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Dates: Received: 04 March, 2015; Accepted: 16
March, 2015; Published: 18 March, 2015

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www.peertechz.com

ISSN: 2455-5282

Commentary

Re-Assessing Red Blood Cell Storage

integrity and function. Adenosine triphosphate (ATP) is such an energy molecule that the cell depends upon to maintain its integrity and function.

Standard clinical practice guidelines dictate that stored RBCs are discarded at 42 days. During this storage interval, alterations in pH and a level of hypoxia occurs, as well as the accumulation of toxic substances which can interact with the RBCs, including its membrane. A state of reactive oxygen radicals and the formation of advanced glycation end products can ensue, both of which can produce detrimental effects to these stored cells. Furthermore, once transfused, the damage to the RBC's membrane may also have a negative effect on the recipient's endothelium.

Although RBCs may appear to survive in storage for five or six weeks, they actually develop "storage lesions", characterized by both biochemical and biomechanical changes that compromise their ability to accept, transport and unload oxygen to the tissue [1]. Changes during storage can involve a lower environmental pH, the accumulation and attacking of free radicals, and the exhaustion of energy substrates, all of which play a significant role in producing these lesions and the cells subsequent function at the time of transfusion. Alterations in metabolic compounds such as ATP and 2,3-DPG occur during storage, as well as changes in the cytoskeletal framework of these cells have been documented [2-5]. Morphologically, studies have shown that "old" stored RBCs demonstrate gaps in their membranes when compared to a more "young" stored RBC [6]. As stated previously, at the time of transfusion, these damaged cells could have negative consequences on the recipient's endothelium, as reported by Mangalmurti et al. and others [7,8].

Clinically, reports are surfacing that within the accepted 42 days of RBC storage, a difference in mortality and morbidity of the recipients once transfused has been observed. A study at the Cleveland Clinic cast doubts about the survivability of RBCs even after a short storage interval of 14 days [9]. Additional published reports have also observed complications, post-transfusion of "old" RBCs, in critically ill patients, the pediatric population, and in individuals requiring large amounts of transfused blood, such as occurs in trauma with extensive blood loss [10-12].

What methods could be employed to detect metabolic and structurally unfit RBCs prior to transfusion? Studies have also reported that due to these altered changes in the cell, the assessment of biomarkers may be beneficial. The measurement of these biomarkers could have the potential to provide a measure as to the state of these cells prior to transfusion; and therefore, potentially eliminate to reduce the likelihood of post-transfusion complications. These markers could involve autoantibodies, markers showing an alteration in the cell structure, as well as cellular *in vitro* byproducts [13-15]. Secondly, the creation of a novel storage solution that

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Numerous reports have surfaced over the past decade centering on the potential for complications when transfusing "new" versus "old" stored red blood cells (RBCs). The transfusion of whole blood and packed RBCs has been a standard medical treatment since Landsteiner in 1900 developed red cell ABO typing, leading to compatible transfusions from donor to recipient. Nearly fifteen million units of whole blood are donated in the United States each year by approximately eight million volunteer blood donors. These donor units are transfused to about four million recipients. Unfortunately, despite the great need and the generous contributions of volunteers, blood is always in short supply; and therefore, the need for donated blood continues. On any given day, approximately 35,000 units of blood are needed to treat surgical patients, accident victims, and patients who are anemic from leukemia, cancer, or other diseases.

Manufactured in the bone marrow, RBCs are enucleated, biconcave discs that are continuously being produced. Once circulating, these RBCs serve a great purpose of delivering oxygen to tissues; however, overtime these RBCs brake down, lose their efficiency and ultimately are eliminated. The biconcave disc shape is crucial to the function of RBCs, presenting a maximal surface area for the capture of oxygen in the lungs and its subsequent release to the tissue beds. The cells are flexible and able to change their shape in order to traverse the tiny tubules of the capillary beds. Since the cells are enucleated and lack mitochondria, they are unable to carry out cellular repair of damage or enzyme inactivation and therefore must rely on anaerobic glycolysis for energy.

Structurally, RBCs depend on an intact membrane and an internal cytoskeleton to function normally. This cytoskeleton, the structural support that maintains the RBC's biconcave shape, is made of protein microfilament, intermediate filaments, and microtubules.

Functioning RBCs have very high levels of 2,3 diphosphoglycerate (2,3 DPG), in which 2,3, DPG binds the beta chain of deoxyhemoglobin in a pH dependent environment. Adequate levels of 2,3 DPG are necessary to lower the oxygen affinity for hemoglobin, thereby increasing oxygen tissue delivery. Therefore, RBC function centers on the ability of an RBC to bind oxygen and to have the ability, if the RBC has a normal biochemical environment and sound structure or morphology, it functions normally by releasing the carried oxygen to the tissues. Furthermore, as part of this process, each RBC must have an energy supply to survive and maintain its

could provide the adequate metabolic substrates and a more ideal storage environment to eliminate structural damage due to oxygen free radicals and advanced glycation end products. The capability of transfusing RBCs has provided the means to aid, including survival, in critically ill individuals. With these recent studies questioning the functionality of “old” stored RBCs, further evaluation should be sought and if correct, novel methods must be developed to secure the safety during and following RBC transfusions.

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Citation: Shechterle LM, Terry KR, St. Cyr JA (2015) Re-Assessing Red Blood Cell Storage. *Global J Med Clin Case Reports* 2(1): 001-002. DOI: 10.17352/2455-5282.000015