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## Strategy of Blood Component Production for Transfusion: The Best Method for Developing Countries

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### Summary

*The current standard blood processing practice is to split blood into its various components usually done by a process such as aphaeresis or whole blood donation involving centrifugation and filtration. This paper review the elements that should be considered when choosing a method and which components to produce based on the risks and benefits to the blood system operation, the donor and the recipient. Specific haemotherapy is safer than the use of whole blood. Overall, considering efficacy and economy, merits and demerits, bottom and top (buffy coat) whole blood processing method is the ideal method for developing countries such as Nigeria.*

**Keywords:** Strategy, Blood Component, Transfusion, Developing Countries

### Introduction

Blood component production is the art of splitting blood into its various components for optimal usage

in transfusion therapy. It is the most effective way of making optimal use of donated whole blood to patients. Blood splitting makes it possible for a patient to be transfused with only the specific component which they require, referred to as specific haemotherapy (Overfield *et al*, 2008). It results in the wider availability of good products with an advantage of the patient being exposed to few transfusion transmissible risks. In addition, component production has made it feasible to channel a single donation for multiple purpose, with red blood cells (RBCs) and platelets going for immediate use in patients, and plasma to be fractionated for the isolation of specific coagulation factors, immunoglobulins or albumin. This benefit is matched by an increased number of donor exposures for patients receiving component therapy when multiple types of components are required in the clinical treatment. An overarching driver for blood systems is the production of high quality blood



products that presents minimal risk to recipients, and that are collected without causing undue risk to the donor.

Other advantages of component productions include, providing the patient's requirement at maximal concentration using small volume, storage of component at ideal condition, utilizing component of a single donation to treat multiple patients with different needs. It enables the transfusion of only specific patient's requirement, thereby maximising the use of limited resource, therefore it is economical. Component separation reduces red cell viscosity thereby ease in transfusion. Filtration removes leucocytes which reduce the chances of transfusing prion, the causative agent of vCJD. Leucocytes are reservoir of prion (Coste, 2013; Mohabir Lionel, 2013). Leucodepletion reduces HLA alloimmunization by removing leucocytes intact. Leucocytes transmit viruses, bacteria and other pathogens. Thus, leucodepletion reduces the risk of transmitting transfusion transmissible disease such as cytomegalovirus (Sharma and Marwaha, 2010). In seeking to establish and optimize a system for component production, there are many factors that come into play in the decision making. The focus of this paper is to review the factors that should be considered in making such decisions.

### **Blood Component Preparation**

The choice of possible methods for blood components production varies with respect to risks and benefits to the blood system operation, the donor and the recipient (Devine and Serrano, 2012). Therefore, an understanding of these risks is

required when choosing what component preparation method to pursue.

The two major methods for component production are:

1. Aphaeresis
2. The production of components from whole blood donations.

Virtually most methods split blood into its various components by mechanisms involving centrifugation and filtration.

#### **1. Aphaeresis**

Aphaeresis is a technique in which whole blood is withdrawn from a donor or patient and separated extracorporeally, that is separating the portion desired to be removed from the whole blood and transfusing back the remaining component of the blood or infusing a substitute. This allows the desired portion such as plasma to be removed and the remainder returned to the aphaeresis donor or infusing a substitute as the case of a patient.

The Aphaeresis machine uses filtration, centrifugation or both.

- Filtration: Use membrane filter etc. Blood flow at the rate of 150ml/min.
- Centrifugation: Blood flow rate 10 to 100ml/min.
- Combined centrifugation and filtration: This used both membrane and centrifugation to achieved the separation of components

**Operating steps:** Aphaeresis machines are wheeled to the bedside of a donor or patient. Sterile large-bore intravenous catheters/tubing sets, also called

phaeresis are connected. As the donor/patient's blood is pumped into the machine, an anticoagulant is automatically added and the mixture enters the chamber. In the chamber, blood components are separated using centrifugation or filtration or both; the method of separation depends on the product that is to be removed or collected from the blood. For centrifugation, the blood enters the centrifuge bowl. The denser elements, namely the erythrocyte, settle to the bottom with less dense elements such as leucocytes and platelets overlying the erythrocyte layer and finally, plasma at the very top. For filtration, the blood passes through a membrane filter bed that separate the component based on the pore size of the membrane filter (Ward, 2011; Rock *et al.*, 2003 and Jonsson, 1992). Processing can be continuous or discontinuous.

