**Storage Lesions in Whole Blood: Effects and Implications after 72 Hours of Preservation**

# Abstract

Blood transfusion is a medical procedure in which donated blood or blood components (such as red blood cells, plasma, platelets, or clotting factors) are transferred into a person's bloodstream to treat a variety of health conditions. The primary goal of a blood transfusion is to replace lost blood or improve the blood's ability to function, particularly in patients who have suffered significant blood loss, have certain medical conditions, or need additional support for their blood components. Blood transfusion is a critical and life-saving procedure that involves transferring blood or its components to a patient. It is commonly used to treat blood loss, anemia, clotting disorders, and conditions that affect blood cell production. While generally safe, transfusions come with some risks, which are carefully managed through blood testing, monitoring, and modern medical practices to ensure patient safety. Transfusing whole blood stored for more than 72 hours in a refrigerator can be problematic due to deterioration of red blood cells, coagulation factors, and platelets, leading to reduced oxygen-carrying capacity, impaired clotting, and other complications. The blood may also be at an increased risk of bacterial contamination and metabolic changes. Therefore, it is generally avoided in favor of fresh or appropriately stored components such as red blood cells, plasma, or platelets, which are stored according to recommended guidelines

***Keywords****: Whole blood storage, Storage lesions, Red blood cell viability, Biochemical changes, Extended storage effects*

# Introduction

Blood transfusion is a medical procedure in which donated blood or blood components (such as red blood cells, plasma, platelets, or clotting factors) are transferred into a person's bloodstream to treat a variety of health conditions(1). The primary goal of a blood transfusion is to replace lost blood or improve the blood's ability to function, particularly in patients who have suffered significant blood loss, have certain medical conditions, or need additional support for their blood components(2).Red blood cells (RBC) contain hemoglobin and supply the cells of the body with oxygen. White blood cells are not commonly used during transfusions, but they are part of the immune system and also fight infections(2). Plasma is the "yellowish" liquid part of blood, which acts as a buffer and contains proteins and other important substances needed for the body's overall health(3). Platelets are involved in blood clotting, preventing the body from bleeding. Before these components were known, doctors believed that blood was homogeneous. Because of this scientific misunderstanding, many patients died because of incompatible blood transferred to them. Different types of blood transfusion in hospital due to different needs of the patients, blood like other medicine also need special care and attention during transfusion, is recommended that patient can transfused blood according to the needs to avoid transfusion reaction(4). The following are the types of blood transfusion, Whole Blood Transfusion: Involves the transfusion of all components of blood, including red blood cells, plasma, white blood cells, and platelets. However, whole blood transfusions are less commonly used today compared to more specific components. Red Blood Cell (RBC) Transfusion: This is the most common type of blood transfusion. It is used to treat anemia or blood loss due to trauma or surgery. The transfusion provides the body with oxygen-carrying red blood cells to improve oxygen delivery to tissues and organs.Plasma Transfusion: Plasma is the liquid portion of blood, containing water, electrolytes, proteins, and other components. Plasma transfusions are used for patients who have a deficiency of clotting factors or have been severely burned or injured, as well as for patients with liver disease or certain bleeding disorders. Platelet Transfusion:Platelets are responsible for blood clotting. A platelet transfusion is used to treat conditions such as thrombocytopenia (low platelet count), which can occur in diseases like leukemia or as a result of chemotherapy or certain medications. Clotting Factor Transfusion: For patients with clotting disorders like hemophilia, transfusions of clotting factors (such as factor VIII or factor IX) are given to help prevent or treat bleeding episodes(5).

Blood transfusion is critical procedure which require more attention, also not any patients who have anaemia required for whole blood transfusion, laboratory results only is not enough to rule out for blood transfusion. Blood transfusion is rarely indicated when hemoglobin levels are greater than 10g/dl, and is usually indicated when hemoglobin concentrations are less than 5g/dl. However, even severely anemic patients (Hb<5g/dl) who are clinically stable may not require transfusion. The decision to transfuse should be based on an estimate of the patient’s risk for developing complications of inadequate tissue-oxygen delivery. A patient should be re-evaluated by clinical and nursing staff immediately prior to blood transfusion to ensure that the transfusion is still required. Surgeons must adhere to good anesthetic and surgical management, to minimize blood loss during surgery. Using alternative approaches such as desmopressin, aprotinin or erythropoietin where appropriate is encouraged(6).

