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Review article *Platelets*

Platelets and its Importance in the Human Body

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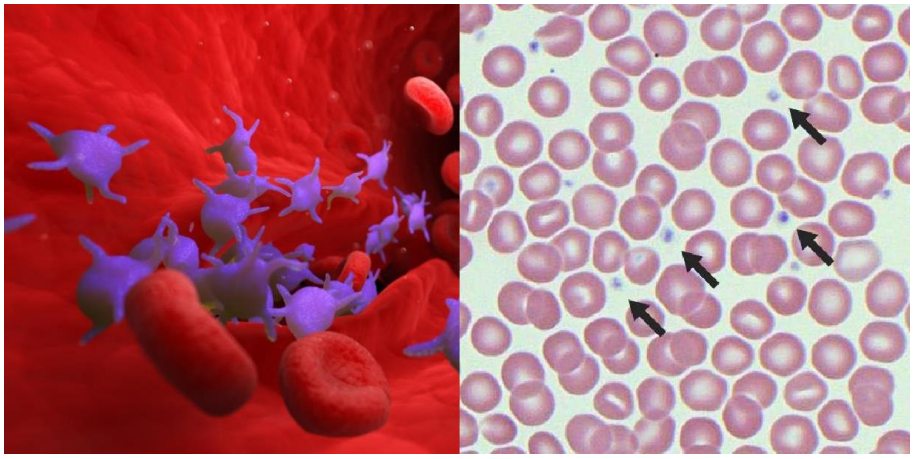
ABSTRACT

There are primarily three types of cells in human blood. White blood cells , platelets, and red blood cells. The smallest of them, biconvex and without a nucleus, cells are known as platelets. Despite their small size, platelets have important roles in vascular healing, hemostasis, and thrombosis, according to a study of numerous literature. Serotonin, a hormone involved in biological processes like learning and happiness as well as physiological processes like sleep and appetite, is also produced by platelets. Platelets aid the adaptive immune system's antimicrobial response. Thrombocytopenia, a low platelet count, and thrombosis, a high platelet count, constitute related medical disorder in the human body. Studies have also been done on the platelet storage procedure. With incubation and agitation, platelets can be kept for up to 5 days in the blood center. Due to their shorter lifespan, platelets' constant availability is a major problem. The super specialty health care center uses platelets additive solution as one of the products to extend the shelf life of the platelets for preserving the platelets in the blood center. In light of the extensive literature review, it is clear that platelets are a crucial type of human cell, actively participating in a variety of biological and physiological processes within the body. On the other hand, because of its limited lifespan, storing platelets is a difficult task for every time availability.

Keywords: Platelets, Hemostasis, Thrombosis, Serotonin, Immune response, Storage, Life span, PAS solution.

INTRODUCTION

Plasma makes up 55% of blood, platelets 1%, white blood cells (WBCs) 1%, and red blood cells 44%. (RBCs). Platelets are biconvex, non-nucleated cells that are generated from bone marrow megakaryocytes. [1]. Platelets are the initial line of defense for the body. To stop bleeding, platelets form clots. Adhesion is the process of spreading platelets across the surface of a damaged blood artery to halt bleeding [2]. Platelets arrive at the location of the injury, develop sticky tentacles that aid in adhesion, and send out chemical signals that attract more platelets. Aggregation is the process through which more platelets build upon the clot. Many immunological tasks, such as hemostasis, are performed by them. [2].Platelets play a pivotal role in hemostasis and vascular repair upon accidental injury[3]. The normal platelets count is approximately 1,50,000/micro liter to 3,50,000/micro liter of blood in adults[4]. Platelets are required for transfusion to patients in many surgical and medical procedures[5].



A peripheral blood smear surrounded by red blood cells as seen using a light microscope (40x). Platelets are tiny and have a purple color (black arrows).

Fig 1: Platelets and red blood cells in the blood flow are depicted graphically.

Production of Platelets

Non-nucleated cells that appear plate-shaped that originate from megakaryocytes in the bone marrow are the platelets [6]. Platelets are irregular in shape can be found as single or in the form of clusters. Platelets don't have a nucleus. But they have mitochondria to produce ATP and ADP. The mitochondrial DNA is also present inside it.

