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Conversion from Platelet-Rich Plasma Platelet Production to Buffy Coat Platelet Component Production: Benefits and Limitations

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Abstract

Blood transfusion centers are under considerable pressure to produce platelet concentrates with high quality and safety due to the short shelf life of 3-5 days as well as possible bacterial and viral contaminations. For a variety of reasons, many Europeans have changed their methods of component production from whole blood using the North American standard platelet-rich plasma method to the buffy coat method of platelet production. Many advantages and some limitations during conversion from platelet-rich plasma method to buffy coat method have been observed. It seems that decisions to switch from platelet-rich plasma method to buffy coat method with whole blood component production should be considered; the benefits from increased platelet yield, improved platelet quality, increased plasma recovery, reduced blood transfusion adverse reactions and lower pathogen transmission rates compared to the platelet-rich plasma method outweigh any transient difference in red cell parameters or inconsiderable reduction of factor VIII activity. The purpose of this review is to discuss the quality, safety and economic aspects of blood components production during conversion from platelet-rich plasma to buffy coat method in preparing blood components which may benefit developing countries.

Keywords: Buffy coat, platelet-rich plasma, platelet concentrates, blood components.

Introduction

Blood transfusion centers are under considerable pressure to produce platelet concentrates (PC) with high quality and safety due to the short shelf life of 3-5 days as well as possible bacterial and viral contaminations. One of the approaches to solve the shortage of platelet concentrates is using platelet substitutes such as infusible platelet membrane[1-6], lyophilized platelets [7] and other similar products; but conversion from conventional production process of PC to the new buffy coat (BC) method is the more feasible approach. Many blood transfusion centers have changed their methods of component production from whole blood using the North American standard platelet-rich plasma (PRP) method to the BC method of platelet (PLT) production. The change arose from dissatisfaction with the infranatant RBCs left after the removal of PRP. They were heavily contaminated with white blood cells (WBCs), which caused febrile, nonhemolytic transfusion reactions [8]. Furthermore, PLTs and WBCs contributed to the formation of microaggregates in the RBCs, which were thought to be deleterious for the recipient [9]. BC method was developed by investigators in the Netherlands and Sweden in the mid-1970s [10]. At the present time, this method is used predominantly in Europe, Canada and most of the Latin America countries, except USA. The aim of this study is to describe quality, safety and economic aspects during conversion from PRP method to BC method in preparing blood components which may benefit developing countries.

Methods of platelet pre-paration

In the early 1960s, PRP was used without further manipulation to reduce the incidence of hemorrhage in thrombocytopenic patients[11]. In that period, blood was processed under refrigeration,

and irreversible platelet clumping was observed when efforts were made to concentrate the platelets further with a hard spin. This problem was solved in the late 1960s by dual modification of processing the blood and PRP at room temperature (22°C) and holding the sedimented platelets stationary for 30 to 60 minutes before resuspending them as a platelet concentrate [12]. This method of production has been remained as a standard platelet component production method in the United States and many other countries since then.

The BC production method reverses the sequence of centrifugation steps compared to PRP. A hard spin is used initially to separate whole blood into three components: plasma, red blood cells (RBCs), and a BC layer. Using semiautomated extraction, the most common configuration uses a so-called top-and-bottom collection set in which plasma and RBCs are transferred to storage containers and the BC is left in the donation bag. This BC contains platelets, white blood cells (WBCs), plasma, and some RBCs. ABO-matched BCs are pooled together with one plasma unit from one of the donors or one unit of platelet additive solution using a sterile docking device. The pooled BC is then given a soft spin, and the PRP is extracted with or without leukofiltration to produce a pooled PC. Although both methods produce a platelet product, the products may have somewhat different in vitro characteristics [13].

Quality aspects of blood component products

Platelet concentrate

There is a remarkable quality improvement in laboratories marking platelets using buffy coat (BC-PC) method relative to platelets produced by PRP (PRP-PC) method [10,13-16]. The second centrifugation in the preparation of PC in PRP-PC method is associated with reversible platelet aggregation and contact with non-biological surface, which probably is induced by activation due to the close contact between platelets in the platelet pellet while, BC-PC method does not involve significant close cell contact between platelets in a pellet. In addition, PRP-PC method may stimulate more degranulation or activation during hard spin centrifugation without the presence of WBC and RBC as a barrier “biologic cushion” to lower these stresses. Some studies considering the BC-PC method have indicated lower platelet activation (P-selectin or Annexin V) [13,15-23], higher morphology score [13,21,23,24], equal or better extend shape of change (ESC) and hypotonic shock response (HSR) [13,23,25], higher pH [13,20,22,25], lower residual WBCs [13,20-22,26] higher platelet yield [13,14,21,22,26-29], better aggregation response to ADP [21,30,31], higher recovery and survival [22,25], lower bacterial infections [32-37], lower release of α-granular contents 38-40, higher glucose [41], lower contaminated RBC [31] and higher total ATP [23] in comparison with PRP-PC method. But, there are some other studies that show no significant differences between the two methods in platelet activation such as P-selectin or annexin V[22], WBC residual [31], pH [22,20,21,42], extend shape change (ESC) 22,42, hypotonic shock response (HSR) [22,31,42], morphology score [31,42], glucose [22,42], lactate [22.42], ATP[21,42], PO2 and PCO2 [21,42], platelet yield [20,26,28,40,43,44], corrected count increment (CCI) [45-47], recovery and survival [22,26,42,48], RBC contamination [20] and even bacterial contamination [49,50] in BC-PC method.

In general, there is more evidence that indicate noticeable quality improvement in laboratory markers of BC-PC relative to PRP-PC.

Packed red blood cells

One of the major aims of BC removal was the improvement of RBC quality. In fact, it cannot be claimed that this improvement was completed, particularly considering the recent technical advances. There are some disadvantages of BC-PC method that have been reported for packed red blood cells such as loss of RBC about 10% or more [43,51], lower survival [52], lower 2,3-diphosphoglycerate [53-59] (2,3-DPG), lower pH [54,60,61], lower bicarbonate concentration [54], higher lactate [54], lower glucose [54], lower viability [62-66], increase in the volume of RBC [67], significant increase in the number of residual WBCs in the 24-hold RBC units [68] and lower post transfusion recovery [69].

The most important concern associated with the overnight storage of whole blood (WB) is the significant increase in the number of residual WBCs in the 24-hour RBC units. Several researchers have demonstrated that RBC unit temperature, age and the number of residual platelets considerably influence the leukoreduction efficiency of RBC units [70-80]. Albeit, WBC reduction in these studies, was performed on WB donations or on RBC units obtained by the BC method or within 8 hours of

collection in PRP method. Due to these problems, investigations concerning the effects of simple operational modifications such as decreasing the temperature of RBC units before leukoreduction, increasing the filtration time and optimizing centrifugation steps are being continued. It is noteworthy that when WBCs are exposed to the acidic conditions of storage and refrigerated in red blood cells concentrates, they respond with activation and cytokine production before they die [81]. After they die, the WBCs break down and release constituents including enzymes such as phospholipase-A2. Phospholipase-A2 in turn attacks and breaks down phospholipids released by red blood cells, creating lysophospholipids such as the dialkyl glycerol platelet-activating factor. The longer the red blood cells are stored, the more of these biologically active lipids are produced. Leukoreduction of red blood cell concentrates shortly after collection markedly reduces the concentrations of lysophospholipids. Leukoreduction also decreases the changes that cause stored red blood cells to stick to endothelial cells in culture and probably to post-capillary venules in the circulation [82]. Five years of follow-up in France has shown significant less residual WBCs in red blood cells concentrates after leukoreduction [83].