Some general administration principle of blood: There must be detailed patient identification and verification with the unit delivered for transfusion, detailed inspection of the unit for evidence of macroscopic contamination, delivered blood must be compatible: whole blood and PRBC must be ABO and Rh-D compatible with the recipient(6).Also we need to understand that blood transfusion is not a cure for anemia. Blood transfusion is used to relieve the clinical signs of cardiac or respiratory distress, but the underlying cause of the anemia needs to be investigated and treated(7). The indications for blood transfusion are frequently urgent conditions. Efforts should first be made to stabilize patients without the use of blood through prompt and appropriate supportive care: Blood transfusion is required in different reasons in hospital, such as Blood Loss: Trauma, surgery, or childbirth complications can lead to significant blood loss, requiring a transfusion to restore blood volume and function. Anemia: Conditions like iron deficiency anemia, sickle cell anemia, or chronic kidney disease can lead to a low red blood cell count, and a transfusion may be necessary to increase oxygen-carrying capacity. Clotting Disorders:Patients with conditions like hemophilia or liver disease may require clotting factors or plasma to help their blood clot properly and prevent excessive bleeding. Cancer Treatment: Chemotherapy or radiation therapy can reduce the production of blood cells in the bone marrow, leading to the need for RBC or platelet transfusions. Bone Marrow Disorders: Certain diseases, such as leukemia or aplastic anemia, can interfere with the bone marrow's ability to produce sufficient blood cells, necessitating transfusions(8).

During blood transfusion several blood Transfusion Process required due to safety of patients such as: Compatibility Testing: Before transfusion, blood from the donor is carefully matched with the recipient's blood to ensure compatibility, particularly in terms of blood type (e.g., A, B, AB, O) and Rh factor (positive or negative). Crossmatching and antibody screening are performed to minimize the risk of a reaction. Preparation of Blood Components: Blood is usually separated into its individual components (RBCs, plasma, platelets, etc.) to be transfused based on the patient's needs. Administration:Blood is administered intravenously (IV) through a blood transfusion line, typically over the course of a few hours, depending on the type of transfusion. Monitoring: During the transfusion, the patient is closely monitored for any signs of adverse reactions, such as fever, chills, or allergic reactions. Vital signs, including heart rate, blood pressure, and oxygen levels, are also checked regularly(9).

Blood transfusion procedure also may have potential risks and complications to the recipients While blood transfusion is generally safe, there are some risks associated with the procedure:these riskare : Allergic Reactions: Some individuals may develop mild allergic reactions to proteins in the transfused blood, leading to symptoms like rash, itching, or fever. Hemolytic Reactions: If the donor blood is not properly matched to the recipient, hemolysis (destruction of red blood cells) can occur, which can lead to serious complications like kidney failure and shock. Infections: Although rare, there is a very small risk of transmitting infections like HIV, hepatitis, or bacterial infections through transfusion. Blood banks rigorously test all donated blood for infectious diseases to minimize this risk. Iron Overload: Repeated transfusions, especially of red blood cells, can lead to iron overload (excess iron in the body), which can damage organs over time, including the heart and liver. Transfusion-Related Acute Lung Injury (TRALI): TRALI is a rare but serious complication of blood transfusion that can lead to lung injury and respiratory distress. Graft-Versus-Host Disease (GVHD): This is a rare, life-threatening complication where the transfused donor white blood cells attack the recipient's tissues. It is most common in immunocompromised patients(1).Blood transfusion is a critical and life-saving procedure that involves transferring blood or its components to a patient. It is commonly used to treat blood loss, anemia, clotting disorders, and conditions that affect blood cell production. While generally safe, transfusions come with some risks, which are carefully managed through blood testing, monitoring, and modern medical practices to ensure patient safety.