From the common myeloid progenitor cells in the bone marrow, platelets form pro-megakaryocytes and then change further into megakaryocytes. Megakaryocytes are the largest cells in the body and are found initially in the bone marrow. Platelets are the fragments of megakaryocytes. The megakaryocytes then tend to produce pro-platelets in the cytoplasm. The pro-platelets are basically the projections on platelet precursor cells. Once the pro-platelets move into the blood stream, they start to release the thousands of platelets in the blood[7].

The production of platelets and megakaryocytes is regulated by the hormone thrombopoietin. This hormone is secreted by the liver and kidney. One megakaryocyte can produce around 1000platelets in its whole life cycle. With the release of thrombopoietin hormone myeloid stem cells turn into megakaryoblast which further changes into Megakaryocyte. Then megakaryocytes start to form projection of platelet precursors. At the end, platelet projections release the platelets in the circulating blood. The floating platelets travels in the blood circulation and the stock of platelets is found reserved in the spleen. The average life span of the platelets is around 8-9 days inside the body[7].

Platelets have the cell membrane and cytoplasm which they get from megakaryocytes. The cell membrane of the platelets is known as glycoprotein cell membrane and is made up of lipid bilayer with the outer layer of carbohydrates and protein [8].Platelets are having receptors which are located on the outer membrane that helps platelets to stick with endothelial tissue at the time of injury. There are two main types ofreceptorsgp-1b and GP-2b/3a.

The cytoplasm of the platelets has actin and myosin for the contraction and release of the granules. They also have special type of protein called thrombosthenin inside the cytoplasm. This protein gives strength to the platelets for the contraction and release of the granules. These granules are the small fragments of Golgi bodies and residuals of rough endoplasmic reticulum which is required for the synthesis of enzymes.

Granules in platelets are divided into three categories: α-granules, dense granules, and lysosomes. A normal platelet's function depends on proteins, chemokine, cytokines, and growth factors found in α-granules. The dense granules contain a variety of small molecules linked to hemostasis, including ADP, serotonin, polyphosphates, glutamate, histamine and calcium.

Platelet lysosomes contain enzymes that are glycohydrolases as well as enzymes that degrade glycoproteins, glycolipids, and glycosaminoglycan [9].

Role of platelets

Platelets control bleeding in the human body. If a blood cell wall injured, they form a blood clot which adhere at the site of injured wall to stop the bleeding.

Hemostasis and thrombosis

Platelets play the key role in formation of blood clot to stop the bleeding in human body. The process to stop the bleeding is called hemostasis and the clot formation is known as thrombosis. At the time of bleeding, collagen is exposed and platelets get activated inside the body and thenplateletsgatheratthesiteofbleedingtoformplateletsplug.Adhesion,activation and aggregation are three main steps of clot formation [10].

The von Willebrand factor (vwf) which is found in the alpha granules of the platelets, involvedin the haemostasis and thrombosis process. At the time bleeding the von Willebrand factor helpsplatelets to stick with the injured wall by binding the collagen with the platelets. The surface receptors arresting the platelets and form a thrombus (clot) at the bleeding site.The von willebrand factor also protects the factor VIII, which plays the role in the intrinsic coagulation pathway[11].

As the von Willebrand factor helps the platelets to form the blood clot, the deviation of this factor in the plasma effects the condition of human body. The decrease in plasma level leads to the bleeding disorder and increase in plasma indicates the occurrence of thrombosis. Hence the cardiovascular rmorbidity can be reduced by the controlling the role of VWF.

Physiological role of platelets as Serotonin source

As per the literature review it was noticed that platelets also

have role in our routine function in gas it has Serotonin inside it. Serotonin act as hormone which is involved in the biological function like learning, memory, happiness and as well as in the physiological activities like regulation of sleep, behavior and appetite of the body. Around 8 % of the Serotonin is found inside the platelets. Serotonin acts as a vasoconstrictor. At the time of bleeding the serotonin is released from the platelets and helps to constrict the smooth muscles at the site of tissue injury or bleeding. Besides that after many studies it was also observed that serotonin interacts with the neurotransmitters and plays a big role in the our body routine processes such as bowel function, mood, nausea, blood clotting, bone density etc.[12]

Interaction of platelets with leucocytes in response to adaptive immune system

At the time of pathogen exposure, platelets act as an immedia te response to innate immunity. Platelets are having receptors on the surface of the cell which getsactivated when exposed to the pathogens. The interaction between bacteria and platelets enhanced the production of antimicrobial peptides. The glycoprotein IIb-IIIa, glycoprotein Ib α , fcyriia , complement receptors, and toll-like receptors influence these interactions . In the recent years, few studies had acknowledged the role of platelets when any foreign body attacks on the body and it was found that platelets play the role as an immediate responder against and also communicate the message to the other circulating cells of the body to attack on these foreign particles [9].