Today, by using improved systems based on Top and Bottom (TAB) technology, adequate adjustment of the centrifugation and fractionation system configuration parameters can compensate RBC loss affording maximum yield from each donation and the production of blood components of increased quality [28, 84,85]. On the other hand, a use should be found for these lost RBCs in BC-PC method. They could be used for the preparation of therapeutic hemoglobin solutions. In addition, these low density RBCs are enriched with young reticulocytes (neocytes). These cells are less dense than older red cells and will end up in the upper layer of the red cell fraction. Transfusion of neocytes can prolong the interval between transfusions in chronically transfused patients [86-88].

Frozen plasma

The subject of method of production of plasma for transfusion has received relatively little consideration. In organizations that fractionate derivatives such as IVIG or factor VIII (FVIII) from plasma, the efforts are generally conducted to recover the maximum amount of plasma with maximum functional activity. The production of transfusion plasma from the whole blood uses either a shortened production time to prepare so-called 'fresh frozen plasma' or a longer production time to produce a routine frozen plasma product. Reports indicate that these products are not so very different from one another with respect to the functional activity of coagulation and anti-coagulant proteins [53,89,90].. The characteristics of frozen plasma which is prepared 24 hours at room temperature before freezing has demonstrated similarity to fresh frozen plasma , except for a 15% to 20% reduction of FVIII [91,92]. Sheffield et al. between 2006 and 2008 observed neither significant reductions in fibrinogen, factor V, ABO-matched FVIII or antithrombin, nor prolonged APTT or PT results when comparing frozen plasma derived by BC (FP-PC) to frozen plasma derived by PRP (FP-PRP) method [93]. No differences have been observed by other studies among FP-BC, FP-PRP or FFP, with exception of the well-known reduction in FVIII activity that supports longer times between donation and freezing [68,94-97].

Safety of blood components

Adverse reactions to transfusion

It has been shown that the use of PRP-PC is much more associated with adverse reactions in recipient than BC-PC [98-100], and their occurrence is strongly correlated to the amount of IL-6 in PC[98]. In addition, no significant increase in the levels of TNF-alpha is observed in BC–PC during storage period, while levels increase significantly in PRP–PC on day 1 [101]. Febrile non-hemolytic transfusion (FNHTR) reactions are the most common adverse reactions to platelet transfusions [102].

The frequency of febrile or urticarial transfusion reactions have been reduced by using BC method and sodium chloride, adenine, glucose and mannitol (SAGM) in comparison with traditional red cell concentrates due to removal of excess plasma [103,104].

Reactions to platelets are caused by leukocyte-derived cytokines and proinflammatory mediators that accumulate in the component during storage. Most blood services have implemented additive solution for BC-PC. The use of platelet additive solution which results in reduction of remaining plasma can lead to significant reduction of allergic

transfusion adverse events [105-107].

Transfusion related acute lung injury (TRALI) is caused by white blood cell antibodies in transfused blood components [108]. It occurs mainly after transfusion of fresh frozen plasma and PC. Pooled PCs contain less plasma from each donor, in particular if the pooled PCs are prepared with additive solution. However, in special cases, it has been demonstrated that even small plasma volumes can cause TRALI [109].

Leukocytes in the PCs can cause transfusion-associated graft-versus-host disease (TA-GVHD). TA-GVHD is mediated by the engraftment of allogeneic T-lymphocytes [110]. The risk of developing TA-GVHD depends on the viability and number of contaminating lymphocytes, the susceptibility of the recipient's immune system to their engraftment and the degree of HLA disparity between donor and recipient. Leukocyte filtration is not effective enough to produce the level of lymphocyte removal required to prevent TA-GVHD [111]. In this respect, a recipient of a pooled PC has a high risk of receiving a PC which contains plasma of a donor carrying WBC antibodies.

The use of universal leukoreduction, implemented in a growing number of countries, is a major decision to improve transfusion safety by drastically reducing the incidence of HLA immunization [112], and adverse reactions in patients [100,113].

Bacterial and viral contaminations

Some reports have demonstrated that buffy coat platelets have contamination rates similar to apheresis platelets but PRP method has higher contamination [114,115]. This phenomenon is presumably due to increased time for leukocyte-mediated bacterial killing provided by overnight hold of the whole blood which is an optional step in the process of buffy coat platelet production.

The theoretical argument of increased risk for transfusion-transmitted infections (TTI) due to a "pooling" of infectious agents in BC-PC may create a new challenge. It has been demonstrated that the use of apheresis PC leads to lower donor exposure of the recipient [116,117]. That means if platelets of four or five donations are pooled, the risk of infection is increased compared to a single unit. In the case of pooling there might be a chance that if one of the donors is infectious for hepatitis B, another donor contributing to the pooled PC product carries an amount of neutralizing antibodies. Due to the higher risk for TTI in first time donors [37,118,119], only repeat donations should be used for preparation of pooled BC-PC. Theoretically, higher leukoreduction in BC-PC relative to PRP-PC can enhance safety against TTI in cell-associated transmission of infections such as CMV, EBV, HIV, Toxoplasma gondii and similar infections. Therefore, it can be concluded that using modern whole blood processing techniques may prevent bacterial contamination [120].

Extended storage of buffy coat platelet concentrates

The most recent development in platelet component processing involves the use of platelet additive solutions (PAS) to dilute the BC before PC separation [121-124]. Use of PAS allows maximal plasma and platelet harvest if before PAS addition the BCs are pooled with a sterile tubing welder [125]. Since the first attempts to use platelet additive solutions, many improvements have been achieved, and although in vivo recovery of platelets is slightly decreased, many advantages are related to their use [126]. Among them, a significant reduction in adverse allergic reactions to transfusion is clearly demonstrated [106,107,127-129].

Buffy-coat processing allows for the use of PASs that reduces plasma-associated transfusion reactions and conserves plasma for transfusion or fractionation. Newer PASs, for example, SSP+ and Composol, can maintain PLT integrity and moderate metabolism similarly to plasma but offer consistently lower PLT recoveries and limited osmotic balance [130]. One recent study has shown that BC-PC stored in either plasma or 65% Plasmalyte meets FDA's post-storage viability criteria for 6 days [41]. Another study has indicated that rapid cooling of whole blood to room temperature is not required to meet FDA quantity and quality platelet standards. Eliminating the need to use cooling plates would represent a substantial cost-saving to blood centers [131].

Automation and standardization

The two production methods have differences that affect the operational efficiency of a production laboratory. For example, with the PRP method, there are more stringent limitations on the allowable production time that may limit the preparation of certain components such as platelets. With the buffy coat method, these production time

limits are less stringent thereby facilitating both laboratory workflow and increasing the ability to prepare components from the greatest proportion of whole blood collections. For the production laboratory, buffy coat platelets production method may require more overall effort than PRP method, but the finished product is generally leukoreduced with better quality. Overall, new technologies are coming that further improve the process control and increased use of automation in component production [132,133].

In addition, PRP–PC preparation is fully manual, and has at least one highly sensible step in term of platelet activation after the high speed centrifugation, while BC–PC can be produced with an automatic process with a high and reproducible platelet recovery [134].

Blood fractionation systems that include removal of the buffy-coat layer have evolved considerably in the past two decades, with a shift from manual extraction procedures to fully automated systems that allow standardized extraction and contribute to good laboratory practice in the preparation of blood components. The use of quality control systems in blood banks has made it necessary to adopt working methods that guarantee reproducible obtainment of the blood components; this in turn accommodates quality analyses of the products obtained on a routine basis, with careful control of the processing procedures involved [135].