**Continuous aphaeresis:** blood is processed and separated in a continuous way. It enables simultaneous blood removal and return (requires two access sites). Once the tubing set is primed, the separation chamber is not emptied till the end of the process. The two catheters lines, one will be connected to the left arm and the other to the right arm serving as giving in and giving out line respectively.

**Discontinuous aphaeresis:** it is an intermittent manner with draw and return via the same line. Processing is in batches of a size that can be tolerated by the subject. Once the separation of that blood is completed, the separation chamber must be emptied to repeat the cycle again (Mabuchi *et al.*, 1987).

### Donor and therapeutic types of aphaeresis

- a. **Donor collection aphaeresis:** This is the collection of a blood component from an allogeneic donor and returning the other component back to the donor. Platelet, red cell or plasma can be removed and the remainder components transfused back to the donor.
- b. **Therapeutic exchange and therapeutic removal aphaeresis:** Therapeutic aphaeresis assures the immediate removal or exchange of abnormal substances from the circulation, which are either present in plasma or tightly bound to plasma proteins. Removing undesirable or excess substances such as antibodies, white blood cells, platelets, red cell in a diseased individual are the main goals.
  - (i) **Therapeutic exchange aphaeresis** involves removal of undesirable elements such as sickled erythrocyte and transfusing back a normal red cell, removal of bilirubin, low density lipoprotein cholesterol from plasma and replaces it with normal plasma or crystalloids.
  - (ii) **Therapeutic removal aphaeresis** involves removal of an undesirable or excess element such as erythrocytes in polycythaemia, paraprotein in multiple myeloma, leucocytes in leukaemia, LDL cholesterol in atherosclerosis. This is usually done without any replacement (Kobayashi *et al.*, 2006).

### 2. Whole Blood Donations

In whole blood donation method, blood is usually kept overnight at 22°C which allows platelet

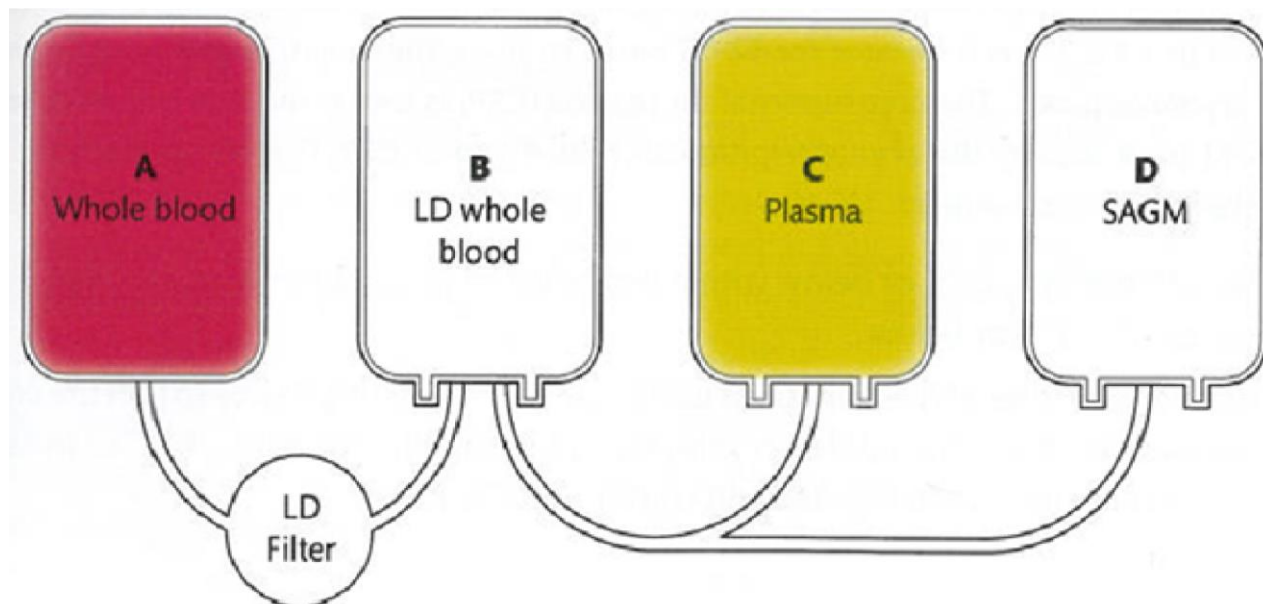


recovery and as well allows white blood cells to undergo phagocytosis to engulf some pathogens such as viruses and bacteria in the blood bag thereby reduces some number of pathogens if present (El-Danasoury *et al.*, 2014; Wang *et al.*, 2013 and Slichter *et al.*, 2012). Two type of method can be used.