Antimicrobial response of the platelets

Besides the role of platelets in the haemostasis , platelets have the broad role in invading pathogens inside the body .Their role starts by attaching themselves with neutrophils and leucocytes. Due to the adhering quality, platelets use their adhesive proteins and chemokine to attach with the leucocytes and carry them at the site of pathogen attack. There is also link between the platelets and neutrophils . Platelets get activated and communicate the message to the neutrophilstoreleasetheneutrophilextractiontrapsfromtheneutr ophilstoengulfthemandstopsthefurther spreading of infection. Thus platelets play a big role to kill the bacterial ,viral or any other allergen that attacks the body[13].

Platelets form antibodies on the first attack of the pathogens. On the next attack of the same pathogens, these platelets form an antigen- antibody complex on the surface of the pathogens and accelerate the immune response[14].

The presence of seven thrombin-releasing antimicrobial peptides from human platelets was observed, including platelet factor 4 (PF-4), RANTES, connective tissue activating peptide 3 (CTAP-3), platelet basic protein, thymosin β-4 (Tβ-4), fibrinopeptide B (FP-B), and fibrinopeptide A (FP-A). [15].

Role in angiogenesis and metastasis

Platelets are having some micro particles which are small plasma membrane vesicles shed from cells at the time of activation. These micro particles are involved in the angiogenesis (growth of new blood vessels that tumours need to grow) and tumour metastasis(spreadofcancercells).The platelets dense granules releases ADP, polyphosphates which promotes the growth of cancer cells [16].

Role in tissue regeneration

Besides the role of haemostasis platelets are having some growth factors which helps in organ transplant, tissue regeneration, tissue repairs. Patients suffering with chronic liver disease can get affected with decreased production of thrombopoietin which results the thrombocytopenia in the body. Growth factors released by platelets include platelet-derived growth factor (PDGF) and hepatocyte growth factor (HGF), which promote liver regeneration [17].

Disorders and diseases that involves platelets / Importance of platelets

Thrombocytopenia

The decrease in the platelets count is termed as thrombocytopenia. It can cause the bleeding intothe tissues that lead to bruising and red rashes on the body. The low platelets count also resultsthe slow process of blood clotting. The most cause of thrombocytopenia may be contrasted such as any bacterial or viral infection, liver illness, immunesystem abnormality, disseminated intravascular coagulation, pregnancy, drugs, and coagulation deficiency. It can be a bone marrow disorder ortheside effect of some specific medication. Any age group can be affected by this disorder. Treatment is decided through the under lying reason of the thrombocytopenia.

The thrombocytopenia can be mild to moderate depending the cause of low platelets count. Thrombocytopenia is caused when platelets count is below 1,50,000/microliter. But if there is critical fall of platelets count (less than 10,000) can be fatal to the body which can lead to bleed. The primary reason of decrement in platelets might be destruction of platelets, less production or trapping of platelets into the spleen.

Usually, spleen stores the platelets and release them to circulate in the blood when needed. The spleen also fights with the foreign particles to stop the infection and filters the waste material from the blood. But in case of any disorder the spleen gets enlarged. This enlargement of the spleen starts holding the platelets inside it which results the less number of platelets in the blood circulation. The production of the platelets takes place in the bone marrow. The decrease in the production may cause the prolonged bleeding into the tissues and lesser the time of clotting to the injured part.

