**PRESERVATION OF BLOOD COMPONENTS BY ADDITIVES TO INCREASE SELF LIFE**

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**Abstract:**

A life-saving procedure known as a blood transfusion uses blood and its constituent parts for treatment.Transfusion supports various forms of medical care and hence, there is an ever-increasing need and demand for blood. The main principles of transfusion lie in safe and effective blood supply. The whole blood which is a mixture of cells, colloids and crystalloids can be separated into different blood components namely packed red blood cell (PRBC) concentrate, platelet concentrate, fresh frozen plasma and cryoprecipitate. Each blood component is used for a different indication; thus the component separation has maximized the utility of one whole blood unit. For a component to be therapeutically effective, it must meet certain temperature and storage requirements. In order to ensure sufficient quality of blood transfused and to prevent wastage, component therapy was introduced. Instead of transfusing complete blood, it entails transfusing a specific component(s). In this chapter we learn about the separation of blood component and blood bags (single bag, double bag, triple bag, and quadruple bag) use for the storage of different components with suitable preservatives..

The history of storage and the most recent advancements in blood and its component storage techniques are also covered in this chapter. With the addition of preservative solutions, blood and its constituent parts can be preserved in a number of conditions.

**Key words:**Introduction, History,Blood Bag System, Components, Component Therapy, Storage and Expiration, , Blood Preservatives

**Introduction:**

As is common knowledge, blood banks are facilities where transfusion-ready supplies of blood or plasma are stored.

or

A blood bank is a facility where donated blood is collected and maintained for use in blood transfusions in the future. The phrase "blood bank" normally refers to a division of a hospital, commonly located within a clinical pathology laboratory, where blood products are stored and pre-transfusion and blood compatibility testing are carried out.However, it sometimes refers to a collection centre, and some hospitals also perform collection. Blood bank plays an important role in modern medical facilities.[1]In case of an emergency, they keep blood on hand and can provide it to patients. How then does a blood bank function? Blood is drawn from donors, type-matched (a test transfusion to see how your blood will respond to potential donor blood) and stored or conserved before being given to recipients.

Dr. Bernard Fantus founded the first blood bank in the country in 1937 at Chicago's Cook County Hospital. Blood couldn't be kept in storage for more than a few days at the time. Most transfusions were person-to-person, a dangerous process which made it hard to find donors.

Dr. Fantus started testing various blood storage techniques in an effort to find a solution to this issue. He altered the name of the facility from the Blood Preservation Laboratory to "blood bank" because he thought it would be less intimidating to potential donors. The capacity to collect and preserve blood for a long time revolutionized how medical professionals cared for patients. Blood donation was no longer a dangerous procedure, and patients in need could now get the blood they required to survive.Numerous lives have been saved because of blood banking over the years. Currently, over 13.6 million units of blood are donated annually. Each day, around 36,000 units of blood are required. Blood banks can now keep donations of blood safely and process and test blood to ensure everyone's safety thanks to advancements in medical technology.[2]

**HISTORY:**

 In 1818, British scientist and obstetrician Dr James Blundell executed the first known transfusion of human blood. Dr Blundell was consulted by a patient suffering from severe bleeding. With no treatment available for this condition back then, Dr Blundell got to thinking. He assumed that if the patient is losing blood, then supplying him with blood would help restore his health. Sounds logical too, right? So, Dr. Blundell injected the patient with 12–14 ounces of blood from numerous donors. Despite these efforts, the patient eventually passed away. Why? Blood groups! Yes, the blood group types were not matched before the transfusion! But there’s no way Blundell knew about this since blood groups weren’t discovered yet. The world, for the first time, got acquainted with the three main blood groups (A, B, and O) after Austrian physician Karl Landsteiner discovered them in 1901. While the first [blood transfusions](https://en.wikipedia.org/wiki/Blood_transfusion) were made directly from donor to receiver before [coagulation](https://en.wikipedia.org/wiki/Blood_coagulation), later it was discovered that by adding [anticoagulant](https://en.wikipedia.org/wiki/Anticoagulant) and [refrigerating](https://en.wikipedia.org/wiki/Refrigeration) the blood it was possible to store it for some days, thus opening the way for the development of blood banks. [John Braxton Hicks](https://en.wikipedia.org/wiki/John_Braxton_Hicks) was the first to experiment with chemical methods to prevent the coagulation of blood at [St Mary's Hospital, London](https://en.wikipedia.org/wiki/St_Mary%27s_Hospital%2C_London), in the late 19th century. His attempts, using [phosphate of soda](https://en.wikipedia.org/wiki/Sodium_phosphates), however, were unsuccessful.[3]