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## **Red Blood Cell (RBC) degradation**

Red Blood Cell (RBC) degradation during whole blood storage is an important process to understand, as it directly affects the quality and effectiveness of stored blood for transfusions. While blood transfusion is a life-saving procedure, the storage of whole blood and its components over time leads to biochemical, morphological, and functional changes in RBCs(10). These changes, collectively known as storage lesions, can compromise the ability of RBCs to perform their primary function of oxygen delivery.Mechanisms of RBC degradation during storage are influenced by several factors such as storage conditions (temperature, pH, and oxygen levels), age of blood, and the presence of various metabolic byproducts. Here are the main mechanisms involved: Loss of Membrane Integrity: The RBC membrane plays a crucial role in maintaining cell shape, flexibility, and structural integrity. During prolonged storage, lipid peroxidation and protein damage occur, which result in the loss of membrane integrity. Phospholipid breakdown: leads to changes in the membrane's structure and fluidity, making RBCs more fragile and prone to hemolysis (the breakdown of RBCs). This process reduces the flexibility of RBCs, making it difficult for them to pass through smaller capillaries and perform their oxygen-carrying function. Dehydration of RBCs: During storage, RBCs undergo a loss of intracellular water, which leads to a decrease in their volume and an increase in hemoglobin concentration. This dehydration further contributes to the rigidity of RBCs and affects their ability to deform and squeeze through small blood vessels. Dehydrated RBCs also show a higher concentration of potassium in the surrounding plasma and lower levels of intracellular ATP, further impairing their functionality(10).

Loss of ATP and Other Energy Stores: RBCs are anaerobic (they don't have mitochondria and depend on glycolysis for energy production). As RBCs age in storage, their ATP levels decrease. This depletion of energy stores impairs ion pump function (such as the Na+/K+ ATPase pump), which is crucial for maintaining the osmotic balance and proper cell function. The loss of ATP also leads to a failure to maintain proper membrane stability, resulting in increased cell fragility and osmotic stress(11).Accumulation of Metabolic Byproducts: The metabolism of glucose in stored RBCs results in the production of lactate and protons (acid), which leads to a drop in pH (acidification of the storage solution). The acidic environment contributes to the breakdown of key metabolic processes, including the depletion of 2,3-DPG (2,3-diphosphoglycerate)(11). 2,3-DPG is essential for RBCs to release oxygen to tissues. Its depletion reduces the RBC's ability to offload oxygen in peripheral tissues, leading to reduced oxygen delivery during transfusion(12).Hemolysis and Free Hemoglobin Release: As RBCs degrade during storage, hemolysis occurs, leading to the release of free hemoglobin into the plasma. Free hemoglobin is harmful because it can be toxic to kidneys, leading to acute kidney injury. The presence of free hemoglobin can also trigger inflammatory reactions in the recipient and can increase the risk of transfusion reactions(13). Oxidative Stress: RBCs are highly susceptible to oxidative stress due to their exposure to molecular oxygen and reactive oxygen species (ROS). Over time, oxidative damage to lipids, proteins, and hemoglobin occurs, leading to the formation of methemoglobin (an oxidized form of hemoglobin) and hemichromes (denatured forms of hemoglobin), which further compromise the RBC's ability to carry oxygen. The degradation of membrane proteins also contributes to the formation of senescent RBCs that are more prone to clearance by the spleen and hemolysis(11). Changes in RBC Morphology: During storage, RBCs can become more spherical (as opposed to their normal biconcave shape), a condition known as spherocytosis. This loss of normal shape reduces their ability to deform and navigate through narrow capillaries. Other morphological changes include the formation of echinocytes (spiky or crenated RBCs) or burr cells, which also impair normal RBC function(14).RBCs are the most critical component of whole blood for oxygen delivery. However, during storage, RBCs undergo hemolysis (destruction of red blood cells), leading to the release of hemoglobin into the plasma. This free hemoglobin can be toxic and cause renal injury if the blood is transfused. Reduced RBC Function: The RBCs’ ability to carry oxygen decreases over time due to the degradation of cell membrane integrity and decreased hemoglobin affinity for oxygen. After 72 hours, RBCs in stored whole blood become less effective at carrying oxygen to tissues. Potassium Leakage: Stored RBCs may leak potassium into the plasma as they break down, increasing the plasma potassium concentration. High potassium levels can be dangerous when transfused, especially for patients with cardiac conditions(15).