There are some conditions that can cause the body to destroy platelets faster than they can be produced, resulting in a deficiency of platelets in the bloodstream. These conditions include:

- **Pregnancy**.
  Gentle thrombocytopenia happens amid pregnancy and generally it progresses before long after childbirth.
- **Immune thrombocytopenia.** Auto-Immune system , such as lupus and rheumatoid joint pain, cause this sort.Bodyitselfproduceanti-plateletsandtheseantibodyattacksonthe platelets and destroy them. The obscure reason named as idiopathic thrombocytopenic purpura. This sort more regularly influences children.
- **Bacterial infection in blood.** The bacterial infection in blood can destruct the platelets.
- **Thrombotic thrombocytopenic purpura**. This can be an uncommon condition
  that happens when little blood clots abruptly frame all through your body, utilizing up huge numbers of

platelets.

- **Haemolytic uremic syndrome**. This uncommon disorder causes a sharp drop in platelets, destroying of red blood cells and affects kidney function.
- **Medications.** There are certain medicines that can decrease the number of platelets in your blood. Sometimes a medication unbalanced the immune system which results destruction of platelets such as heparin, quinine, sulfa-containing antibiotics and anticonvulsants.

Thrombocytosis

The increase in the platelets count is termed as thrombocytosis. It is a disorder when body can produce a large number of platelets. The increase in platelets count in the circulating blood can cause stroke, cardiac arrest, clotting in blood vessels. There are two kinds of thrombocytosis, Primary and secondary. The primary thrombocytosis can be a cause of large number of production of platelets in the bone marrow due to some abnormality. It is also called essential thrombocythemia. It can be a genetic disorder.

The secondary condition of thrombocytosis is called when the patient is suffering from some disease which causes the high number of platelets into the blood circulation. There are some conditions such as anemia because of iron deficiency, Cancer, Inflammation or any infection, surgical procedure, especially removal of the spleen due to which the platelets count can increase.

Storage of platelets in blood centre

The storage of platelets is an *in vivo* process under which the platelets are being separated from the whole blood of the donor by component separation techniques. Usually, the platelets are stored up to 5 days in the blood centre. However, in some blood centre services, the storage time is extended up to 7 days. After the preparation of the platelets the platelets are stored in the agitator cum incubator at 20-24^0 C. The storage area must be sterile. The bags using for the storage are gas permeable to breath the platelets well. Mainly there are two ways to prepare the platelets from the donors. Component separation and apheresis techniques. The component separation is done after the collection of whole blood from the donors within 4-6 hrs after collection. In this technique main three components are prepared and stored as per the standard guidelines.

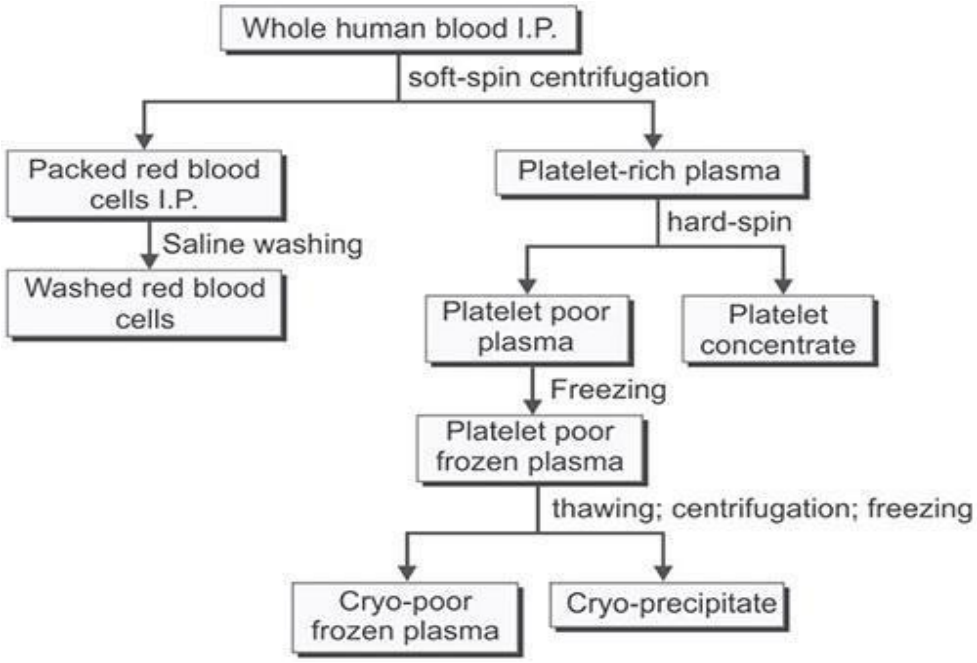


Fig 2: Blood component separation flow chart.

