The protocols of rHuEPO administration differed significantly in the different studies evaluating the perisurgical use of the drug. The differences involved both the total dose of rHuEPO administered during the study treatment, the duration of treatment (from 1 to 3 weeks) and the interval between dosing (from daily to weekly). Altogether, however, these studies showed a reduction in allogeneic transfusion rate in treated Pts compared with controls. In our Institute a short-term perisurgical treatment was used in a pilot study. Twenty Pts for whom predeposit was contra-indicated for various clinical reasons and who were about to undergo major orthopaedic surgery with a predicted transfusion requirement of 2-3 units of blood were enrolled in the study.

The protocol involved subcutaneous administration of r-HuEPO at a daily dose of 100 IU/Kg beginning 4 days before surgery (day-4) up to the second day following surgery (day + 2). On the first day of treatment, one 200 IU/Kg bolus was also administered intravenously. Intravenous iron sucrose was administered concomitantly at a total dose of 600 to 1000 mg, according to baseline iron reserve levels. The treatment produced a 2% to 7% increase in Hct, with average increase in circulatory RBC mass of some 100mL (from 0 to 245) before surgery. Sixteen of the 20 Pts did not require allogeneic transfusion, whereas a total of 6 units of blood was transfused in the remaining 4 Pts. These findings suggest that rHuEPO administration together with IV iron during a pre-operative period of 4-5 days is able to stimulate erythropoiesis significantly and reduce the transfusion requirement in Pts who, for clinical or logistic reasons are not able to deposit autologous units prior to elective surgery. Because of the short time period, this protocol could also be offered to a proportion of trauma surgical Pts, when surgery is planned to take place 4-5 days after injury.

It can be concluded that rHuEPO therapy may be safe and effective, in selected surgical Pts, in stimulating erythropoiesis, in increasing the volume of AB that can be collected pre-operatively, in expanding circulating RBCs volume preoperatively and, consequently, in reducing the exposure to homologous blood. Therapy with rHuEPO may prove to be a useful addition to existing strategies of blood conservation to minimise the use of allogeneic blood.

However owing to the high cost of rHuEPO treatment, its routine use is unlikely to be cost-effective and should be discouraged. Candidates to rHuEPO treatment should be selected on the basis of appropriately calculated transfusion need of the single specific Pt and rHuEPO should be used only when it can't be expected to cover the patient surgical need only when the use of other less expensive blood conservation techniques.

In general, Pts who would most benefit are those with low circulating RBC volume due to anemia (comprising also Pts with ACD), those with small body mass, those with irregular RBC antibodies, those who refuse transfusions for religious reason, and those with transfusion surgical need exceeding 5 units or for whom the interval before surgery is too short to allow the donation of sufficient blood.

Acute Normovolemic Haemodilution

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Allogenic blood transfusion, although often needed in major surgery with large per- and post-operative bleeding, is fraught with dangers such as clerical mishandling, immuno-suppression and blood-borne infections. Acute normovolemic hemodilution (ANH) is a method to diminish blood loss but is not without its own panorama of risks and benefits.

The patient donates blood just before surgery. A central venous catheter is normally used. Normovolemia is essential. When bleeding occurs during surgery, the patient will lose fewer erythrocytes. The saved blood is given back to the patient at the end of surgery.

The advantages of ANH remain unclear. While it is certain that the amount of blood saved correlates well with the permitted hemodilution of the patient, there are no strict rules about “safe” hemodilution levels, nor the quantity of blood saved. The blood saved is, however, limited and with the target hematocrit (hct) of 28, only 0.5 units of blood are probably saved. The risk with lower hct is mainly cardiac ischemia in patients with coronary artery disease. Therefore, lower values than hct 30 are not recommended in these patients. Other risks with this method are hypovolemia, peripheral edema and increased lung water.

In later years, ANH has often been compared with pre-donation of autologous blood where the patient donates his/her own blood during a period of up to six weeks before the operation. Pre-donation has very few risks for the patient but is cumbersome and needs planning. One disadvantage with the method is that the quantity of blood actually saved is much lesser than the amount donated. The blood saving capacity of the two methods has been shown to be equal. Which of these two methods is better in healthy patients depends on the organization of the hospital but for cardiac-sick patients, pre-donation seems to be preferable.