The first non-direct transfusion was performed on March 27, 1914, by the [Belgian](https://en.wikipedia.org/wiki/Belgium) doctor [Albert Hustin](https://en.wikipedia.org/wiki/Albert_Hustin), though this was a diluted solution of blood. The [Argentine](https://en.wikipedia.org/wiki/Argentina) doctor [Luis Agote](https://en.wikipedia.org/wiki/Luis_Agote) used a much less diluted solution in November of the same year. Both used [sodium citrate](https://en.wikipedia.org/wiki/Monosodium_citrate) as an anticoagulant.[1]

**Facts about blood banking**

The American Association of Blood Banks reports that:

* Each year, 6.8 million volunteers donate blood.
* Every day, 36,000 units of blood are required.
* About 13.6 million blood units are donated each year.
* Blood is divided up into individual components. These include platelets, cryoprecipitate AHF (cryo), a white blood cell, plasma, and red blood cells. One unit of whole blood and its parts may be transfused to several people. Each person may have a different need.
* Each year, more than 21 million different blood components are transfused.

## What are the components of blood?

Although blood or one of its components can be transported, each one also has a variety of other purposes, such as the following:

* **Red blood cells.**These cells carry oxygen to the tissues in the body and are commonly used in the treatment of anemia.
* **Platelets.** They help the blood to clot and are used in the treatment of leukemia and other forms of cancer.
* **White blood cells.**These cells help to fight infection, and aid in the immune process.
* **Plasma.**the liquid, watery portion of blood in which platelets, white blood cells, and red blood cells are suspended. The numerous components of the blood must be transported through the bloodstream via plasma.

 Plasma serves many functions, including the following:

* + Helps to maintain blood pressure
	+ Provides proteins for blood clotting
	+ Balances the levels of sodium and potassium
* **Cryoprecipitate AHF.** The portion of the plasma that contains clotting factors that help to control bleeding.

Albumin, immune globulins, and clotting factor concentrates may also be separated and processed for transfusions.

**Disposable Blood Bag System**

A disposable bio-medical equipment called a blood bag system is used to collect, store, transport, and transfuse human blood and blood components. The system is made up of one or more blood bags that are connected to one another by tubes, needles, needle covers, clamps, etc. The blood bags are constructed of plastic that is compatible with blood.

Blood systems have relied on polyvinyl chloride plastic bags with suitable various anticoagulants inside of them since the 1950s because they offer an amazing storage life of up to 49 days. Now, the next generation PVC blood bags are imminent.[13] PVC blood bags allow a long shelf life for the blood. The blood can last up to 49 days when refrigerated. Despite the fact that most blood is used within a few weeks, a storage period of up to 49 days is essential for a number of reasons. Currently, the plasticizer DEHP is used to make blood bags flexible, stabilising the red blood cells and ensuring a long storage period. However, the substance has come under scrutiny by authorities and regulators. The value chain for PVC medical devices is looking for substitute plasticizers to take its place. DEHT is an acceptable replacement, according to the Swedish Karolinska Institute, while BTHC and DINCH, according to recent study by the national Dutch blood bank Sanquin, can take the place of DEHP. The continued availability of blood bags plasticized with DEHP is essential for patient safety in the meantime.

The technology has been licensed to four Indian businesses with a combined annual manufacturing capacity of 3 million bags, bringing the nation's overall production capacity to 12 million bags. Currently, it is anticipated that the nation as a whole needs 10 million bags annually. However, the product has gained acceptance on a global scale and there is a substantial market demand for it, providing excellent export possibilities.[14]

A complete line of blood bags created to improve the quality of blood collection, processing, product separation, and storage.All bags have required international licences and certificates. Products can be customized to fit individual and country- specific requirements, including bag configurations, safety methods, filtration and sampling methods.

**Single blood bag:**

 Single blood bag is used for collection of whole blood with anticoagulant CPDA-1 solution. The single bag system with primary bag contains anticoagulant CPDA-1 (Citrate-Phosphate-Dextrose-Adenine) which preserve red blood cells up to 35 days at 2-6ºC.

**Double blood bag:**

 Double blood bag system is used for separation of two components from whole blood. The double bag with anticoagulant CPDA-1 and one emptysatellite bag.