While the apheresis technique is the medical procedure in which the whole blood from the individual person is removed and the particular component from that blood is extracted.The left blood components are then returned back into the bloodstream of that same person.

In both procedures , the storage protocols of platelets are same. To maintain the good quality of platelets invivo, the platelets must be stored as per the below mentioned protocols.

- Temperature for storage must be room temperature(between20-25degree centigrade)
- Thereshouldbegentleagitationtotheplateletsbag.Theagitationshouldbecircularoraflatbedmovement. The quality of agitation affects the quality of platelets.
- The collection bag should be gas–permeable so that platelets can breathe.
- The area of storage should be clean, dry and sterile.

Due to the gas permeability of the platelets collection bags, the storage time of platelets has been increased from three to seven days.[18]

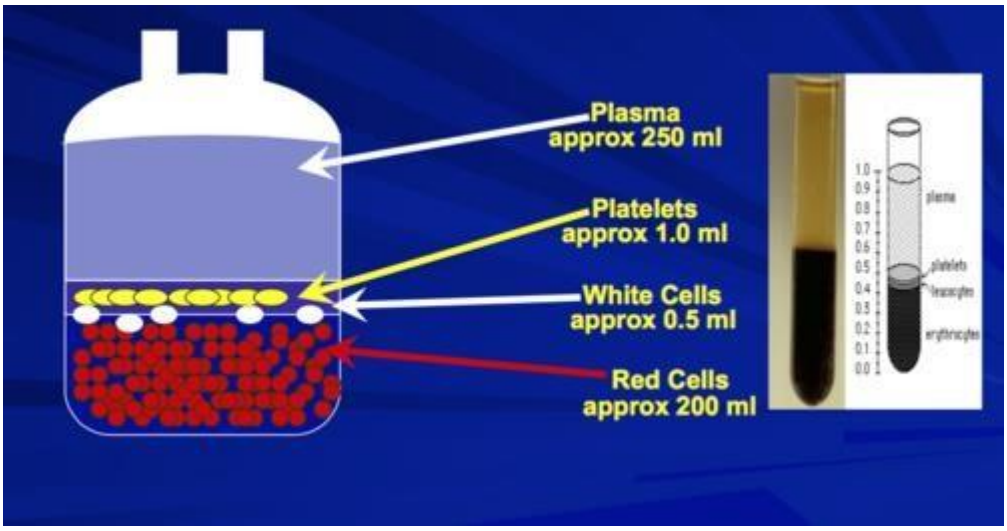


Fig 3: Diagram showing composition of Blood stock .

The anticoagulant which are commonly used for the storage of platelets are.

- CPDA-Citrate phosphate dextrose agar
- ACD-Acid citrate dextrose

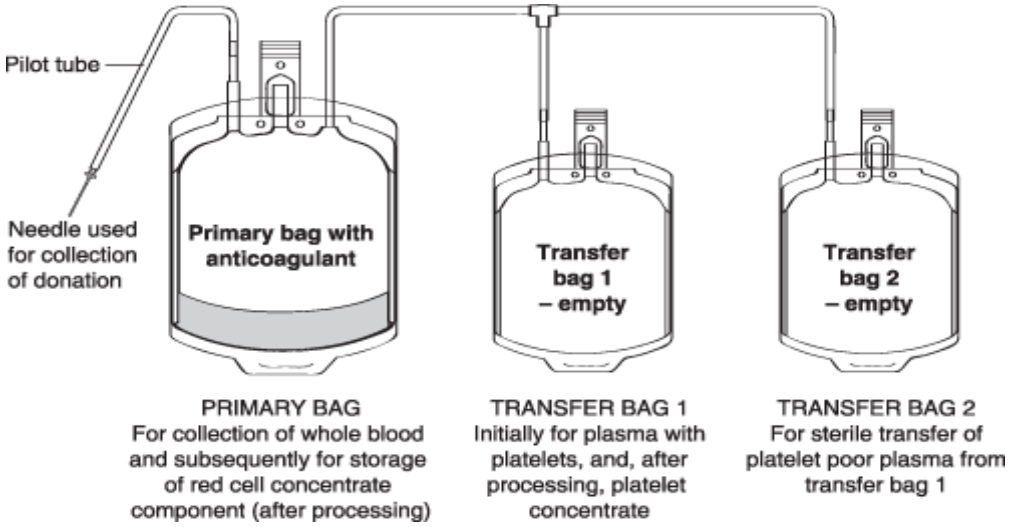


Fig 4: Blood bag system used for blood component separation.