Cost-effective benefits

The main topic of cost also comes into consideration when decisions are made. Unfortunately, there are no published comparisons of each blood component's costs from country to country determined by using the same criteria. For the manufacturer, BC-PC is a cost-effective method, due to the increased recovery of plasma and a 24-hour production window that permits all manufacturing to be done on the day after collection. Furthermore, BC pooled platelets reduce the cost of platelet therapy, because the BC-PC is pooled during production, it has lower overall leukoreduction costs than PRP-PC and can be used by both the blood transfusion services and the hospitals without further modification [136]. In addition, new technologies are being developed that further improve the process control in component production such as decreased RBC, platelet, BC and plasma discard rates, improved labor productivity with better yields for platelets, plasma and RBCs [132,133].

To date, formal cost-effectiveness analyses on leukodepletion are scarce and are mainly derived from observational, retrospective data. However, the few studies that are available show a favorable economic profile for selected clinical indications. For instance, utilizing observational clinical data in an economic model, leukodepletion of platelets appears to be cost-saving when applied in adult acute myelogenous leukaemia[137].

Furthermore, leukodepletion of platelets in acute myelogenous leukemia and lymphoma patients and leukodepletion of whole blood in colorectal surgery have shown lower hospital costs compared to unfiltered blood products [138,139]. In coronary artery bypass graft surgery patients, leukodepletion of erythrocytes was cost-saving[140]. The Canadian Coordinating Office for Health Technology Assessment concluded that universal leukodepletion would not be cost-saving but that selective leukodepletion, that is, applying it to all patients who had an established indication for its use (such as frequently transfused patients), might be cost-saving [141].

In addition, use of neocyte therapy by using the Neocel® System that is a simple method and relatively low cost can benefit the majority of chronically transfused patients by reducing transfusional iron overload and related complications in BC-PC method 88. On the other hand, extension of the platelet shelf life by 2 to 3 days in BC-PC method can improve platelet inventory and efforts of donor recruitment tremendously, as well as the overall cost of this type of product to patients.

Finally, it is logically clear that lower risk of infections and adverse reactions in BC-PC relative to PRP-PC can improve safety public health and minimize the healthcare cost.

Summarizing the advantages and disadvantages

As mentioned above, some disagreements are observed in the results of the reports about BC -PC method versus PRP-PC method. For example, neither the HSR, nor the ESC showed sensitivity to time in storage [16,142] and the test results are significantly affected by the test diluents [143] which may reflect inconsistency among the protocols used by different laboratories. Other differences may be

related to the protocol of platelet preparation, pooling kit method or the chain method [144,145], type of additive solution [146-149], type of storage container [150-153], rapid cool down of whole blood after collection [154], type of cell separators [155,156] and the timing of BC preparation from either fresh or overnight-stored whole blood that influences metabolic activity, storage lesion and platelet count [145].

Incompatibility between in vivo and in vitro studies is another challenge for platelet products. It is accepted that the assessment of platelet quality is normally made in the first instance using in vitro laboratory assays. Unfortunately, there is no single laboratory test than can accurately predict the efficacy of a platelet transfusion [157]. Meanwhile, poor correlations between in vitro assays and in vivo survivability of PCs are sometimes seen in α-granule release [158], morphology score [159], P-selectin [160-162] and pH [163]. A possible explanation for this inconsistency is that platelet activation/degranulation is an independent process that sometimes, but not always, runs in parallel to the mechanism that leads to decreasing platelet viability. In the quest for an in vitro assay that can predict in vivo outcome, one must also consider that the platelet storage lesion appears to be somewhat reversible; platelets regain lost function after transfusion [164]. In addition, in vitro quality of platelets and the in vivo effectiveness of platelets depend on various factors like leukoreduction [165], storage temperature [166-169], the plastic material of the storage bag [162] gas exchange capabilities of the PLT storage container [153,170], platelet concentration in the storage container [171,172], and duration of storage [173,174], the type of anticoagulant used, the platelet concentration in the bag and the agitation[175].

These facts may also help to explain why poor correlations between in vitro assays and in vivo survivability or discrepancies in results are sometimes seen in the reports.

In acute transfusion reactions, it should also be considered that quality of the product in terms of residual WBCs, plasma content, storage period and patient factors may be more important than platelet product type.

In summary, the advantages of BC-PC relative to PRP-PC include: increase in leukoreduction of blood components, decrease in TRALI and TA-GVHD adverse reactions to blood components, decrease in in-vitro platelet activation, possible extension of platelet storage beyond 7 days, better process control by semi-automated production equipment and more efficient use of staff, more cost-effectiveness due to increase in recovery of plasma for fractionation industry, reduction in microaggregation formation and its consequences in transfused patients, lower cost of platelet transfusion therapy, reduction in post-transfusion infections such as CMV, HIV, EBV, possible reduction in the incidence of bacterial contamination of blood components, increase in the removal rate of plasma in BC-PC that may reduce allergic transfusion adverse events and pathogen reduction, decrease in platelet alloimmunization and refractoriness, possible improvement of platelet yield, equal or better in vivo platelet recovery and survival, lower work load due to a 24-hour production window and standardization, lower leukocytes interaction and cytokine release, possible separation of blood components by differential centrifugation and possible improvement by new additive solutions, high applicability to pathogen reduction/inactivation systems, possible lower hematocrit levels in BC-PC, decrease in loss of red blood cells and possible preparation of therapeutic hemoglobin solutions (neocytes).

On the other hand BC-PC relative to PRP-PC may have some limitations such as: equal or lower platelet recovery, identical platelet survival and viability, lower quality of RBC in red cell units, increase in the number of residual WBCs in the 24-hour RBC units before leukodepletion step and possible lower quality of frozen plasma due to small decrease in factor VIII activity.

Above evidence show that BC-PC has a better quality than PRP-PC. This is due to these facts that most European countries have adopted this technique [10].

Conclusion

Decisions to convert from PRP-PC to BC-PC method in whole blood component production should be made. The benefits from increased platelet yield and quality, reduced bacterial contamination rates as well as cost-effectiveness compared to the PRP method might outweigh any transient difference in red cell parameters. It seems, in the process of converting, the prominent challenge is probably between the improvement

of the quality/safety of platelet and saving more plasma on one side, and the lower quality of red blood cells and somewhat frozen plasma units on the other side.

Furthermore, the products need regular re-assessment since new developments may have impact on the quality of various product types. From a risk management point of view it is advisable that a blood transfusion service should keeps both methods of preparation on hand. Further studies are recommended to assess the clinical significance of these two methods and in vivo results in terms of clinical efficacy and the viability of the stored platelets to patients.

