

# The Blood Banking Controversy: How Old is that Red Blood Cell

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## Introduction

The American Association of Blood Bank (AABB) is one of the main or crucial international associations of blood banks and this includes hospitals, community blood centers, transfusion services and transplantation services. AABB is usually the organization that is responsible for accreditation; while, the FDA (Food and Drug Association) is responsible for regulation. The blood bank is a place where blood and blood products undergo extensive testing and every task associated with the work performed is scrutinized to ensure the quality and safety of both the services and products provided [1]. The blood bank is responsible for collecting, storing, processing and distributing human blood and blood products for the purpose of transfusion. The blood donated and collected is whole blood and is separated into RBCs, plasma and platelets; the components are transfused depending on the patient's need.

The first transfusion dates back to the 17th century when scientists were finally able to describe the circulation and properties of blood. An important part of the history of blood banking occurred in 1901, when an Austrian physician by the name of Karl Landsteiner, made reference of the first three human blood groups namely A, B and O. This was based upon the substances found on the blood cells. Possibly, there would be no blood banking today, if this phenomenon was not discovered followed by more recent research. Science has become more advanced which has led to the collection and storage of the human blood followed by blood preservation methods necessary for human blood transfusion. One such preservation was founded in 1914, which was long-term anticoagulants including sodium citrate being developed and tested in Europe hoping to provide longer periods of blood preservation [2]. The first blood bank itself became established during the First World War where army doctors collected and stored type O blood using citrate glucose solution. Many methods of storage and preservation of blood components have since been developed before standardization was achieved.

There are certain equipments needed in the storage and preservation of blood such as: a refrigerator for the storage of packed red blood cells and freezers for the storage of RBCs frozen in 40% glycerol (-65%). Granulocytes are transfused within 24 hours of being donated. The transfusion of red cell concentrates is indicated in order to achieve a fast increase in the supply of oxygen to the tissues, when the concentration of hemoglobin is low and/or the oxygen carrying capacity is reduced, in the presence of inadequate physiological mechanisms of compensation. The most widely used protocol for the storage of red blood cells are the collection of blood into anticoagulant solution typically citrate-dextrose-phosphate. A definitive protocol that reconciles long term storage is based on both safety and the efficacy of the transfusion therapy. Studies suggest that the quality of red blood cells decreases in proportion to the time the storage period is prolonged. The current standard requirements suggested in the

recommendation of the European Council are essentially based on two parameters: the level of hemolysis which is below the threshold of 0.8% at the end of the storage period, following the introduction of the '95/95' rule and the survival rate of the transfused cells of more than 75% at 24 hours after transfusion. Numerous clinical studies have been carried out to identify possible relationship between the duration of storage of red blood cells, the changes observed at a molecular level and side effects in the transfused patients, in order to determine whether and, if so, to what extent red blood cells stored for a long time lose safety and efficacy. It was discovered that storage has the potential to reduce the efficacy of transfused blood components by reducing their flow, functional capacity, and survival. Storage time also allows the accumulation of leaked potassium from red cells and the growth of contaminating bacteria. Regulatory decisions about product storage have been conservative, and largely based on historic patterns of use [3].

Packed red blood cells (RBCs) are prepared from whole blood by removing approximately 250 mL of plasma by centrifugation and then re-suspending the red cells in citrate based anticoagulant preserving solution to prolong storage time. Packed cells are stored in a SAG-M (saline-Adenine-Glucose Mannitol) solution to increase their shelf life to 5 weeks at 2-6°C. Weinstein, in his article stated that "Packed, Red blood cell transfusions are used to treat haemorrhage and to improve oxygen delivery to tissues [4]". Indications for transfusion include symptomatic anaemia (causing shortness of breath, dizziness, congestive heart failure, and decreased exercise tolerance), acute sickle cell crisis, and acute blood loss of more than 30 percent of blood volume. Chronic renal failure (describes the gradual loss of kidney function). Septic shock (Septic shock is a life-threatening condition that happens when your blood pressure drops to a dangerously low level after an infection), failure of erythropoiesis (lack of production of red blood cells), haemorrhage, dilutional anaemia following severe burns and megaloblastic anaemia (a blood disorder in which the number of red blood cells is lower than normal), gastrointestinal haemorrhage, bone marrow transplant. The main goal of blood preservation is to provide viable and functional blood components for patients requiring blood transfusion. According to an article written by Samuel Antwi-Baffour and company "More than 70% of red blood cells should remain viable in circulation 24 hours after transfusion of stored blood in CPDA-1 for 35 days. The blood is stored at 2-6°C to maintain optimal viability [5]".