## **Coagulation factor deterioration**

The deterioration of coagulation factors during the storage of whole blood is a significant concern in transfusion medicine, particularly in the context of patients requiring clotting support. Coagulation factors are proteins in the blood that work together to form a clot and prevent excessive bleeding. When whole blood is stored for transfusion, particularly for longer periods, coagulation factors can deteriorate, affecting the blood's ability to promote proper clotting.Coagulation factors (such as factor V, factor VIII, and fibrinogen) present in the plasma part of whole blood undergo deterioration over time. After more than 72 hours of refrigeration, the ability of the blood to clot may be compromised, leading to an increased risk of bleeding.Factor degradation makes whole blood less effective in treating conditions like bleeding disorders or hemorrhagic shock that require functioning clotting factors for adequate hemostasis(16).During the storage of whole blood (usually at 1-6°C), coagulation factors experience deterioration due to a combination of factors, including the loss of enzymatic activity, changes in the blood's pH, and the depletion of necessary cofactors and substrates. This process is typically referred to as storage lesions.

## 2.3. Platelet function loss

Platelets are typically stored in whole blood or as separated components (e.g., platelet concentrates) at room temperature (20-24°C) with gentle agitation. Unlike red blood cells (RBCs), which are stored at colder temperatures (1-6°C), platelets require room temperature to maintain their function(17). However, even under optimal storage conditions, platelets undergo deterioration in functionality over time, a process known as storage lesion(17).Factors Contributing to Platelet Function Loss: Platelets lose their function during storage due to several factors, including structural changes, metabolic alterations, and activation. Here are the key factors contributing to platelet dysfunction during storage:Platelet Activation: During storage, platelets can become spontaneously activated, leading to platelet aggregation and the formation of microthrombi. When activated, platelets lose their ability to respond effectively to stimuli during transfusion. They also begin to consume ATP and calcium, which are critical for their function. The activation of stored platelets results in the expression of surface proteins like P-selectin and glycoprotein IIb/IIIa, which are important for platelet adhesion and aggregation. However, excessive activation can impair their ability to form stable clots in recipients(17). Loss of Membrane Integrity: The platelet membrane undergoes structural changes during storage, including lipid peroxidation and membrane fragmentation, which reduce their ability to interact properly with other cells and components of the coagulation system. These membrane changes result in the loss of key surface glycoproteins, such as GPIb-IX-V (important for platelet adhesion to the vascular wall) and GPIIb/IIIa (important for platelet aggregation)(17). This leads to decreased platelet adhesion to the site of vascular injury and impaired aggregation in response to activation signals. Loss of Platelet Shape and Deformation: Healthy platelets are discoid in shape, which allows them to deform and squeeze through small capillaries and adhere to damaged blood vessels. During storage, platelets often undergo a change in shape, becoming more spherical. This loss of flexibility impairs their ability to interact with injured vasculature and limits their functional capacity to stop bleeding. The loss of platelet shape change and aggregation potential can also result in reduced ability to form a stable clot(18). Metabolic Changes: ATP depletion is a key event in the loss of platelet function during storage. Platelets rely on glycolysis for energy production, and during prolonged storage, ATP levels decline. ATP is necessary for the activation of platelet signaling pathways, as well as for maintaining membrane integrity and shape change(17). Calcium is also critical for platelet activation and aggregation. During storage, calcium homeostasis becomes disrupted, which impairs platelet responsiveness to activation signals and reduces their ability to form clots.Increased Release of Reactive Oxygen Species (ROS): Platelets are highly sensitive to oxidative stress, and reactive oxygen species (ROS) can accumulate during storage. ROS can damage platelet membrane lipids, proteins, and enzymes, impairing their function. The oxidative damage compromises the platelets' ability to respond to hemostatic demands after transfusion(17). Decreased Platelet Glycoprotein Expression: Storage leads to a decrease in the expression of key platelet glycoproteins involved in platelet adhesion and aggregation. Specifically, glycoprotein IIb/IIIa (integrin αIIbβ3) plays a central role in platelet aggregation by binding to fibrinogen and other adhesive molecules. Decreased expression of these glycoproteins reduces platelet function and impairs their ability to form stable clots in recipients(19). Release of Inflammatory Mediators: During platelet storage, there is an increase in the release of pro-inflammatory cytokines and biologically active molecules, such as thromboxane A2 and serotonin. These mediators contribute to platelet activation and aggregation but also have the potential to disrupt normal platelet function in the recipient. Platelet function loss during the storage of whole blood is a significant concern in transfusion medicine. Platelets are essential for primary hemostasis, as they help form blood clots to stop bleeding after injury(20). However, platelets deteriorate over time during storage, which affects their ability to properly support clot formation. This is particularly important in situations where transfusions are required to manage bleeding disorders or in patients undergoing major surgeries, trauma, or chemotherapy. If whole blood contains platelets, their functionality rapidly declines after storage. Platelets in stored blood become less effective at aggregating and forming clots, significantly reducing the hemostatic capacity of the transfused blood. After more than 72 hours, the platelets may be effectively non-functional, further increasing the risk of bleeding in transfusion recipients(21).Impact of Platelet Function Loss on Transfusion Therapy, Reduced Hemostatic Capacity: the primary concern with platelet function loss during storage is that transfused platelets may not effectively stop bleeding in patients who are thrombocytopenic (low platelet count) or who require platelet support after surgery, trauma, or chemotherapy. Platelet concentrates stored for 5–7 days or longer can show significantly reduced hemostatic capabilities. Platelet aggregation and adhesion are often impaired, meaning that platelet transfusion may not achieve the desired therapeutic effect. Risk of Thrombosis: Although stored platelets may become spontaneously activated and form microclots, they still might not function adequately at the site of injury. In some cases, this pre-activation can increase the risk of thrombotic events in transfusion recipients, especially in critically ill patients. Transfusion Reactions: The degradation of platelets during storage can lead to the release of inflammatory cytokines and bioactive molecules that can provoke immune responses or contribute to transfusion-related complications, such as TRALI (transfusion-related acute lung injury)(17).