References

1. Chao FC, Kim BK, Houranieh AM, Liang FH, Konrad MW, Swisher SN, et al. Infusible platelet membrane microvesicles: a potential transfusion substitute for platelets. Transfusion. 1996;36(6):536-42.
2. Nasiri S, Heidari M, Rivandi S. Evaluation of hemostatic effectiveness of infusible platelet membrane in rabbits as a potential substitute for platelet transfusion. Journal of Drug Delivery & Therapeutics. 2012;2(5):1-3.
3. Nasiri S, Heidari M, Rivandi S. Infusible platelet membranes improve hemostasis in thrombocytopenic rabbits: studies with two different injection doses. International Journal of Pharmaceutical Sciences Research. 2012;3(12):4895-8.
4. Nasiri S. Platelet membranes versus intact platelets: Feasibility as a potential platelet substitute. World Journal of Pharmacy and Pharmaceutical Sciences. 2013; 2(3):763-81.
5. Nasiri S. Infusible platelet membrane as a platelet substitute for transfusion: an overview. Blood Transfus. 2013;11(3):337-42.
6. Nasiri S, Mousavi Hosseini K. Infusible platelet membrane versus conventional platelet concentrate: benefits and disadvantages. Iranian Journal of Blood and Cancer. 2014;6(2):87-93.
7. Nasiri S, Khosroshahi BN. Lyophilization of human platelet and study of its aggregability International Journal of Drug Delivery. 2012;3:241-4.
8. Brittingham TE, Chaplin H Jr. Febrile transfusion reactions caused by sensitivity to donor leukocytes and platelets. J Am Med Assoc.. 1957;165(7):819-25.
9. Prins HK, de Bruijn JC, Henrichs HP, Loos JA. Prevention of microaggregate formation by removal of buffy-coats. Vox Sang. 1980;39:48-51.
10. Murphy S. Platelets from pooled buffy coats: an update. Transfusion. 2005;45(4):634-9.
11. Freireich EJ. Kliman A, Gaydos LA, Natan M, Frei E. Response to repeated platelet transfusion from the same donor. Ann Intern Med. I963;59:277-87.
12. Mourad N. A simple method for obtaining platelet concentrates free of aggregates. Transfusion. 1968;8(1):48.
13. Levin E, Culibrk B, Gyöngyössy-Issa MI, Weiss S, Scammell K, LeFresne W, et al. Implementation of buffy coat platelet component production: comparison to platelet-rich plasma platelet production. Transfusion. 2008;48(11):2331-7.
14. Gulliksson H. Platelets from platelet-rich-plasma versus buffy-coat-derived platelets: what is the difference? Rev Bras Hematol Hemoter. 2012; 34(2): 76-7.
15. Sweeney JD, Kouttab NM, Holme S, Kurtis JD, Cheves TA, Nelson EJ. Prestorage pooled whole-blood-derived leukoreduced platelets stored for seven days, preserve acceptable quality and do not show evidence of a mixed lymphocyte reaction. Transfusion. 2004;44(8):1212-9.
16. Turner CP, Sutherland J, Wadhwa M, Dilger P, Cardigan R. In vitro function of platelet concentrates prepared after filtration of whole blood or buffy coat pools. Vox Sang. 2005;88(3):164-71.
17. Devine D, Bradley A, Maurer E, Levin E, Chahal S, Serrano K, et al. Effects of pre-storage white cell reduction on platelet aggregate formation and the activation state of platelet and plasma enzyme systems. Transfusion. 1999;39(7):724-34.
18. Tibbles HE, Navara CS, Hupke MA, Vassilev AO, Uckun FM. Thrombopoietin induces p-selectin expression on platelets and subsequent platelet ⁄ leukocyte interactions. Biochem Biophys Res Commun. 2002; 292(4):987-91.
19. Metcalfe P, Williamson LM, Reutelingsperger CP, Swann I, Ouwehand WH, Goodall AH. Activation during preparation of therapeutic platelets affects deterioration during storage: a comparative flow cytometric study of different production methods. Br J Haematol. 1997;98(1):86-95.
20. Soleimany Ferizhandy A. Platelet activation in stored platelet concentrates: comparison of two methods preparation. J Hematol. 2012;1(1):15-9.
21. Mrowiec ZR, Oleksowicz L, Dutcher JP, De Leon-Fernandez M, Lalezari P, Puszkin EG. A novel technique for preparing improved buffy coat platelet

concentrates. Blood Cells Mol Dis. 1995;21(1):25-33.
22. Dumont LJ, Dumont DF, Unger ZM, Siegel A, Szczepiorkowski ZM, Corson JS, et al. A randomized controlled trial comparing autologous radiolabeled in vivo platelet (PLT) recoveries and survivals of 7-day-stored PLT-rich plasma and buffy coat PLTs from the same subjects. Transfusion. 2011;51(6):1241-8.
23. Bertolini F, Rebulla P, Porretti L, Murphy S. Platelet quality after 15-day storage of platelet concentrates prepared from buffy coats and stored in a glucose-free crystalloid medium. Transfusion. 1992;32(1):9-16.
24. Kunicki TJ, Tuccelli M, Becker GA, Aster GH. A study of variables affecting the quality of platelets stored at "room temperature". Transfusion. 1975;15(5):414-21.
25. Bertolini F, Rebulla P, Riccardi D, Cortellaro M, Ranzi ML, Sirchia G. Evaluation of platelet concentrates prepared from buffy coats and stored in a glucose-free crystalloid medium. Transfusion. 1989;29(7):605-9.
26. Singh RP, Marwaha N, Malhotra P, Dash S. Quality assessment of platelet concentrates prepared by platelet rich plasma-platelet concentrate, buffy coat poor-platelet concentrate (BC-PC) and apheresis-PC methods. Asian J Transfus Sci. 2009;3(2):86-94.
27. Holme S, Moroff G, Whitley P, Hallinen D, Heaton A. Properties of platelet concentrates prepared after extended whole blood holding time. Transfusion. 1989;29(8):689-92.
28. Pietersz RN, de Korte D, Reesink HW, Dekker WJ, van den Ende A, Loos JA. Storage of whole blood for up to 24 hours at ambient temperature prior to component preparation. Vox Sang. 1989;56(3):145-50.
29. van der Meer PF, de Wildt-Eggen J. The effect of whole-blood storage time on the number of white cells and platelets in whole blood and in white cell-reduced red cells. Transfusion. 2006;46(4):589-94.
30. Washitani Y, Irita Y, Yamamoto K, Shiraki H, Kiyokawa H, Maeda Y, et al. Prevention of acquired defects in platelet function during blood processing. Transfusion. 1988;28(6):571-5.
31. Rácz Z, Thék M. Buffy coat or platelet-rich plasma? Comparison of two platelet-processing techniques. Vox Sang. 1984;47(2):108-13.
32. van der Meer PF, Pietersz RN, Reesink HW. Storage of platelets in additive solution for up to 12 days with maintenance of good in-vitro quality. Transfusion. 2004;44(8):1204-11.
33. Sanz C, Pereira A, Vila J, Faundez AI, Gomez J, Ordinas A. Growth of bacteria in platelet concentrates obtained from whole blood stored for 16 hours at 22°C before component preparation. Transfusion. 1997;37(3):251-4.
34. Pietersz RN, Reesink HW, Pauw W, Dekker WJ, Buisman L. Prevention of Yersinia enterocolitica growth in red-bloodcell concentrates. Lancet 1992;240(8822):755-6.
35. Hogman CF, Gong J, Hambraeus A, Johansson CS, Eriksson L. The role of white cells in the transmission of Yersinia enterocolitica in blood components. Transfusion. 1992;32(7):654-7.
36. Reesink HW, Hanfland P, Hertfelder HJ, Scharf RE, Högman CF, Hoppe PA, et al. International forum. What is the optimal storage temperature for whole blood prior to preparation of blood components. Vox Sang. 1993;65(4):320-7.
37. Högman CF, Gong J, Eriksson L, Hambraeus A, Johansson CS. White cells protect donor blood against bacterial contamination. Transfusion. 1991;31(7):620-6.
38. Snyder EL, Koerner TA Jr, Hezzey A. Platelet concentrates. Influence of different preparative protocols on the in vitro release reaction. Vox Sang. 1982;43(2):71-5.
39. Ledent E, Wasteson A, Berlin G. Growth factor release during preparation and storage of platelet concentrates. Vox Sang. 1995;68(4):205-9.
40. Fijnheer R, Pietersz RN, de Korte D, Gouwerok CW, Dekker WJ, Reesink HW, et al. Platelet activation during preparation of platelet concentrates: a comparison of the platelet-rich plasma and the buffy coat methods. Transfusion. 1990;30(7):634-8.
41. Slichter SJ, Bolgiano D, Corson J, Jones MK, Christoffel T, Bailey SL, et al. Extended storage of buffy coat platelet concentrates in plasma or a platelet additive solution. Transfusion. 2014 Mar 28. (Epub ahead of print)
42. Keegan T, Heaton A, Holme S, Owens M, Nelson E, Carmen R. Paired comparison of platelet concentrates prepared from platelet-rich plasma and buffy coats using a new technique with 111In and 51Cr. Transfusion. 1992;32(2):113-20.
43. Murphy S, Heaton WA, Rebulla P. Platelet production in the Old World and the New. Transfusion. 1996;36(8):751-4.
44. Hirosue A, Yamamoto K, Shiraki H, Kiyokawa H, Maeda Y, Yoshinari M. Preparation of white cell poor blood components using a quadruple bag system. Transfusion. 1988;28(3):261-4.