ANH has a limited blood saving capacity and should therefore preferably be combined with adjuvant techniques. It can, for instance, be combined with immediate preoperative platelet rich plasma (PRP) harvest with additive blood saving effect. Maybe the most promising development in the ANH concept is to combine this method with an oxygen carrier, either hemoglobin-based or perfluorocarbons (PFC). PFC in combination with ANH has, in some promising

studies, been shown to be more effective in blood saving than colloids or ANH alone.

In conclusion, ANH has limited effects and may be dangerous for the cardiac-sick patient. To optimize the effect it should be combined with other blood saving methods such as auto-transfusion or platelet rich plasma harvest. The combination of ANH with PRC treatment seems very promising for the future.

Retransfusion of salvaged blood

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The surgeon and obstetrician James Blundell first described retransfusion at 1818, who held the chair of Midwifery and Physiology and worked at St. Thomas and Guy's hospital in London. Due to the high mortality rate among women giving birth due to post partum bleedings, he developed a method for collection, temporary storage and reinfusion of the shed blood and mortality decreased to 50%. He is often called "father of autotransfusion". Later in 1885-86 two Scottish surgeons, Miller and Duncan independently reported successful reinfusion of shed blood after lower-extremity amputation. Anticoagulation was done with "a solution of phosphate of soda".

In 1968 the first autotransfusion prototypes were built and also tried. Coagulopathy and lethal air embolism were common. These early devices were refined with a better collection reservoir and a centrifugation bowl. In orthopaedic surgery a primary arthroplasty of the hip or knee bleeds a total of around 1500 ml and usually requires 2 units of blood. In revision arthroplasties and major spinal surgery these amounts are exceeded. In Sweden it is estimated that orthopaedic surgery alone accounts for around ¼ of the total of 400.000 units transfused allogeneic blood.

The blood lost at or after the operation can be salvaged in different ways. The possibility for salvage and the methods that can be utilised depends on if the operation is done with or without tourniquet, and if drain is used or not. During the operation blood can be salvaged through suction from the wound. The blood is anticoagulated and usually collected in a reservoir. The erythrocytes are separated, washed, hemoconcentrated and stored for retransfusion. The plasma is wasted and this loss of volume must therefore be replaced together with the retransfusion.

The perioperative cell separation can be done by three different methods. The first and most used method is to collect the blood in a special reservoir and use separate centrifugation bowls intermittently. The erythrocytes are separated and are retransfused intermittently.

The second method uses a special Vortex hemofiltration filter, where blood is washed and erythrocytes are concentrated. The third method is also a centrifugation, but uses a special washing chamber where the blood can be washed and centrifuged continuously.

The cell separation technique has the advantage of providing erythrocytes with uncompromised functional capacity. The erythrocyte concentrate is practically free from contaminating particles and has low contents of different cytokines. The disadvantage is that the method needs trained staff, is fairly expensive and not all blood can be salvaged.

There are reports on cases where the method has concentrated catecholamines, anaphylatoxines and endotoxines. If centrifugation is done discontinuously, some fat will remain in the retransfused solution. Retransfusion of large volumes can disturb

the acid-base balance, raise the level of Hb/s and cause bleeding disorder.

Nowadays the problem with micro- and air embolism is extremely rare.

Intraoperative salvage is mainly indicated in emergent procedures like major trauma and in elective surgery where the anticipated preoperative blood loss is more than 1-1,5 L. The method can also be used in patients with religious objections, blood incompatibilities or limited supply of allogeneic blood. In septic and intraabdominal surgery the method is contraindicated. In tumour surgery there is a debate whether to use it or not. If blood is diluted with ascites, amnion fluid or urine blood salvage is usually not done.

