INTRODUCTION
Platelets, or thrombocytes, are one of the formed elements in vascular circulation. Platelets are produced in the bone marrow, which includes femurs, hip, ribs, sternum, and other bones. The progenitor cell for platelets is the megakaryocyte. In the steady state, where platelet production equals platelet destruction, daily production is 30,000 to 40,000/µL. Platelet production is stimulated by the hormone thrombopoietin. When platelet levels are adequate, serum levels of thrombopoietin remains low. When hemorrhage occurs, platelet production can increase up to eight times normal.

The circulating life of a platelet is 9-12 days with approximately two-thirds of the platelets circulating and one-third in the splenic pool, bone marrow, or other extravascular locations. The reference range, established by each institution, is generally 150,000 to 350,000/µL.

The diameter of a platelet is approximately 2-4 µm, compared to a red blood cell of 7 µm. Like red blood cells, platelets are anuclear and discoid when resting. Upon activation, platelets undergo a shape change to a globular form with pseudopodia.

Glycoproteins (GP), embedded in the phospholipid bilayer membrane, are the receptors for activation and interaction with other cells. Organelles that serve as storage granules are evenly distributed in the cytoplasm of resting platelets. Some granules contain fibrinogen, thrombospondin, factor V, von Willebrand Factor, platelet factor 4, etc. Following activation, platelets release their granular contents contributing to diverse interaction with other platelets or other cells.

ANTIGENS ON PLATELETS
Antigens on platelets include:
1. HPA
2. HLA
3. ABO

PLATELETS IN HEMOSTASIS
The role of platelets in hemostasis, which depend on an adequate number of circulating platelets and normal platelet function, are to:
1. Maintain vascular integrity
2. Arrest bleeding by formation of a platelet plug
3. Stabilize the plug by contributing to the process of fibrin formation
When blood is exposed to a denuded arterial wall, platelets cover the surface in a monolayer.

**Step 1: platelet adhesion**
- Platelets are activated when brought into contact with collagen, which is exposed when the endothelial blood vessel lining is damaged.
- Other platelet activators include von Willebrand factor, thrombin, thromboxane A₂, adenosine diphosphate (ADP), adrenaline, and serotonin.

**Step 2: platelet aggregation**
- Granular contents are released from the platelets causing platelet aggregation.
- Platelets adhere to each other via adhesion receptors and to the endothelial cells in the blood vessel wall, forming a plug in conjunction with fibrin.

Any disruption in the thrombotic process or platelet production will cause platelets to malfunction.
- Aspirin inactivate cyclooxygenase and inhibits platelet thromboxane production. Platelets harvested from donors who have ingested aspirin should not be used as the sole platelet transfusion source.
- Thienopyridines (e.g., ticlopidine [Ticlid] and clopidogrel [Plavix]) inhibit platelet adenosine diphosphate (ADP) receptor.
- Glycoprotein inhibitors (e.g., abciximab [ReoPro], eptifibatide [Integrilin], and tirofiban [Aggrastat]) are potent inhibitors of platelet aggregation that block a receptor for fibrinogen and vWF.

**PLATELET COLLECTION, PRODUCTION, AND STORAGE**

Some platelet components include:
- Platelets: prepared from a single unit of whole blood.
- Pooled Platelets: two or more units of platelets that have been combined into one bag.
- Apheresis Platelets: a suspension of platelets in plasma prepared by cytapheresis.
- Apheresis Platelets Leukocytes Reduced: platelets collected by apheresis in which the residual leukocyte number is <5 x 10⁶.

**Preparation**
- In the United States, two main platelet products are apheresis platelets and whole-blood-derived platelets (using the platelet-rich plasma method).
- In Europe, Canada and other countries, platelet concentrates are prepared by the buffy coat method. Whole blood is to be stored and transported toward a temperature range of 20 to 24 C when platelets are being manufactured.
- Apheresis platelets have the advantages of limiting the recipient exposure to a single donor, which potentially reduces the possibility of infection and alloimmunization.