45. Hogge DE, Thompson BW, Schiffer CA. Platelet storage for 7 days in second-generation blood bags. Transfusion. 1986;26(2):131-5.
46. Dijkstra MJ, Hendriks ECM , van der Meer PF, Pietersz RNI , Reesink HW, Huijgens PC. Clinical effectiveness of leukocyte depleted platelet concentrates that were stored for up to 7 days. Vox Sang. 2002;83(suppl 2):7-8.
47. van Rhenen DJ, Gulliksson H, Cazenave JP, Pamphilon D, Davis K, Flament Jet al. Therapeutic efficacy of pooled buffy-coat platelet components prepared and stored with a platelet additive solution. Transfus Med. 2004;14(4):289-95.
48. Cardigan R, Williamson LM. The quality of platelets after storage for 7 days. Transfus Med. 2003;13(4):173-87.
49. Vasconcelos E, Figueiredo AC, Seghatchian J. Quality of platelet concentrates derived by platelet rich plasma, buffy coat and Apheresis. Transfus Apher Sci. 2003;29(1):13-6.
50. Heaton WA, Rebulla P, Pappalettera M, Dzik WH. A comparative analysis of different methods for routine blood component preparation. Transfus Med Rev. 1997;11(2):116-29.
51. Andreu G, Vasse J, Sandid I, Tardivel R, Semana G. Use of random versus apheresis platelet concentrates. Transfus Clin Biol. 2007;14(6):514-21.
52. Moroff G, AuBuchen J, Heaton A, Holme S. Preparation of components from units of whole blood held for 24 hours at 20-24°C (abstract).Vox Sang 1994;67(Suppl 2):48.
53. Rácz Z, Baróti C. Storage of platelet concentrates from overnight-stored blood and overnight-stored buffy coat: in vitro studies. Vox Sang. 1995;68(3):160-3.
54. Högman CF, Knutson F, Lööf H. Storage of whole blood before separation: the effect of temperature on red cell 2,3 DPG and the accumulation of lactate. Transfusion. 1999;39(5):492-7.
55. Valeri CR, Hirsch NM. Restoration in vivo of erythrocyte adenosine triphosphate, 2,3-diphosphoglycerate, potassium ion, and sodium ion concentrations following the transfusion of acid-citrate-dextrose-stored human red blood cells. J Lab Clin Med. 1969;73:722-33.
56. Beutler E, Wood L. The in vivo regeneration of 2,3-diphosphoglyceric acid (DPG) after transfusion of stored blood. J Lab Clin Med. 1969;74(2):300-4.
57. Hogman CF, Akerblom O, de Verdier CH. Optimal use of different storage procedures. Bibl Haematol. 1971;38:175-82.
58. Heaton A, Keegan T, Holme S. In vivo regeneration of red cell 2,3-diphosphoglycerate following transfusion of DPG-depleted AS-1, AS-3 and CPDA-1 red cells. Br J Haematol. 1989;71(1):131-6.
59. Matthes G, Strunk S, Siems W, Grune T. Posttransfusional changes of 2,3-diphosphoglycerate and nucleotides in CPD-SAGM-preserved erythrocytes. Infusionsther transfusionsmed. 1993;20(3):89-92.
60. Rosenthal TB. The effect of temperature on the pH of blood and plasma in vivo. J Biol Chem. 1948;173(1):25-30.
61. Severinghaus JW. Blood gas calculator. J Appl Physiol. 1966;21(3):1108-16.
62. Jandl JH, Tomlinson AS. The destruction of red blood cells by antibodys in man. II. Pyrogenic, leukocytic and dermal responses to immune hemolysis. J Clin Invest. 1958;37(8):1202-28.
63. Mollison PL. Blood transfusion in clinical medicine. 5th ed. Oxford: Blackwell, 1972:55.
64. Shields CE. Studies on stored whole blood. IV. Effects of temperature and mechanical agitation on blood with and without plasma. Transfusion. 1970;10(4):155-62.
65. Ruddell JP, Lippert LE, Babcock JG, Hess JR. Effect of 24-hour storage at 25 degrees C on the in vitro storage characteristics of CPDA-1 packed red cells. Transfusion. 1998;38(5):424-8.
66. Högman CF, de Verdier CH, Ericson A, Hedlund K, Sandhagen B. Studies on the mechanism of human red cell loss of viability during storage at +4 degrees C in vitro. I. Cell shape and total adenylate concentration as determinant factors for posttransfusion survival. Vox Sang. 1985;48(5):257-68.
67. Cohle SD, Saleem A, Makkaoui DE. Effects of storage of blood on stability of hematologic parameters. Am J Clin Pathol. 1981;76(1):67-9.
68. Thibault L, Beauséjour A, de Grandmont MJ, Lemieux R, Leblanc JF. Characterization of blood components prepared from whole-blood donations after a 24-hour hold with the platelet-rich plasma method. Transfusion. 2006;46(8):1292-9.
69. Heaton WA. The quality of red blood cells. Immunol Invest. 1995;24(1-2):371-90.
70. Pietersz RN, van der Meer PF, Seghatchian MJ. Update on leucocyte depletion of blood components by filtration. Transfus Sci. 1998;19(4):321-8.
71. Beaujean F, Segier JM, le Forestier C, Duedari N. Leukocyte depletion of red cell concentrates by

