

Blood banking and blood component storage routines: Opportunities for improvement

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DOI: <https://doi.org/10.5281/zenodo.7791053>

Published Date: 01-April-2023

Abstract: Blood banks strive to maximize the supply of blood from the right donor to the right patient in a timely manner.

They attempt to ensure effectiveness by requiring proof that a reasonable proportion of red blood cells, platelets, and plasma proteins survive storage before allowing new blood storage systems or blood-regulating products such as leukopenia filters^{4,5}. However, a reasonable ratio for erythrocytes is 75%, for platelets 67% and for plasma proteins 80%. Standards, such as insisting that every unit of blood be tested for HIV, only work if the tests are allowed to detect circulating virus, a moving target.

Keywords: blood banking, blood component, storage, transfusion.

1. INTRODUCTION

Blood banks are medical logistics operations. It strives to deliver the life-saving benefits of blood transfusion to patients in need by making blood components readily available, safe, effective and inexpensive¹. Blood banks strive to maximize the supply of blood from the right donor to the right patient in a timely manner. The easiest way to ensure timely blood availability is to always have a sufficient stock of blood on the shelves. Blood bank standards have evolved to address issues observed in the past². The donor must be free of syphilis, hepatitis, and human immunodeficiency virus (HIV) as well as a range of other illnesses. The donor arm cleaning method should work. Blood bags must contain appropriate solutions and be sterile. The system for identifying donors and patients, identifying antigens on their blood cells and antibodies in their serum, and the processes and procedures used to collect and store this information must be robust.

Regulatory bodies, such as the United States (U.S.) The Food and Drug Administration (FDA), which is responsible for ensuring that blood products are safe and effective³. They strive to ensure safety by applying the above-mentioned standards. They attempt to ensure effectiveness by requiring proof that a reasonable proportion of red blood cells, platelets, and plasma proteins survive storage before allowing new blood storage systems or blood-regulating products such as leukopenia filters^{4,5}.

However, a reasonable ratio for erythrocytes is 75%, for platelets 67% and for plasma proteins 80%. Standards, such as insisting that every unit of blood be tested for HIV, only work if the tests are allowed to detect circulating virus, a moving target. A better understanding of basic biology and better tests is needed to underpin better standards. If we better understand the changes that occur with the storage of red blood cells, platelets, and plasma, we can design better storage systems and regulate storage more efficiently. If we know more about viruses and bacteria as well as the cytokines and blood breakdown products that threaten the safety of blood, then we can establish control measures to further improve them. and the safety of blood. This paper will explore some specific examples.

2. RED CELL COLLECTION AND STORAGE

Units were collected as whole blood in bags containing citrate anticoagulant and nutritional phosphate and dextrose (CPD) or by decantation in acid citrate dextrose (ACD). white blood cells and platelets, and the plasma on top. This is called the padding method and the pockets that support it are called the top and bottom pockets. Other methods include less vigorous centrifugation of the blood to retain more of the platelets that are still suspended in the plasma. This is known as the production method of the platelet-rich plasma component. Normally, the red blood cells concentrate is then passed through a leukopenia filter, which removes most of the white blood cells and platelets, and an additive solution containing more nutrients. For filtrate units, the collection method removes most of the white blood cells and platelets, and the additive solution is added directly to the collected packed red blood cells. These methods of separating blood components are essentially equivalent, although each has its advocates. The platelet-rich plasma method loses and eventually damages platelets, the buffer coat method loses red blood cells, and the apheresis method is expensive. The use of ACD and CPD is legacy since they are the best available 3-week whole blood storage solution⁸. However, mixing whole blood with these acidic anticoagulants immediately causes the pH of the resulting suspension to drop to about 7.1, causing rapid decomposition of 2,3-diphosphoglycerate (2, 3-DPG) of red blood cells. Over subsequent weeks of storage, red cells consume dextrose through glycolysis and the hexose monophosphate shunt to produce adenosine 5'-triphosphate (ATP) and reducing substances. Conventional red cell additive storage solutions support stored red cells for about 6-weeks of storage but fail rapidly thereafter. Between a pH of 7 where red cell storage typically starts and 6.5 where it ends, a unit of red cells can buffer about 7 mEq of protons.

3. RED CELL RECOVERY

In the U.S. and Europe, the licensure of red blood cell storage systems has been based on measures of the viability and physical integrity of the stored cells⁴. The viability of red cells is typically measured as the fraction of cells at the end of storage that are able to circulate. In making this measurement, about 15 mL of stored red cells are labeled with chromium 51- and reinfused into the original donor¹¹. A major remaining problem associated with red cell storage is that viability is very different from one donor to another. In a typical study, the individual donors red cells may have viabilities at the end of storage that range from less than 60 to more than 95%. Being able to identify those donors whose cells store well is potentially useful for recipients such as children with thalassemia or sickle cell anaemia who can become iron overloaded from repeat transfusions. Measures that would allow a blood banker to choose the best red cells for this situation could improve care and markedly reduce health system cost. For general surgical patients whose transfusions are replacement for blood lost, the extra iron helps them rebuild their own blood, but the load of effete red cells that must be cleared in the first 24 hours after the transfusion of poorly stored blood may cause additional problems¹³. Increased incidences of both post-operative pneumonia and metastatic cancer after transfusion are well-recognized phenomena and may in part be related to the number of non-viable red cells presented to limited clearance mechanisms¹⁴. Except for a few specific severe enzymatic defects that limit blood donation anyway, it is not known whose red cells are most susceptible to damage or if the addition of antioxidants such as vitamin E or n- acetyl cysteine can safely improve storage.