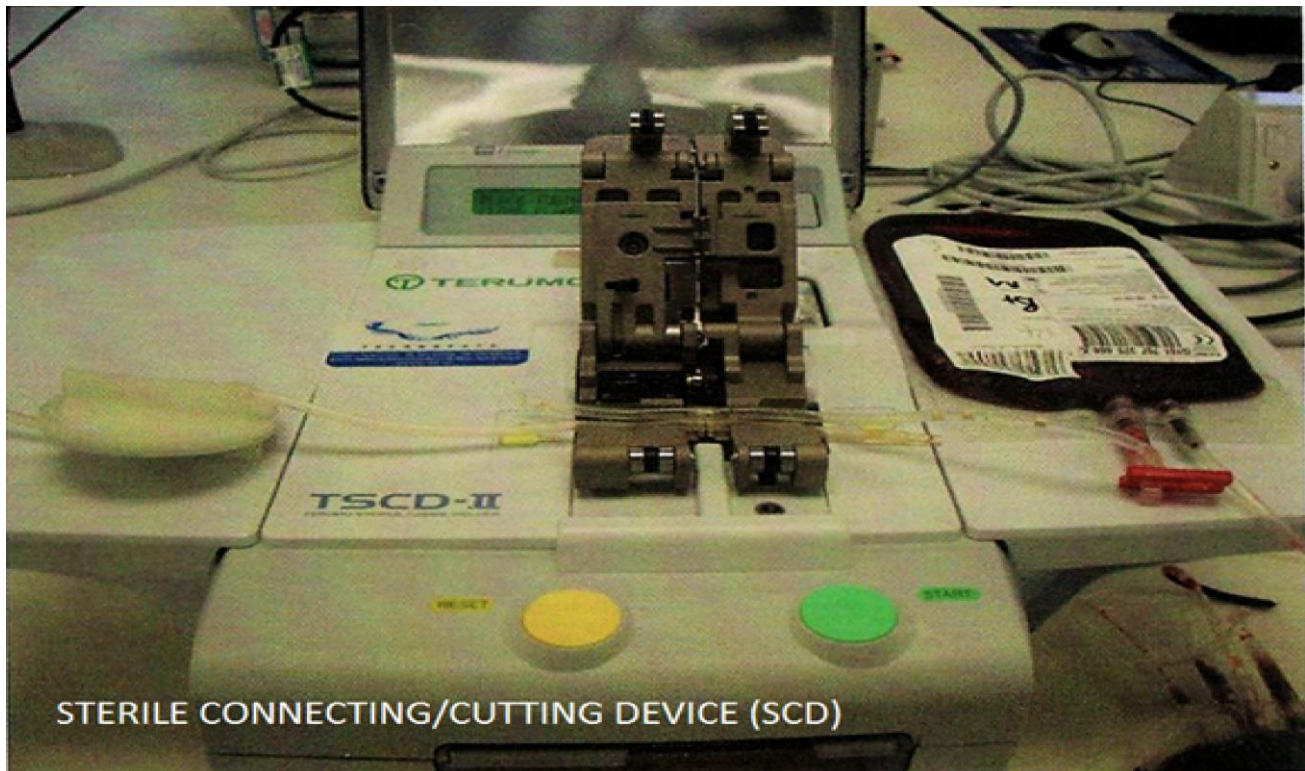
- a. Top and Top (TOP) or platelet rich plasma (PRP) method:
- b. Bottom and Top (BAT) or Buffy Coat method:

**a. Top and Top or PRP:** In this method, the blood is first filtered from the first bag (labelled A) of the quadruplet set (Figure 1) via the LD filter into the second bag (labelled B). After filtration, the bag labelled A is cut off with the aid of sterile connecting device (SCD). The leucodepleted whole

blood in bag B together with bag C and D are centrifuged to separate it into two fractions - a red cell concentrate and a mix of platelets and plasma. With the aid of Optipress (Figure 4), the plasma platelet mixture is pressed out of bag B into bag C. Bag C will then undergo a second low centrifugation, which separates the plasma from the concentrated platelets. The content of bag D (Saline Adenine Mannitol) is then transferred into the concentrated whole blood in bag B. In the procedure, an instrument called sterile connecting/cutting device (SCD), sterile connecting or cutting device is used wherever cutting or connecting tubes is necessary. This device cuts or connects bleeding line and tubes in an enclosed sterile manner (Wang *et al.*, 2013 and Knight, 2012). An image of the device is shown in Figure 2.