filtration: influence of blood product temperature. Vox Sang. 1992;62(4):242-3.
72. Rogers SE, Edmondson D, Goodrick MJ, Standen GR, Franck V, Reppucci A, et al. Prestorage white cell reduction in saline-adenine-glucose-mannitol red cells by use of an integral filter: evaluation of storage values and in vivo recovery. Transfusion. 1995;35(9):727-33.
73. Ledent E, Berlin G. Factors influencing white cell removal from red cell concentrates by filtration. Transfusion. 1996;36(8):714-8.
74. van der Meer PF, Pietersz RN, Nelis JT, Hinloopen B, Dekker WJ, Reesink HW. Six filters for the removal of white cells from red cell concentrates, evaluated at 4 degrees C and/or at room temperature. Transfusion 1999;39(3):265-70.
75. Smith JD, Leitman SF. Filtration of RBC units: effect of storage time and temperature on filter performance. Transfusion. 2000;40(5):521-6.
76. Shinar E, Prober G, Yahalom V, Michlin H. WBC filtration of whole blood after prolonged storage at ambient temperature by use of an in-line filter collection system. Transfusion. 2002;42(6):734-7.
77. van der Meer PF, Pietersz RN, Reesink HW. Influence of temperature, filter wettability, and timing of filtration on the removal of WBCs from RBC concentrates. Transfusion. 2001;41(4):540-4.
78. Steneker I, Prins HK, Florie M, Loos JA, Biewenga J. Mechanisms of white cell reduction in red cell concentrates by filtration: the effect of the cellular composition of the red cell concentrates. Transfusion. 1993;33(1):42-50.
79. Royer D, Pommier P, Polidori Y, Païtard V, Arinal P, Verdrel N, et al. The platelet leukocyte ratio in red blood cell concentrates is an essential indicator of leukocyte removal filter efficiency which limits their use. Transfus Clin Biol. 2000;7(1):70-5. (Article in French)
80. Alcorta I, Pereira A, Sanz C, Terol MJ, Ordinas A. Influence of the red blood cell preparation method on the efficacy of a leukocyte reduction filter. Vox Sang. 1996;71(2):78-83.
81. Weisbach V, Wanke C, Zingsem J, Zimmermann R, Eckstein R: Cytokine generation in whole blood, leukocyte-depleted and temporarily warmed red blood cell concentrates. Vox Sang. 1999; 76(2):100-6.
82. Anniss AM, Sparrow RL: Storage duration and white blood cell content of red blood cell (RBC) products increases adhesion of stored RBCs to endothelium under flow conditions. Transfusion. 2006; 46(9):1561-7.
83. Chabanel A, Carrat F, Begue S, Masse M, Perrault MP, Andreu G. Quality of leucoreduced red blood cell concentrates: 5 years of follow-up in France. Vox Sang. 2008;94(1):41-7.
84. Kretschmer V, Tesche U, Richter P. Improvement of the separation of blood by modification of separators Optipress and Biotrans Separator. Beitr Infusionsther. 1992; 30:112-21.
85. Hurtado C, Bonanad S, Soler Mf, Mirabet V, Blasco I, Planelles Mf, et al. Quality analysis of blood components obtained by automated buffy-coat layer removal with a top & bottom system (Optipress (R)II). Haematologica. 2000;85(4):390-5.
86. Piomelli S, Seaman C, Reibman J, Tytun A, Graziano J, Tabachnik N, et al. Separation of younger red cells with improved survival in vivo: An approach to chronic transfusion therapy. Proc Natl Acad Sci. 1978;75(7):3474-8.
87. Graziano JH, Piomelli S, Seaman C, Wang T, Cohen A, Kelleher J, et al. A simple technique for preparation of young red cells for transfusion from ordinary blood units. Blood. 1982;59(4):865-9.
88. Spanos T, Ladis V, Palamidou F, Papassotiriou I, Banagi A, Premetis E, et al. The impact of neocyte transfusion in the management of thalassaemia. Vox Sang. 1996;70(4):217-23.
89. Serrano K, Scammell K, Weiss S, Culibrk B, Levin E, Gyöngyössy-Issa M, et al. Plasma and cryoprecipitate manufactured from whole blood held overnight at room temperature meet quality standards. Transfusion. 2010;50(2):344-53.
90. Cardigan R, van der Meer PF, Pergande C, Cookson P, Baumann-Paretti B, Cancelas JA, et al. Coagulation factor content of plasma produced from whole blood stored for 24 hours at ambient temperature: results from an international multicenter BEST Collaborative study. Transfusion. 2011;51(suppl 1):50S-57S.
91. Alhumaidan H, Cheves T, Holme S, Sweeney J. Stability of coagulation factors in plasma prepared after a 24-hour room temperature hold. Transfusion. 2010;50(9):1934-42.
92. Alhumaidan H, Cheves T, Holme S, Sweeney J. A Comparison of Clotting Factors in Fresh Frozen Plasma and 24 Hour Room Temperature Hold Frozen Plasma. Transfusion. 2010;50 (suppl 2).Abstract 8A.
93. Sheffield WP, Bhakta V, Jenkins C, Devine DV. Conversion to the buffy coat method and quality of frozen plasma derived from whole blood donations

in Canada. Transfusion. 2010;50(5):1043-9.
94. O'Neill EM, Rowley J, Hansson-Wicher M, McCarter S, Ragno G, Valeri CR. Effect of 24-hour whole-blood storage on plasma clotting factors. Transfusion. 1999;39(5):488-91.
95. Cardigan R, Lawrie AS, Mackie IJ, Williamson LM. The quality of fresh-frozen plasma produced from whole blood stored at 4 degrees C overnight. Transfusion 2005;45(8):1342-8.
96. Smith JF, Ness PM, Moroff G, Luban NL. Retention of coagulation factors in plasma frozen after extended holding at 1-6 degrees C. Vox Sang. 2000;78(1):28-30.
97. Runkel S, Haubelt H, Hitzler W, Hellstern P. The quality of plasma collected by automated apheresis and of recovered plasma from leukodepleted whole blood. Transfusion. 2005;45(3):427-32.
98. Muylle L, Wouters E, Peetermans ME. Febrile reactions to platelet transfusion: the effect of increased interleukin 6 levels in concentrates prepared by the platelet-rich plasma method. Transfusion. 1996;36(10):886–90.
99. Oksanen K, Ebeling F, Kekomaki R, Elonen E, Sahlstedt L, Volin L, et al. Adverse reactions to platelet transfusions are reduced by use of platelet concentrates derived from buffy coat. Vox Sang. 1994;67(4):356–61.
100. Anderson NA, Gray S, Copplestone JA, Chan DC, Hamon M, Prentice AG, et al. A prospective randomized study of three types of platelet concentrates in patients with haematological malignancy: corrected platelet increments and frequency of non haemolytic febrile transfusion reactions. Transfus Med. 1997;7(1):33–9.
101. Chaudhary R, Aggarwal A, Khetan D, Dayal R. Cytokine generation in stored platelet concentrate: comparison of two methods of preparation. Indian J Med Res. 2006;124(4):427-30.
102. de Rie MA, van der Plas-van Dalen CM, Engelfriet CP, von dem Borne AE. The serology of febrile transfusion reactions. Vox Sang. 1985; 49(2):126–134.
103. Högman CF, Akerblom O, Hedlund K, Rosén I, Wiklund L. Red cell suspensions in SAGM medium. Further experience of in vivo survival of red cells, clinical usefulness and plasma-saving effects. Vox Sang. 1983;45(3):217-23.
104. Liedén G, Hildén JO. Febrile transfusion reactions reduced by use of buffy-coat-poor erythrocyte concentrates. Vox Sang. 1982;43(5):263-5.
105. Andreu G, Vasse J, Herve F, Tardivel R, Semana G: Introduction of platelet additive solutions in transfusion practice. Advantages, disadvantages and benefit for patients. Transfus Clin Biol. 2007; 14(1):1006. (Article in French)
106. Kerkhoffs JL, Eikenboom JC, Schipperus MS, van Wordragen-Vlaswinkel RJ, Brand R, Harvey MS, et al. A multicenter randomized study of the efficacy of transfusions with platelets stored in platelet additive solution II versus plasma. Blood. 2006; 108(9):3210–5.
107. de Wildt-Eggen J, Nauta S, Schrijver JG, van Marwijk KM, Bins M, van Prooijen HC. Reactions and platelet increments after transfusion of platelet concentrates in plasma or an additive solution: a prospective, randomized study. Transfusion. 2000;40(4):398-403.
108. Bux J, Sachs UJ. The pathogenesis of transfusion-related acute lung injury (TRALI). Br J Haematol. 2007; 136(6):788-99.
109. Win N, Chapman CE, Bowles KM, Green A, Bradley S, Edmondson D, et al. How much residual plasma may cause TRALI? Transfus Med. 2008;18(5):276-80.
110. Brubaker DB. Human posttransfusion graft-versus-host disease. Vox Sang. 1983;45(6):401-20.
111. [No authors listed]. Guidelines on gamma irradiation of blood components for the prevention of transfusion-associated graft-versus-host disease. BCSH blood transfusion task force. Transfus Med. 1996;6(3):261-71.
112. Andreu G, Dewailly J. Prevention of HLA alloimmunization by using leukocyte-depleted components. Curr Stud Hematol Blood Transfus. 1994(60):29-40.
113. Enright H, Davis K, Gernsheimer T, McCullough JJ, Woodson R, Slichter SJ. Factors influencing moderate to severe reactions to PLT transfusions: experience of the TRAP multicenter clinical trial. Transfusion. 2003;43(11):1545–52.
114. Ness P, Braine H, King K, Barrasso C, Kickler T, Fuller A, et al. Single-donor platelets reduce the risk of septic platelet transfusion reactions. Transfusion. 2001;41(7):857-61.
115. Jenkins C, Ramírez-Arcos S, Goldman M, Devine DV. Bacterial contamination in platelets: incremental improvements drive down but do not eliminate risk. Transfusion. 2011;51(12):2555-65.
116. Heuft HG, Mende W, Blasczyk R. A general change of the platelet transfusion policy from apheresis platelet concentrates to pooled platelet concentrates is associated with a sharp increase in donor exposure and infection rates. Transfus Med Hemother. 2008;35(2):106-13.