## **Bacterial Contamination**

Bacterial Contamination: The presence of microbial contamination in stored blood can significantly contribute to inflammatory responses. While rare, contamination of blood products with bacteria (especially Gram-negative bacteria) can lead to the release of endotoxins, which trigger a severe inflammatory response in the recipient. Bacterial contamination may be more common in platelet concentrates (stored at room temperature) than in whole blood stored at refrigerated temperatures, but the risk of bacterial growth is still a concern, especially with longer storage times. Endotoxins and Sepsis: The release of lipopolysaccharide (LPS), a component of Gram-negative bacterial cell walls, can lead to sepsis-like symptoms, including fever, hypotension, and organ failure. Although bacterial contamination is a concern for all blood products, the risk increases if the blood is stored improperly or for too long. After 72 hours, if the blood isn’t kept under ideal conditions, bacteria may proliferate, increasing the risk of transfusion-related infections. Blood banks implement strict protocols to minimize contamination, but the risk still exists as blood ages, particularly if there are any breaches in sterile technique or if refrigeration is inadequate(22).

## **Metabolic Changes**

The metabolic changes that occur during the storage of whole blood at refrigerated temperatures (typically 1–6°C) over a period of 72 hours can have significant implications for the functionality of the blood components, including red blood cells (RBCs), platelets, and plasma. Understanding these changes is critical to ensuring the quality and safety of blood used for transfusion purposes.Metabolic waste products accumulate in stored blood, including lactate and carbon dioxide, due to the lack of circulation and cellular metabolism. The accumulation of these waste products can affect the pH of the blood and lead to acidosis upon transfusion.The increase in lactate can be harmful to the recipient, particularly in patients with poor metabolic reserves (e.g., infants, elderly patients, or those with organ dysfunction)(23).Decreased pH and Increased Lactate Concentrations: As the blood is stored, metabolic processes (particularly anaerobic glycolysis) lead to an accumulation of lactate, which causes a decrease in pH (becoming more acidic). The pH of blood typically decreases to around 6.5 to 6.8 after 72 hours of refrigeration. This acidification impacts the functionality of several blood components: Red blood cells (RBCs): A lower pH reduces the RBC’s ability to effectively release oxygen to tissues (due to the Bohr effect). Platelets: Low pH leads to platelet dysfunction, inhibiting their ability to aggregate and form clots(24). Coagulation Factors: A more acidic environment can impair the activity of clotting factors, leading to compromised hemostatic potential in the stored blood.Loss of Albumin Function: Plasma albumin, an important protein for maintaining oncotic pressure, also experiences decreased functionality during storage. Although albumin itself remains in the plasma, its ability to maintain osmotic balance and transport various molecules becomes less effective as metabolic disturbances (such as acidosis) increase.Cytokine Release and Inflammation: As stored blood ages, platelets and leukocytes in the blood can release pro-inflammatory cytokines such as interleukins and tumor necrosis factor (TNF), which contribute to systemic inflammation and potentially trigger immune responses in the recipient(24).The storage of whole blood at refrigerated temperatures for 72 hours induces a series of metabolic changes that affect the functionality of its components, especially RBCs, platelets, and coagulation factors. The accumulation of lactic acid, ATP depletion, and oxidative stress contribute to the deterioration of blood quality over time. While blood stored for up to 72 hours can still be useful for transfusion, storage lesions increase as time progresses, affecting the hemostatic capacity of the blood, particularly in terms of platelet aggregation and coagulation. Therefore, optimizing storage conditions and minimizing storage duration can help preserve blood function and improve the efficacy of transfusions(25).