Utility and storage of platelets

Patients suffering from thrombocytopenia or platelets dysfunction, leukaemia, myelodysplasia, aplastic anaemia, solid tumours, congenital or acquired/medication-induced platelet dysfunction, needs platelets to be transfused to treat the active platelet-related bleeding or as prophylaxis in the seat serious risk of bleeding. In the current scenario , platelets are stored as platelets concentrate or platelets rich plasma in blood centre where plasma works as a travel agent for transfusion.

Platelets can be stored with the platelets additive solutions (PAS) to increase the shelf life of the platelet. These solutions are named as platelet additive solutions. In this, method the plasma is replaced by PAS. At current few of the corporate and super specialty hospital blood centre are using pas.

Platelets additive solutions (PAS) are the electrolyte solute solution which has some chemical components. These chemical components help to maintain the ph of the platelets during the storage. Plasma is replaced by this PAS by which the storage time can be extended [19]. The lifespan of platelets in plasma is upto 5 days. Due to less storage time platelets are being wasted sometimes. So, by using PAS solutions the life span of the platelets can be increased. Around 70-80 percent of plasma is replaced by PAS solutions which is beneficial for patients as well as for the blood centre.

Advantages of using PAS solutions

- Minimizes the risk of transfusion (plasmatic reactions / a febrile reactions) reaction as low volume of plasma induced
- Plasma stock in the blood centre would be maintained which is needed for burning patients, coagulation therapy, patients with excessive bleeding, in therapeutic plasma exchange, Guillain-Barre syndrome patients.
- Cryoprecipitate (Cryoprecipitated antihemophilic factor [AHF]; cryo) availability could enhanced. The Cryoprecipitate isa blood product derived from plasma

that carries fibrinogen (factor 1),factor V111,factor X111,von wille brand factor, and fibron ectin and is used for coagulation therapy.

- The cost effectiveness of the Platelet additive solutions (PAS) also studied and observed that the usage of new generation PAS is cost-effective than platelets with plasma bags as it minimizes the risk of transfusion reaction and decrease the total amount of the expenditure . They also observed that the source of microbial contamination inside the platelets can be plasma, the ambient temperature for the bacterial growth (room temperature),and can be the permeability of the bag.[20]

Platelets are the most required blood products. But due to short life span and the storage condition, availability of the platelets all the time is quite difficult. Platelets can store only upto 5 days at room temperature inside the blood centre which is a very short period of time for the survival of platelets. Also, the temperature of storing is very prone to the occurrence of the bacterial contamination. Storage of the platelets is very great concern now a days. Many researches are going on for better availability of the platelets. Different storage conditions are studied to maximize the availability of platelets. The activities on alternate conditions of the storage were monitored like change in storage solutions, temperature for storing, results after transfusion and concluded that by using of platelet additive solutions the shelf life of the stored platelets can be increased.Also, the transfusion transmitted reactions would be minimized.(kellee capocelliet. currhematol, 2014).

CONCLUSION

Even though platelets are the smallest cells in the body, they play a significant role in human daily life, it has been discovered after reviewing a vast amount of literature. Numerous diseases or abnormalities in the body can be born from low platelet counts.

It can be challenging to balance platelet availability during the peak platelet demand season.The blood centers with the modern amenities are attempting to store enough platelets to meet patient demand for their treatment. However, the stock is difficult to maintain due to its short lifespan. Additionally, we learned that platelet additive solutions (PAS) are used in some superspeciality healthcare settings to extend the shelf life of platelets from 5 to 10 days after collection. Although using PAS solution has some advantages, such as a low risk of allergic reactions and transfusion-transmitted infections, its use is still very restricted because of its high cost.

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