**Triple blood bag:**

 Triple blood bag system is used for separation of three components from whole blood, the triple system includes one primary bag with anticoagulant CPDA-1 solution and two emptysatellite bag. Triple SAG-M blood bag system includes one primary bag with anticoagulant CPD solution and SAGM solution in another bag and one empty satellite bag.

**Quadruple blood bag:**

 Quadruple blood bag system is used for separation of three components of blood through Buffy coat method. Quadruple blood bag system includes one primary bag with anticoagulant CPD solution, one bag with SAGM solution and two empty bags.

**Top to bottom blood bag:**

Top to bottom blood bag also used for separation three components of blood through buffy coat method however it provides process to extract red blood cells from the bottom and plasma from the top side.

**COMPONENT THERAPY**

Instead of entire blood transfusions, component therapy uses specific component transfusions.

. Component therapy can be carried out by:

1. separating blood components by centrifugation after whole blood donation or
2. Aphaeresis .

The technique of aphaeresis is unique to component therapy, which is defined as the withdrawal of blood from the donor, removal of the component required for transfusion and the remaining components transfused back into the donor , with the utilization of an automated aphaeresis instrument.[4]Component therapy reduces the risk of blood exposure and adverse transfusion-related consequences by ensuring that one unit of whole blood is utilised for several patients. In situations of significant blood loss, whole blood is transfused. In situations of anaemia, erythrocytes are transfused; in cases of thrombocytopenia and clotting problems, platelets are transfused. Plasma and its associated factors are transfused in liver diseases and coagulation factor deficiencies .[5]

**WHOLE BLOOD TO COMPONENTS**

In order to separate blood components from one unit of whole blood, a specific piece of equipment known as a chilled centrifuge was created in 1960. Only PRBC and fresh frozen plasma (FFP) are prepared using a single-step heavy spin centrifuge, but platelet concentrates (PLTCs), PRBC concentrates, and FFP are prepared using a two-step centrifuge. The platelet-rich plasma (PRP) method or the BC method are the two basic ways to prepare PLTC.[6] Algorithms 1 and 2 are provided as a basis for the two methods of separation. The PRBC, PLTC or random donor platelet (RDP), FFP, cryoprecipitate, cryo poor plasma (CPP), and Plasma fractionation products are the key components of the simple PRP procedure.[7]

**STORAGE AND EXPIRATION**

Presently, whole blood is collected in tubes made of polyolefin or PVC that has been plasticized with various substances, such as triethyl hexyl trimellitate and butyryl-tri-hexyl citrate.[10] In addition to maintaining pH levels above 6, these bags offer nearly double the oxygen permeability of first-generation Di-ethyl hexyl phthalate plasticized PVC containers.In order to maintain the biological activity of the constituents, lower their metabolic activities, and stop bacteria from growing on the blood components, adequate component storage is required. Red blood cells should be stored between +2°C and +6°C, platelets and leucocytes between +20°C and +24°C, and plasma products should be stored below -18°C, according to standard guidelines. All components must be kept in one of three compartments: untested, tested and safe for release, and tested but unsafe or quarantined for disposal.[11]If available, additional equipment is also needed to keep cross-matched units safe. If kept at recommended temperatures, the components can be transported and stored for a maximum of 24 hours. The PRBC must be kept between +2 and +10 degrees. All parts are routinely shipped and stored at temperatures between +20°C and +24°C.[8] All frozen components should be shipped in a way that keeps them frozen. Either personally inspecting each component for signs of deterioration or using indicators fixed to units are two ways to track and record temperature changes. All blood components should be kept in the cold chain up until the point of transfusion.[9]

**The storage and transport equipments used are:**

Refrigerators (+4–2°C) Whole blood and PRBC storage, as well as thawed FFP and other plasma products storage, Agitators for platelet incubators operating at a temperature of (+222°C) and 70 cycles per minute-For the preservation of all platelet products, Deep freezers (80°C) are used to freeze blood components or FFP. Mechanical blast freezers can quickly freeze materials, and they can store frozen PRBC or platelets at temperatures as low as 65 C. freezers (40 °C): storage of all plasma products at a temperature of −30°C or even lower degrees, Transport containers: Transport containers are used to move blood or blood components quickly between two storage locations.Even blood mobiles are equipped with backup power and built-in cold chain storage systems. The choice to transfuse should not be made solely on the basis of test data, but rather should be preceded by a detailed assessment of each patient's clinical condition. In a hospital context, the major goal of transfusion medicine is to guarantee that "the right blood is given to the right patient at the right time and at the right place."[12]