## **Immunologic and Inflammatory Responses**

The immunologic and inflammatory responses that occur during the storage of whole blood at refrigerated temperatures for up to 72 hours are significant concerns in transfusion medicine. These responses can affect the safety and effectiveness of blood transfusions, particularly in relation to immune reactions, allergic responses, and inflammatory processes in the recipient. Below is an overview of the immunologic and inflammatory changes that occur during the storage of whole blood in the refrigerator for 72 hours.Leukocyte Degranulation: As the blood is stored, granulocytes (neutrophils, eosinophils, basophils) and monocytes release various pro-inflammatory cytokines and enzymes such as interleukins (IL-1, IL-6, IL-8), tumor necrosis factor (TNF-α), matrix metalloproteinases (MMPs), and reactive oxygen species (ROS). These molecules contribute to inflammation and immune responses in the recipient(26). Leukocyte Activation and Adhesion Molecules: Leukocytes can become activated and express adhesion molecules (e.g., P-selectin, L-selectin) and integrins. This can lead to intravascular activation of white blood cells, increasing their potential to adhere to the endothelium and contribute to inflammation. The presence of activated leukocytes and the cytokines they release are linked to the risk of transfusion-related reactions(10).Cytokine Accumulation: During storage, stored whole blood tends to accumulate pro-inflammatory cytokines due to the release of these molecules from activated leukocytes, platelets, and endothelial cells. Common cytokines include TNF-α, IL-1, IL-6, IL-8, and IL-10. These cytokines can cause systemic inflammatory responses in the recipient when transfused, leading to adverse reactions such as fever, chills, and more severe conditions like transfusion-related acute lung injury (TRALI).TNF-α: This cytokine is involved in the acute inflammatory response and can increase the permeability of the blood vessels. High levels of TNF-α in stored blood may increase the risk of inflammatory complications post-transfusion(27). IL-1 and IL-6: These cytokines contribute to the acute phase response, influencing the production of acute-phase proteins in the liver and modulating the immune response. IL-6, for example, is linked to fever and systemic inflammation after transfusion. IL-8: This cytokine is a potent chemoattractant that recruits immune cells (especially neutrophils) to sites of inflammation, which can exacerbate inflammatory reactions in the recipient(28).Complement Activation: The complement system, a part of the innate immune response, is often activated during the storage of whole blood. The storage process can lead to the activation of the classical and alternative complement pathways, particularly through the binding of immune complexes and foreign antigens.- C3a and C5a: The activation of the complement system leads to the release of C3a and C5a, which are potent anaphylatoxins. These molecules increase vascular permeability, promote neutrophil chemotaxis, and enhance the inflammatory response, which can contribute to transfusion-related inflammatory reactions in the recipient. Membrane Attack Complex (MAC): Activation of complement can also lead to the formation of the Membrane Attack Complex (MAC), which can directly damage RBC membranes, leading to further hemolysis and the release of pro-inflammatory mediators. Transfusion of stored blood after 72 hours can activate the immune system in the recipient, leading to inflammatory responses. The degradation of RBCs and plasma proteins can trigger the release of cytokines and other inflammatory mediators, leading to fever, chills, or in severe cases, transfusion-related acute lung injury (TRALI).Older blood may also increase the risk of alloimmunization (the formation of antibodies against foreign blood antigens), which can complicate future transfusions(29).The storage of whole blood at refrigerated temperatures for up to 72 hours induces various immunologic and inflammatory responses that can affect the safety and efficacy of transfusions. These responses include the activation of leukocytes, the release of cytokines, platelet activation, and the activation of the complement system. Additionally, hemolysis and the presence of free hemoglobin contribute to an inflammatory milieu. These factors can lead to adverse transfusion reactions such as fever, allergic reactions, TRALI, and alloimmunization. Therefore, it is crucial to monitor storage conditions and minimize storage time to reduce the risk of these reactions and ensure the safety of transfused blood(11).