**Figure 1** Configuration of the satellite packs for leucodepletion of whole blood by Top and Top or Platelet rich Plasma (PRP) method  
Adapted from Knight, R. (2012).

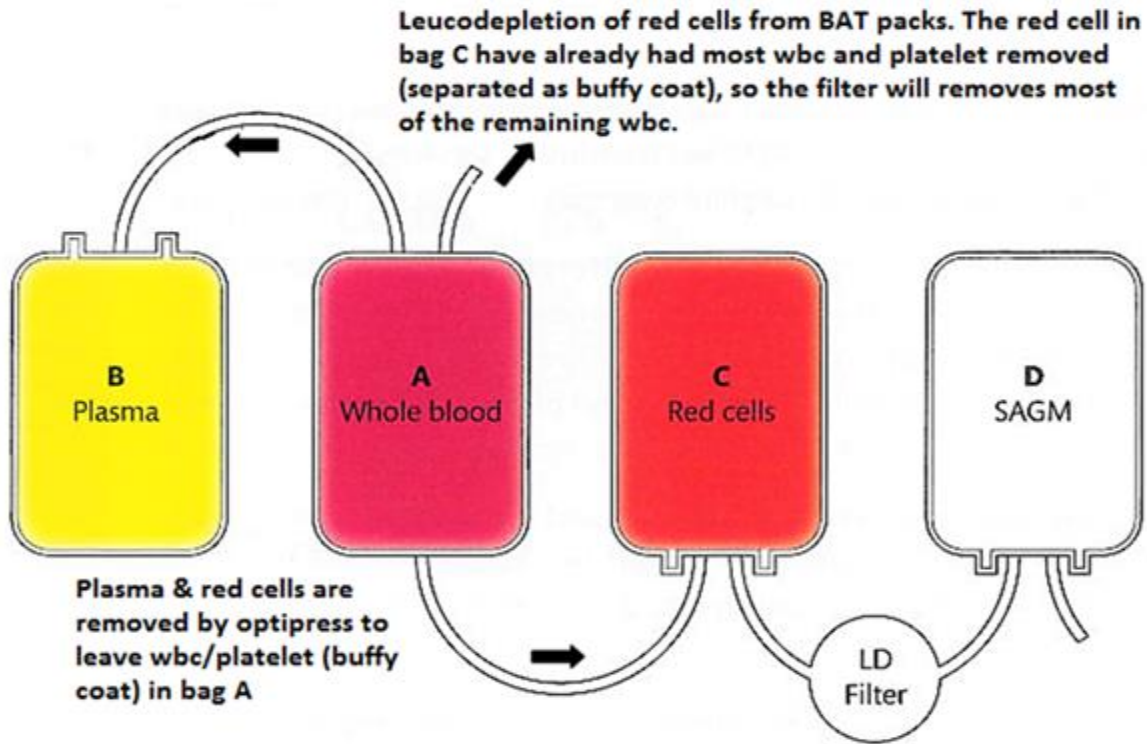


**Figure 2**

Adapted from Knight, R. (2012).

b. **BAT or Buffy coat:** Whole blood is separated into three elements: red cell concentrate, plasma, and buffy coat. For platelet production, the buffy coats of 4-8 units are pooled, centrifuged and platelet rich plasma are removed. Hard centrifugation of the whole blood would produce three layers, red cell at the bottom, buffy coat at the middle and plasma at the top. The bleeding pack is the second bag (labelled A) among the quadruplet set as shown in figure 3. With the aid of Optipress (Figure 4) the red cell at the bottom of bag A is press down to bag C while the plasma is press-up to the bag labelled B leaving the buffy coat in the bleed bag (bag A). Optipress has a sensor which controls the movement of the plasma and red cells out of the bleed pack (Knight, 2012). At the end of the transfer procedure, the two bags; bag C (red cell) together

with bag D (SAGM) and bag B (plasma) B would be cut off from the bleed pack (A) with the aid of Sterile Connecting and Cutting Device (SCD) (Fig 2). The plasma pack B is then labelled and quarantine. The SAGM in bag D would be transferred to bag C via the filter to wet, prime the filter and reconstitute the red cell present in C. Thereafter the reconstituted SAGM red cell in C is transferred back to bag D through the filter for leucodepletion. SAGM leucodepleted red cell in bag D is detached using SCD and the labelled. The buffy coat present in bleed pack A is joining with four other buffy coat of same ABO Rh group with same screening status using SCD. The five joined buffy coat is then used to prepare pooled platelet or granulocyte concentrate (Knight, 2012).