117. Lopez-Plaza I, Weissfeld J, Triulzi DJ. The cost-effectiveness of reducing donor exposures with single-donor versus pooled random-donor platelets. Transfusion. 1999; 39(9):925-32.
118. Hourfar MK, Jork C, Schottstedt V, Weber-Schehl M, Brixner V, Busch MP, et al. Experience of German Red Cross blood donor services with nucleic acid testing: results of screening more than 30 million blood donations for human immunodeficiency virus-1, hepatitis C virus, and hepatitis B virus. Transfusion. 2008;48(8):1558-66.
119. Williams AE, Thomson RA, Schreiber GB, Watanabe K, Bethel J, Lo A, et al. Estimates of infectious disease risk factors in US blood donors. Retrovirus Epidemiology Donor Study. JAMA. 1997;277(12):967-72.
120. Stramer SL, Glynn SA, Kleinman SH, Strong DM, Caglioti S, Wright DJ, et al. Detection of HIV-1 and HCV infections among antibody-negative blood donors by nucleic acid-amplification testing. N Engl J Med. 2004;351(8):760-8.
121. Eriksson L, Htgman CF. Platelet concentrates in an additive solution prepared from pooled buffy coats. 1. In vitro studies. Vox Sang. 1990; 59(3):140-5.
122. Bertolini F, Rebulla P, Marangoni F, Sirchia G. Platelet concentrates stored in synthetic medium after filtration. Vox Sang. 1992;62(2):82-6.
123. Eriksson L, Shanwell A, Gulliksson H, Högman CF, Svensson LA, Kristensen J, et al. Platelet concentrates in an additive solution prepared from pooled buffy coats: In Vivo Studies. Vox Sang. 1993;64(3):133-8.
124. Gulliksson H, Eriksson L, Högman CF, Payrat JM. Buffy-coat-derived platelet concentrates prepared from half-strength citrate CPD and CPD whole-blood units. Comparison between three additive solutions: in vitro studies.. Vox Sang. 1995;68(3):152-9.
125. AuBuchon JP, Pickard C, Herschel L. Sterility of plastic tubing welds in components stored at room temperature. Transfusion. 1995;35(4):303-7,
126. Gulliksson H, AuBuchon JP, Cardigan R, van der Meer PF, Murphy S, Prowse C, et al. Storage of platelets in additive solutions: a multicentre study of the in vitro effects of potassium and magnesium. Vox Sang. 2003;85(3):199–205.
127. Kerkhoffs JL, Eikenboom JC, Schipperus MS, vanWordragen-Vlaswinkel RJ, Brand R, Harvey MS, et al. A multicenter randomized study of the efficacy of transfusions with platelets stored in platelet additive solution II versus plasma. Blood. 2006;108(9):3210-5.
128. Snyder E, McCullough J, Slichter SJ, Strauss RG, Lopez-Plaza I, Lin JS, et al. Clinical safety of platelets photochemically treated with amotosalen HCl and ultraviolet A light for pathogen inactivation: the SPRINT trial. Transfusion. 2005;45(12):1864-75.
129. Kacker S, Ness PM, Savage WJ, Frick KD, McCullough J, King KE, et al. The cost-effectiveness of platelet additive solution to prevent allergic transfusion reactions. Transfusion. 2013;53(11):2609-18.
130. Zhang JG, Carter CJ, Culibrk B, Devine DV, Levin E, Scammell K, et al. Buffy-coat platelet variables and metabolism during storage in additive solutions or plasma. Transfusion. 2008;48(5):847-56.
131. Slichter SJ, Corson J, Jones MK, Christoffel T, Pellham E, Bolgiano D. Platelet concentrates prepared after a 20- to 24-hour hold of the whole blood at 22°C. Transfusion. 2012;52(9):2043-8.
132. Thomas S, Beard M, Garwood M, Callaert M, van Waeg G, Cardigan R. Blood components produced from whole blood using the Atreus processing system. Transfusion. 2008;48(12):2515-24.
133. Sandgren P, Hild M, Sjödin A, Gulliksson H. Storage of buffy-coat-derived platelets in additive solutions: in vitro effects on platelets prepared by the novel TACSI system and stored in plastic containers with different gas permeability. Vox Sang. 2010;99(4):341-7.
134. Larsson S, Sandgren P, Sjödin A, Vesterinen M, Gulliksson H. Automated preparation of platelet concentrates from pooled buffy coats: in vitro studies and experiences with the OrbiSac system. Transfusion. 2005;45(5):743-51.
135. Högman CF, Eriksson L, Ring M. Automated blood component preparation with the Opti system: three years' experience. Beitr Infusionsther. 1992; 30:100-7.
136. Devine DV, Serrano K.. Preparation of blood products for transfusion: is there a best method? Biologicals. 2012;40(3):187-90.
137. Balducci L, Benson K, Lyman GH, Sanderson R, Fields K, Ballester OF, et al. Cost-effectiveness of white cell-reduction filters in treatment of adult acute myelogenous leukemia. Transfusion. 1993;33(8):665-70.
138. Blumberg N, Heal JM, Kirkley SA, DiPersio JF, Rapoport AP, Rowe JM. Leukodepleted-ABO-identical blood components in the treatment of hematologic malignancies: a cost analysis. Am.J.Hematol. 1995;48(2):108-15.
139. Jensen LS, Grunnet N, Hanberg-Sorensen F, Jorgensen J. Cost-effectiveness of blood transfusion and white cell reduction in elective colorectal