4. RED CELL HAEMOLYSIS

The second standard measure in the licensure of red cell storage systems is the percent haemolysis. These numbers are arbitrary, and typical modern red cell storage systems average less than half those values. Some are made as immature red cells, reticulocytes and mature in the circulation and shed membrane to reduce their size and assume the mature biconcave disc form. Others are made by mature red cells as they shed oxidized lipids, and are characterized by high concentrations of these oxidized lipids and the membrane proteins stomatin and flotillin¹⁹. There are three major determinants of the amount of haemolysis in any given unit of red cells. Haemolysis increases with the duration of storage, it is reduced by leukoreduction, and individual variation accounts for most of the remainder²⁰. A typical unit of red cells contains about 69 gm of haemoglobin, one millimole of the 69 kD haemoglobin tetramer. Haemolysis is typically 0.4% at the end of storage, of which only half is free, outside of vesicles. Outside the red cell or the vesicles the tetramer dissociates into dimers, which in turn bind to haptoglobin dimers with 1:1 stoichiometry. Haptoglobin, normally circulates at 10-52 μ M concentration in plasma, so it typically takes at least 15 units of red cells to overwhelm this system.

5. PLATELET COLLECTION AND STORAGE

In Europe, the EU standard has been greater than 200 billion platelets representing the pooling of 3-5 whole blood-derived collections. Prophylactic platelet use ranges from maintaining low blood concentrations in leukemia and stem cell transplant patients to prevent bleeding to attempts to reach higher concentrations to limit bleeding in patients undergoing invasive

bedside procedures or surgery²³. They can be centrifuged from platelet-rich plasma, isolated from buffy coats, or collected directly from the bloodstream by apheresis. There is some evidence that the buffy coat and apheresis methods provide better platelets, with the suggestion that centrifuging platelets against the plastic bag surfaces in the platelet-rich plasma method leads to partial or complete activation of some of the platelets²⁴. Platelets are stored in large flat bags with as high surface to volume ratio and on agitators to facilitate oxygen diffusion. Platelets are stored at room temperature, 20-24 °C, because below 18 °C, their lipid bilayer membrane undergoes a phase change which allows the aggregation of surface glycoproteins²⁶. Platelets are generally stored in the plasma in which they are collected. It is possible to keep platelets for as long as 8-13 days, but blood banks in the U.S. are only allowed to keep them for only 5 days because of bacterial contamination. It would be useful to store platelets longer and detect bacterial contamination sooner³¹. At a regulatory level, the adoption of Scott Murphy's definition of successful platelet storage, 67% of fresh autologous platelet recovery with 58% of autologous fresh platelet survival, has allowed the development of new platelet products to go forward³⁴. In the last year for which data are available, there was one death from bacterial contamination of a blood component, a platelet unit, in the whole U.S.³⁵. While the regulations assure that the average platelet unit collected by any particular method or device is of reasonable quality, the recovery and survival of units from different donors is highly variable.

6. PLASMA COLLECTION AND STORAGE

Plasma is used to control or prevent bleeding and rarely for other uses such as the acute treatment of angioedema in patients who are missing complement-1 esterase activity or chronically in children congenitally deficient of the von Willebrand factor cleaving protease. Plasma for clinical use comes from volunteer donors in the course of routine blood collection. The plasma collection industry, which collects millions of liters of plasma from paid donors for the manufacture of albumin, coagulation factor concentrates and intravenous immunoglobulin, is a separate activity. If FFP is allowed to thaw in the refrigerator, a granular precipitate of fibrinogen, von Willebrand's factor, factor VIII and Factor XIII remains which can be removed to form a 10 mL unit of cryoprecipitate. The plasma remaining after cryoprecipitate removal is used to treat patients with thrombotic thrombocytopenic purpura (TTP) or sold to commercial plasma fractionators to make pooled plasma products. Apheresis plasma can be collected in 600 mL amounts in ACD or buffered citrate, but is usually broken down into 300 mL units to give it the size of normal plasma units. Coagulation factor VIII is poorly soluble and can remain cryoprecipitated even after 30-37°C thawing, but is rarely a problem because haemophilia patients are treated with factor concentrates and trauma patients secrete factor VIII from their shocked endothelial cells. Even under conditions where whole blood is held at room temperature for 24-hours before processing and then the plasma is held thawed for 5-days, total losses of factor VIII are only about 15%. The simple expedient of removing the sugar from the anticoagulant and collecting apheresis plasma and, perhaps even whole blood, in neutral citrate may be impossible because no company would bear the regulatory cost necessary for licensure of such a system³⁷.

7. THE FUTURE OF BLOOD COMPONENTS

Red cells, platelets and plasma all have important roles in medical care, high efficacy for their primary indications, and no obvious replacements in the foreseeable future. Blood collection centres and hospital transfusion services will remain largely as they are in the immediate future. More red cells than that are lost in the lines of the apheresis device used to collect the stem cells. Platelets for transfusion are even less likely to come from alternative sources of production, but donor-derived apheresis platelets already make up almost three-quarters of the national supply. Conventional blood products appear to be with us for the foreseeable future.

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