Blood intended for transfusion must be thoroughly screened. Specific tests have to be conducted before it can be transfused safely to whoever needs it; some of these tests are as follows: ABO and Rh, antibody screening, serologic test for syphilis, West Nile Virus (WNV) RNA, HIV (HIV-1 RNA), Hepatitis B SURFACE antigen (HBsAg), Antibodies to hepatitis C virus (anti-HCV), Antibodies to hepatitis B core antigen (HBc). If the blood meets the proper criteria then proper labelling is done to each component; labelling includes the appropriate

ABO, Rh and expiration date. Blood and its components undergo typing, screening, cross-matching, postpartum and prenatal evaluation and cord blood studies. This is necessary in order to avoid infecting a recipient with a disease and/or causing a transfusion reaction. Transfusion reactions can be immediate or delayed but implications of such reactions can result in organ failure, death and lawsuits for the doctors, medical technologists, and blood donor facilities. According to Fastman, Acute Hemolytic reaction is the most serious and immediate transfusion reaction; this occurs when the recipient receives a blood type that does not match their own [6]. This is caused by human error in labelling or misidentification of a recipient; unfortunately, such an error can prove fatal and if not deadly will cause serious kidney damage that will require a patient to be on dialysis. Anemia may also be developed. The World Health Organization gives a detailed step in the acceptance of donors, the deferral of donors, the responsibility to inform and record information, the donor phlebotomy procedure, transportation and storage; the clinical requirements for transfusion, the requirement of a written informed consent, equipment specifications and the required forms and worksheets. "The most reported complications are because of transfusion of mismatched blood products and are avoidable through clinical vigilance" [7].

There is no way to refute the benefits blood banking has contributed to the world of medicine. However it is still surrounded by great controversial issues. Among these issues the need for the harmonization in the preparation of the stored red blood cell seems to be at the forefront of the argument. The key point of the problem is the lack of universally accepted standard criteria that closely reflect the dramatic molecular changes that occur during prolonged storage of red blood cells which enables "good" blood to be distinguished from no longer sufficiently "good" blood. In 1993, Marik and Sibbald reported that the transfusion of longer-stored units was associated with a decrease in gastric pH in 23 patients in septic shock, each transfused with 3 units of red blood cells as a goal-directed therapy to increase their oxygen delivery in an attempt to increase their oxygen consumption. This was an incidental finding in a larger study in which many factors were analysed [8]. According to Lacroix J et al. [9] in present time, red blood cells are kept in storage up to 42 days in France and Canada. From the 1940's it was agreed that red blood cells units can be stored as long as the average haemolysis is lower than 1% and the proportion of the red blood cells still alive 24 hours' post-transfusion is higher than 70%. There have been studies that show that older blood cell units may jeopardize the outcome of severely ill patients. Other scientists think that storing blood cells for even this length of time is harmful to the patient. According to Aubron et al. [10], a study conducted in healthy volunteers reported the presence of higher extravascular haemolysis after older RBC transfusion (storage of 40-42 days) compared with fresh blood (storage of 3-7 days) illustrating the possible harmful effect of iron delivery. Given these results, wouldn't it be safer to store blood for less than 40 days or for as little time as possible? Blood is considered a source of life and it is yet to be successfully manufactured outside a living body, making donated

blood a precious commodity. This indicates that it would not be wise to discard blood that still has the potential to help a patient in need of it even if it is not freshly drawn. This is the stance on the argument taken by the opposing side that agrees with blood being stored as long as possible. Experts have also argued that it would be difficult to gauge the level of aggregates of any adverse effects caused by an inadequate blood supply as a result of "old" blood transfusion [10]. Controversy will continue to surround this issue until the demand on transfusion becomes significantly less, which according to experts, is not likely.

In conclusion, there is a great wealth of knowledge obtained over decades of research on the safety and efficacy and storage of "old" blood for transfusion. Experts have argued that it would be difficult to gauge the level of aggregates of any adverse effects caused by an inadequate blood supply as a result of "old" blood [10]. This argument is ongoing and an agreement or consensus is yet to be reached. However, some critical questions need to be answered such as; at what point changes affect RBCs during storage process are irreversible? How do the recipient's cells and tissues respond to "old" RBCs after transfusion? Is there a better way of storing "old" blood for transfusion to reduce storage lesion? Controversy will continue to surround this issue until the demand on transfusion becomes significantly less, which according to experts, is not likely. Experiments and studies are still being carried out today to develop and implement preservative solutions that improve buffering capacity and maintain an increase pH which causes delay of critical changes among RBCs to achieve optimal safety and efficacy of blood storage capacity [11].

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