surgery. Transfusion 1995;35(9):719-22.
140. Postma MJ, van de Watering LMG, de Vries R, Versmoren D, van Hulst M, Tobi H, et al. Cost-effectiveness of leucocyte depletion of red-cell transfusions for patients undergoing cardiac surgery. Vox Sanguinis 2003;84(1):65-67.
141. [No authors listed]. Canadian Coordinating Office for Health Technology Assesment. Leukoreduction: the techniques used, their effectiveness and costs. Int J Technol Assess Health Care. 1998;14(3):586-8.
142. Aubuchon JP, Taylor H, Holme S, Nelson E. In vivo and in vitro evaluation of leukoreduced platelets stored for 7 days in CLX containers. Transfusion. 2005;45(8):1356-61.
143. .VandenBroeke T, Dumont LJ, Hunter S, Nixon J, Murphy S, Roger J, et al. Platelet storage solution affects on the accuracy of laboratory tests for platelet function: a multi-laboratory study. Vox Sang. 2004;86(3):183-8.
144. Armstrong B, Hardwick J, Raman L, Smart E, Wilkinson RW. Introduction to Blood Transfusion Technology. Vox Sang ISBT Science Series. 2008; 3:165-67.
145. Dijkstra-Tiekstra MJ, Kuipers W, Setroikromo AC, de Wildt-Eggen J. Overnight or fresh buffy coat-derived platelet concentrates prepared with various platelet pooling systems. Transfusion. 2008;48(4):723-30.
146. Ringwald J, Zimmermann R, Eckstein R.The new generation of platelet additive solution for storage at 22 degrees C: development and current experience. Transfus Med Rev. 2006;20(2):158–164.
147. Cardigan R, Sutherland J, Garwood M, Bashir S, Turner C, Smith K, et al. In vitro function of buffy coat-derived platelet concentrates stored for 9 days in CompoSol, PASII or 100% plasma in three different storage bags. Vox Sang. 2008;94(2):103–112.
148. Gulliksson H, Larsson S, Kumlien G, Shanwell A. Storage of platelets in additive solutions: effects of phosphate. Vox Sang. 2000;78(3):176-84.
149. Gulliksson H, AuBuchon JP, Vesterinen M, Sandgren P, Larsson S, Pickard CA, et al. Storage of platelets in additive solutions: a pilot in vitro study of the effects of potassium and magnesium. Vox Sang. 2002;82(3):131-6.
150. Murphy S, Kahn RA, Holme S, Phillips GL, Sherwood W, Davisson W, et al. Improved storage of platelets for transfusion in a new container. Blood. 1982;60(1):194-200.
151. Simon TL, Nelson EJ, Carmen R, Murphy S. Extension of platelet concentrate storage. Transfusion. 1983;23(3):207-12.
152. Gulliksson H, Shanwell A, Wikman A, Reppucci AJ, Sallander S, Uden AM. Storage of platelets in a new plastic container. Polyvinyl chloride plasticized with butyryl-n-trihexyl citrate. Vox Sang. 1991;61(3):165-70.
153. Turner VS, Mitchell SG, Kang SK, Hawker RJ. A comparative study of platelets stored in polyvinyl chloride containers plasticised with butyryl trihexyl citrate or triethylhexyl trimellitate. Vox Sang. 1995;69(3):195-200.
154. Pietersz RN. Storage of whole blood for up to 24 hours at ambient temperature before component preparation: implementation in the Netherlands. Transfusion. 2011;51(Suppl 1):3S-6S.
155. Holme S, Sweeney JD, Sawyer S, Elfath MD. The expression of p-selectin during collection, processing, and storage of platelet concentrates: relationship to loss of in vivo viability. Transfusion. 1997;37(1):12-7.
156. Krailadsiri P, Seghatchian J. Are all leucodepleted platelet concentrates equivalent? Comparison of Cobe LRS Turbo, Haemonetics MCS+ LD, and filtered pooled buffy-coat-derived Platelets. Vox Sang. 2000;78(3):171-5.
157. Pietersz RN, Engelfriet CP, Reesink HW, et al. Evaluation of stored platelets. Vox Sang. 2004;86(3):203-23.
158. Murphy S, Rebulla P, Bertolini F, Holme S, Moroff G, Snyder E, et al. In vitro assessment of the quality of stored platelet concentrates. Transfus Med Rev. 1994;8(1):29-36.
159. Hoffmeister KM, Felbinger TW, Falet H, Denis CV, Bergmeier W, Mayadas TN, et al. The clearance mechanism of chilled blood platelets. Cell. 2003;112(1):87–97.
160. Michelson AD, Barnard MR, Hechtman HB, MacGregor H, Connolly RJ, Loscalzo J, et al. In vivo tracking of platelets: circulating degranulated platelets rapidly lose surface P-selectin but continue to circulate and function. Proc Natl Acad Sci. 1996;93(21):11877-82.
161. Rinder HM, Murphy M, Mitchell JG, Stocks J, Ault KA, Hillman RS. Progressive platelet activation with storage: evidence for shortened survival of activated platelets after transfusion. Transfusion. 1991;31(5):409-14.
162. Slichter SJ, Bolgiano D, Jones MK, Christoffel T, Corson J, Rose L, et al. Viability and function of 8-day-stored apheresis platelets.Transfusion. 2006;46(1):1763-9.

163. Arnold DM, Heddle NM, Kulczycky M, Carruthers J, Sigouin C, Blajchman MA. In vivo recovery and survival of apheresis and whole blood-derived platelets: a paired comparison in healthy volunteers. Transfusion. 2006;46(2):257-64.
164. Holme S. Storage and quality assessment of platelets. Vox Sang. 1998; 74(Suppl 2):207-16.
165. Muylle L, Peetermans ME. Effect of prestorage leukocyte removal on the cytokine levels in stored platelet concentrates. Vox Sang 1994;66(1):14-7.
166. Pietersz RN, Loos JA, Reesink HW. Survival in vivo of platelets stored for 48 hours in the buffy coat at 4°C compared to platelet rich plasma stored at 22°C. Blut 1987;54(4):201-6.
167. Holme S, Heaton A. In vitro platelet ageing at 22°C is reduced compared to in vivo ageing at 37°C. Br J Haematol. 1995;91(1):212-8.
168. Tablin F, Oliver AE, Walker NJ, Crowe LM, Crowe JH. Membrane phase transition of intact human platelets: correlation with cold-induced activation. J Cell Physiol 1996;168(2):303-13.
169. Murphy S, Sayar SN, Gardner FH. Storage of platelet concentrates at 22°C. Blood. 1970;35(4):549-57.
170. 170. Kostelijk EH, Gouwerok CW, Veldman HA, De Korte D. Comparison between a new PVC platelet storage container (UPX80) and a polyolefin container. Transfus Med. 2000;10(2):131-9.
171. 171. De Wildt-Eggen J, Schrijver JG, Bouter-Valk HJ, Fijnheer R, Bins M, Van Prooijen HC. Improvement of platelet storage conditions by using new polyolefin containers. Transfusion. 1997;37(5):476-81.
172. De Wildt-Eggen J, Schrijver JG, Bins M. WBC content of platelet concentrates prepared by the buffy coat method using different processing procedures and storage solutions. Transfusion. 2001;41(11):1378-83.
173. Holme S, Haeton WA, Whitley P. Platelet storage lesions in second-generation containers: correlation with in vivo behavior with storage up to 14 days. Vox Sang. 1990;59(1):12-8.
174. Dijkstra-Tiekstra MJ, Pietersz RN, Hendriks EC, Reesink HW, Huijgens PC. In vivo platelet increments after transfusions of WBC-reduced PLT concentrates stored for up to 7 days. Transfusion. 2004;44(3):330-6.
175. Slichter SJ, Harker LA. Preparation and storage of platelet concentrates. II. Storage variables influencing platelet viability and function. Br J Haematol. 1976;34(3):403-19.