Postoperatively the blood can be collected and retransfused if drain is used. The usage of drain is debated and the use of drain might increase the bleeding volumes. If drain is used the blood is collected through some kind of filter of 200-280 μ m. The blood can be used for retransfusion the first 6-8 postoperative hours. This can be done either through continuation with a cell separation machine or by retransfusion of filtered but unwashed blood. If filtering technique is used extra filters of different types can be used or some other method to reduce e.g. the fat content. The salvaged blood is always finally given back through a standard 40 μ m blood transfusion filter. With unwashed blood plasma remains including both potentially toxic as well as beneficial contents. Hemolysis is below 1 % of the blood content within the first 24 hours. The blood is defibrinated and slightly diluted and has reduced levels of both leukocytes and platelets. With time glucose is consumed and the blood becomes slightly more acid. Due to the lower amount of leukocytes rheology (resistance to pass narrow pores) is improved. Cytokine levels are raised. Fever reactions occur in the postoperative period but there is no certain link to the reinfusions. The viability and functional capacity of the erythrocytes are unaffected.

Only retransfusion of unwashed salvaged blood can reduce the need for allogeneic blood in hip replacements with $\frac{1}{2}$ and in total knee replacements with $\frac{2}{3}$. The system with salvage and retransfusion of unwashed blood is simple, fairly inexpensive but the use of drain is a prerequisite. Retransfusion of larger volumes (>1,5-2 L) is questionable and should be avoided.

In orthopaedic surgery retransfusion is more troublesome in certain patients. Infected patients autologous salvage is not applicable. If allogeneic blood is used, leukocyte filter should be used to minimise the immunologic response. In tumour surgery recycling has so far not been possible, but there are a few encouraging reports on radiating the washed blood before retransfusion. This way all cells with nucleus are killed including all metastatic tumour cells. By using autologous blood the immunologic response is reduced. In trauma surgery it is important to stop the bleeding first before other actions according to the ATLS protocol. In major trauma blood should be salvaged by the use of a cell separation machine.

Jehovah's witness can be a special problem and it is very important to discuss individually with each patient especially in elective cases. Salvage of blood is usually permitted if a closed system of tubes is arranged so there is no discontinuous tube from the wound to the retransfusion site. Arrangement with stopcocks is no problem.

Retransfusion of blood should be considered in most operations if bleeding is a problem. The best blood in the patient's veins is his own.

Leukocytes Role at Blood Transfusion

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The acute inflammatory response is the first line of defence against microbial infection and is also the primary event in tissue healing. Central within this highly complex process, which involves countless chemical mediators and numerous cell populations, is the polymorphonuclear leukocyte (PMN). PMN are autonomous white blood cells, which are abundant in the blood but are normally absent in other tissues. In reaction to infection or injury the bone marrow produces and releases increased numbers of PMN causing a transient leukocytosis.

The PMN is therefore the key cell of the acute inflammatory response, having three main functions for anti-bacterial defence:

1. Transmigration: the ability of the cells to leave the bloodstream and enter the site of injury.
2. Phagocytosis: the ability to engulf and ingest the foreign microorganisms
3. Bactericidal effects:
 - a. Oxygen dependent – Respiratory burst activity, which involves the release toxic metabolites by the phagocyte to digest the microbe.
 - b. Non-oxygen dependent – degranulation .

Increasing concerns regarding allogenic blood has lead to the search for alternative sources of blood replacement. These concerns have included infection, transfusion reactions and downregulation of the immune system. This immune suppression is multifactorial and has been thought to be related to various aspects including low natural killer cell activity, abnormal immunoglobulin levels, defective phagocytosis and complement- mediated killing capacity.

On the other hand, previous studies have suggested that autologous transfusion may reduce post-operative infection rates but no clear mechanism for this has been offered. It is possible that PMN may play a key role in this increased immunity. This could be due to a heightened response of any of the above functions. A study we have conducted in Cardiff using

Bellovac A.B.T, Astra Tech, has indeed shown that the respiratory burst activity of PMN in total knee arthroplasty patients is augmented following autologous transfusion. This is likely to be due to increased concentration of pro-inflammatory mediators. It suggests that the use of autologous transfusions systems would reduce post-arthroplasty infection rates, compared with no transfusion.