**BLOOD PRESERVATIVES**

**For whole blood and erythrocytes**

Rous and Turner reported successful blood preservation in 1916. Blood was stored in the solution and then transferred to rabbits via transfusion. The solution contained citrate and dextrose. Oswald Robertson employed the same remedy during World War I.[15] During the Spanish Civil War and World War II, Loutit and Mollison developed the acid-citrate-dextrose (ACD) solution. The CPD solution (citrate, phosphate and dextrose) was used extensively for whole blood storage. However, the addition of adenine by Simon caused the emergence of CPDA or CPDA-1 (citrate, phosphate, dextrose and adenine) solutions . As the different types of “additive solutions” were developed, each with their own modifications of the earlier available solutions, there was a concurrent development of new and improved storage containers as well.[16]In place of the outdated method of storing blood in bottles, bags allowed for the separated storage of blood components, creating a demand for and an increase in the availability of solutions for each individual component. The blood was initially drawn into a CPD solution, divided into its constituent parts, and then each part was placed in a separate storage solution.[17] Beutler created the first solution for storing erythrocytes, known as BAGPAM, which included sodium bicarbonate, sodium carbonate, sodium phosphate, adenine, glucose, and mannitol. [18-19]SAG solution, which is composed of saline, adenine, and glucose, was developed as a result of the decrease in ATP during storage in this solution. Later, mannitol was added to the same solution to create SAGM, which is currently the most popular commercial RBC storage method.[20-23] Mannitol has been demonstrated to significantly lessen haemolysis by scavenging free radicals and preserving the erythrocyte membrane. While entire blood can be maintained for 35 days in CPDA-1, blood stored in CPD can only be kept for 21 days. SAGM, on the other hand, permits erythrocyte preservation for 42 days.[24-25]

***For platelets***

The existence of platelets and their role in haemostasis were first described in the 1870s. But it wasn't until 1910 when transfused platelets were demonstrated to lower thrombocytopenic patients' risk of bleeding.[26] Only around the 1970s did platelet transfusions become widely accessible. When Scott Murphy and Frank Gardner discovered that platelets could be kept at 22°C for up to 3 days while still performing their haemostasis function, this was made practical. Platelets can now be used for transfusion even after 5-7 days of storage because to advancements including the use of novel platelet additive solutions (PAS) and better storage containers. Studies are now being done to increase the possibility of prolonged platelet preservation. A significant fraction of the plasma in platelet suspensions is currently replaced with PAS during storage [27]. As a result, there is a lower possibility of germs and viruses contaminating the leftover plasma. Additionally, it enhances storage conditions and lessens transfusion-related negative effects associated with plasma. The amounts of glucose, citrate, phosphate, potassium, magnesium, and acetate in PAS vary. The pH is maintained by acetate, which also acts as a substrate for aerobic respiration. To increase the effectiveness and shelf life of preserved platelets, research is being done. According to Gulliksson, platelets can be kept for 18 to 20 days at 20 to 24°C with an enhanced additive medium that can prevent platelet ageing. The natural lifespan of platelets is 8 to 12 days. However, at 22–24 °C, with agitation, the shelf life of platelets collected for therapeutic or preventive transfusion is now only 5-7 days. By imposing this restriction, the danger of bacterial growth and the consequences of platelet storage lesion (PSL) are reduced. Reduced in vivo recovery and haemostasis activity after transfusion are associated with PSL [28]. PSL comprises of all the deleterious changes that occur from the time of blood collection from the donor until the time the platelet concentrate (PC) is administered to the patient.[29]

***For plasma***

As plasma reflects the changes taking place in blood, it serves as an excellent biomarker of oxidative stress. Human plasma is endowed with a robust antioxidant defense mechanism to combat the changes occurring during storage. Protein sulfhydryl groups have also shown to contribute to the antioxidant capacity and their oxidation indicates protein oxidation [30]. The proteases (serine, cysteine, aspartic and matrix metalloproteases) present in plasma are released from activated, lysed or dying neutrophils and mononuclear phagocytes. Plasma must be frozen immediately after separation, to prevent the proteases from damaging proteins. Plasma also possesses an innate ability to counteract these proteolytic enzymes through protease inhibitors (α1-protease inhibitor, tissue inhibitor of metalloprotease, α2-macroglobulin and plasminogen activator inhibitor-1). Another alternative method is the use of protease inhibitors in the storage solution. Ethylene-diamine-tetra-acetic acid (EDTA) or citrate (Ca2+ chelators) help in preventing not only coagulation, but also in the inhibition of Ca2+-dependent proteases [31]

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