## **Reduced efficacy in Critical Care**

Whole blood that has been stored for extended periods (more than 72 hours) is less effective in treating conditions such as severe anemia, trauma, or hemorrhagic shock. The oxygen-carrying capacity of the RBCs is reduced, and the potential for clotting or hemostasis is impaired due to the deterioration of coagulation factors and platelets(30).

## **Increased Risk of Transfusion Reactions**

The storage lesions that develop in blood after prolonged refrigeration may increase the risk of transfusion reactions. For example, stored blood may cause febrile non-hemolytic transfusion reactions (FNHTR) due to the breakdown of white blood cells and the release of cytokines and other inflammatory mediators. The presence of free hemoglobin and increased potassium may lead to more serious reactions, such as cardiac arrhythmias or renal injury(31).

## **Conclusion**

Transfusing whole blood stored for more than 72 hours in a refrigerator can be problematic due to deterioration of red blood cells, coagulation factors, and platelets, leading to reduced oxygen-carrying capacity, impaired clotting, and other complications. The blood may also be at an increased risk of bacterial contamination and metabolic changes. Therefore, it is generally avoided in favor of fresh or appropriately stored components such as red blood cells, plasma, or platelets, which are stored according to recommended guidelines

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**References**

1. Ackfeld T, Schmutz T, Guechi Y, Le Terrier C. Blood Transfusion Reactions—A Comprehensive Review of the Literature including a Swiss Perspective. Journal of Clinical Medicine. 2022.

2. Booth C, Allard S, Robinson S. Blood transfusion. Medicine (United Kingdom). 2021.

3. Brophy A, Opsha Y, Cardinale M. Blood, Blood Components, Plasma, and Plasma Products. In: Side Effects of Drugs Annual. 2016.

4. Storch EK, Custer BS, Jacobs MR, Menitove JE, Mintz PD. Review of current transfusion therapy and blood banking practices. Blood Reviews. 2019.

5. Ming Y, Liu J, Zhang F, Chen C, Zhou L, Du L, et al. Transfusion of Red Blood Cells, Fresh Frozen Plasma, or Platelets Is Associated With Mortality and Infection After Cardiac Surgery in a Dose-Dependent Manner. Anesth Analg. 2020;

6. Drammeh B, De A, Bock N, Pathak S, Juma A, Kutaga R, et al. Estimating Tanzania’s National Met and Unmet Blood Demand From a Survey of a Representative Sample of Hospitals. Transfusion Medicine Reviews. 2018.

7. SS G, HD C, N S, A A, NK N, R B. Study of Utilization of Blood and Blood Components in a Tertiary Care Hospital. J Blood Lymph. 2017;

8. Brigmon EP, Cirone J, Harrell K, Greebon L, Ngamsuntikul S, Mendoza A, et al. Walking blood bank: a plan to ensure self-sufficiency in an era of blood shortage. Trauma Surgery and Acute Care Open. 2024.