**Figure 3** Configuration of satellite packs red cell, plasma and buffy coat production by Bottom and Top (BAT) or Buffy Coat method

Adapted from Knight, R. (2012).



Knight, R. (2012).  
**Figure 4**

The evolution of aphaeresis technology has resulted in great benefit to patients by improving the access to specialty products such as HLA-matched platelets and multiple transfusion doses from a single collection procedure (Ness *et al.*, 2001). These factors contributed to the widespread use of aphaeresis collection technology in the UK, US and some European countries (Andreu *et al.*, 2004). On the other hand, the two whole blood component preparation techniques have different risk profiles, with overall benefits being more favourable to BAT or buffy coat production methods particularly with respect to improved process control. The widespread use of aphaeresis technology is limited by the cost of equipment and disposables, operational skills. Also, most devices are not portable so use is restricted to permanent facilities.

Furthermore, the procedure itself presents a greater risk to donor than whole blood donation due to the increased infusion of citrate into the donor and albeit rare but known fatality arising from misuse of the equipment (Winters *et al.*, 2006; Follea *et al.*, 2011). Some have reported an increased adverse event risk in donors undergoing aphaeresis procedures (Crocco *et al.*, 2009; Andreu *et al.*, 2004). The cost of platelet dose by aphaeresis is about 10 times costlier than whole blood produced platelet dose. Leucocytes transmit viruses, bacteria and other pathogens. Thus, leucodepletion reduces the risk of transmitting transfusion transmissible disease such as cytomegalovirus (Sharma and Marwaha, 2010). Some comparison of some effects by the procedure are listed in table 1.

**Table 1: Comparison of the effects of aphaeresis and whole blood procedures on blood products** (Andreu *et al.*, 2007; Picker *et al.*, 2007; Van Der Meer *et al.*, 2010; Thomas *et al.*, 2010; Van Der Meer *et al.*, 2011 and Lu *et al.*, 2011).

Parameters	Aphaeresis	BAT or Buffy coat	TOP or PRP
Dose of haemoglobin in a unit	Consistent	None	None
Met-haemoglobin level	Higher	Low	Low
Chances of air embolism	Higher	Low	Low
ATP level	Lower	Higher	Higher
RBC haemolysis level after production	Increased	Low	Low
RBC haemolysis level after storage	Increased	Low	Low
Facilitation for platelet recovery	None	Overnight hold of the whole blood facilitate platelet recovery	Overnight hold of the whole blood facilitate platelet recovery
Leukocyte-mediated bacterial killing	No overnight hold to provide leukocyte-mediated bacterial killing	Overnight hold provide leukocyte-mediated bacterial killing	Overnight hold provide leukocyte-mediated bacterial killing
Incidence of allergic reactions to platelets	Higher	Low	Low
Chances of vascular erosion and perforation	Higher	Low	Low



## Conclusion and Recommendation

Overall, blood production system that utilises whole blood donations is favoured as this helps the range of collection sites, the ease of mobile operations and is generally the most cost effective. Aphaeresis procedures should be included in platelet production options to meet the demand for specific products (HLA-matched, platelet antigen-matched) and to supplement inventory. Whole blood component preparation via the bottom and top (buffy coat) method has increased platelet yield and reduced bacterial contamination rates compared to the top and top (PRP) method hence, outweigh any transient difference in red cell parameters. Buffy coat production of platelets also positions the blood centre to use platelet additive solutions to reduce recipient reactions or pathogen reduction technology, neither of which can readily be applied to PRP platelets. Furthermore, because the buffy coat platelet is pooled during production, it has lower overall leucoreduction costs than PRP platelets and can be used by the hospital without further modification. Lastly, the comparative review suggested the advocacy for Buffy Coat (Bottom and Top) component production method for the developing countries such as Nigeria.

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