9. Argyrou A, Gafou A. Transfusion of blood components in current clinical practice. Arch Hell Med. 2017;

10. Miglio A, Rocconi F, Cremonini V, D’Alessandro A, Reisz JA, Maslanka M, et al. Effect of leukoreduction on the metabolism of equine packed red blood cells during refrigerated storage. J Vet Intern Med. 2024;

11. Pulliam KE, Joseph B, Veile RA, Friend LA, Makley AT, Caldwell CC, et al. Expired But Not Yet Dead: Examining the Red Blood Cell Storage Lesion in Extended-Storage Whole Blood. Shock. 2021;

12. Le Blanc J, Lordkipanidzé M. Platelet Function in Aging. Frontiers in Cardiovascular Medicine. 2019.

13. Eze EM, Christian SG, Jacob RB, Jeremiah ZA, Chuku IDW. Changes in Plasma Haemoglobin Concentration in Citrate Phosphate Dextrose Adenine-1(CPDA-1) Stored Blood. Int Blood Res Rev. 2019;

14. Roussel C, Dussiot M, Marin M, Morel A, Ndour PA, Duez J, et al. Spherocytic shift of red blood cells during storage provides a quantitative whole cell–based marker of the storage lesion. Transfusion. 2017;

15. Xu Z, Zheng Y, Wang X, Shehata N, Wang C, Sun Y. Stiffness increase of red blood cells during storage. Microsystems Nanoeng. 2018;

16. Maulidan EB, Tambunan BA, Hajat A. The effect of storage time on the whole blood (WB) quality at the blood bank of Dr. Soetomo general hospital. Int J Health Sci (Qassim). 2022;

17. Liu C, Su Y, Guo W, Ma X, Qiao R. The platelet storage lesion, what are we working for? Journal of Clinical Laboratory Analysis. 2024.

18. Kim J Il, Bae HC, Park HJ, Lee MC, Han HS. Effect of Storage Conditions and Activation on Growth Factor Concentration in Platelet-Rich Plasma. J Orthop Res. 2020;

19. Stolla M, Wang Y, Miles J, Osborne B, Shen Y, Fang L, et al. Targeted Proteomics Reveals That the Dominant Mechanism of Gpibα Loss during Platelet Storage Depends on Temperature of Storage. Blood. 2020;

20. Rebulla P. The long and winding road to pathogen reduction of platelets, red blood cells and whole blood. British Journal of Haematology. 2019.

21. Pramudita JJ, Widjanarko B, Munadi M, Suwondo A. The effect of storage period on the platelet levels on whole blood in the blood bank refrigerator. Int J Health Sci (Qassim). 2022;

22. Ramirez-Arcos S, Kou Y, Kumaran D, Culibrk B, Stewart T, Schubert P, et al. Assessment of bacterial growth in leukoreduced cold-stored whole blood supports overnight hold at room temperature prior to filtration: A pilot study. Vox Sang. 2022;

23. Bontekoe IJ, van der Meer PF, de Korte D. Thromboelastography as a tool to evaluate blood of healthy volunteers and blood component quality: a review. Vox Sanguinis. 2019.

24. Kondoh H, Kameda M, Yanagida M. Whole blood metabolomics in aging research. International Journal of Molecular Sciences. 2021.

25. Oyet C, Okongo B, Apecu Onyuthi R, Muwanguzi E. Biochemical changes in stored donor units: Implications on the efficacy of blood transfusion. J Blood Med. 2018;

26. Stefani A, Capello K, Carminato A, Wurzburger W, Furlanello T, Bertazzo V, et al. Effects of leukoreduction on storage lesions in whole blood and blood components of dogs. J Vet Intern Med. 2021;

27. Tormey CA, Stack G. Use of a cytokine-release assay to demonstrate loss of platelet secretory capacity during blood bank processing and storage. Arch Pathol Lab Med. 2014;

28. Zhang Y, Wang Z, Ma X, Li Y, Zhou Q, Sun S, et al. Stored whole blood transfusion initiates serum amyloid A activation monitored by real-time dynamic imaging. Blood Transfus. 2023;

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;

30. Gallaher JR, Schreiber MA. A Review of Whole Blood: Current Trauma Reports. Current Trauma Reports. 2019.

31. De Pascale MR, Belsito A, Sommese L, Signoriello S, Sorriento A, Vasco M, et al. Blood transfusions and adverse acute events: A retrospective study from 214 transfusion-dependent pediatric patients comparing transfused blood components by apheresis or by whole blood. Annali dell’Istituto Superiore di Sanita. 2019.