**Quality control (AABB Standards)**
- Platelets from whole blood: at least 90% of units sampled contain ≥5.5 x 10¹⁰ platelets and have a pH >6.2 at the end of allowable storage. The residual plasma is usually 50-70 mL. Pooled platelets of 4 to 6 units will contain roughly ≥3.0 x 10¹¹ platelets.
- Apheresis Platelets: at least 90% of units sampled contain ≥3.0 x 10¹¹ platelets and have a pH >6.2 at the end of allowable storage. The residual plasma is usually 200-400 mL.
- Apheresis Platelets Leukocytes Reduced will meet the same requirements as apheresis platelets but also have a residual leukocyte number <5 x 10⁶ in 95% of units sampled.
Storage

- Platelets are stored at 20-24 C with continuous agitation. The maximum time allowed for all platelets without agitation is 24 hours.
- Platelets expire within 24 hours to five days, depending on the collection system.
- Any platelet component prepared in an open system expires in 4 hours.
- Platelets may be frozen but the post-thaw platelet recovery and function are significantly reduced when compared with those of liquid-stored platelets.
- Irradiation does not shorten the shelf life of platelets.

Storage conditions affect metabolism and function of platelets with the resulting change(s) called platelet storage lesion. These conditions include:
- pH
- Temperature of storage
- Total platelet count
- Volume of plasma
- Duration of storage
- Agitation during storage
- Lactic acid accumulation
- Anticoagulant
- Method of preparation
- Storage container

A reduced pH causes the platelets to change shape from discs to spheres rendering the platelets nonviable after infusion in vivo. The storage container and agitation influence oxygen supply and gas exchange. The number of platelets and their metabolism cause decrease in nutrients from the plasma and changes in pH. Viability of platelets decreases during the storage period.

Platelet additive solutions (PAS) are available. The advantages of PAS include reduction of plasma-associated transfusion reactions, improved platelet storage, and reduction in viral and bacterial contamination.

COMPATIBILITY

Crossmatch

- Crossmatch is not required in routine platelet transfusion unless the platelet component contains >2 mL red cells.

DOSAGE

- A therapeutic dose of platelets for prophylactic therapy in adults is approximately one platelet per 10 kg body weight, which, for an adult, translates to one unit of Apheresis Platelets or 4 to 6 units of whole blood-derived platelets.
- Each unit of platelet concentrate usually increases the platelet count by 5000 to 10,000/µL in the typical 70-kg human. One Apheresis Platelets should increase the platelet count by 30,000 to 60,000/µL.

ADMINISTRATION, LEUKOREDUCTION AND IRRADIATION

- Platelets are administered according to institutional policy using an administration set.
- Leukoreduction filter may be used to reduce the leukocyte count.
- Irradiation of the component is indicated in certain disease states and in the prevention of transfusion-associated graft-versus-host disease (TA-GVHD). Platelets for transfusion are irradiated:
  - The patient is at risk for TA-GVHD such transplant recipients
  - Platelets are from a donor who is a blood relative of the recipient
The platelets are selected for HLA compatibility by typing or crossmatch.

**PLATELET DISORDERS**

- A reduction in the normal platelet count is called thrombocytopenia or thrombopenia. In severe thrombocytopenia, petechiae (perfectly round, purplish red spots caused by intradermal or submucosal hemorrhage), ecchymoses (small hemorrhagic spots, larger than a petechiae), and mucosal or spontaneous hemorrhage may be observed.
- An increase in platelet production and subsequent elevation in platelet count is thrombocytosis.

**INDICATIONS FOR PLATELETS**

The decision to transfuse platelets depends on the cause of bleeding, the patient’s clinical condition, and the number and function of circulating platelets. Significant bleeding due to thrombocytopenia or abnormal platelet function is an indication for “therapeutic” platelet transfusion. Indication include:

- Prophylaxis in patients with thrombocytopenia (e.g., Leukemia, massive transfusion, neonatal alloimmune thrombocytopenia (NAIT)
- Congenital and acquired platelet disorders (e.g., Bernard-Soulier syndrome, platelet storage pool deficiency)
- Active platelet-related bleeding

No universal “trigger” has been identified for prophylactic platelet transfusion. A common threshold for all patients is 10,000/µL for prophylactic transfusion. An alternative approach is:

- 5000/µL: stable patients
- 10,000/µL: patients with fever or recent hemorrhage
- 20,000/µL: patients with coagulopathy, on heparin, or with anatomic lesions likely to bleed.
- 50,000/µL: bleeding patients, patients about to undergo a hemostatic challenge such as surgery
- 100,000/µL: patients with intracerebral, pulmonary, and ophthalmic hemorrhage

Massive transfusion protocols: Platelets as well as plasma are often included. Patients who received a higher ratio of platelets were reported to have improved survival.

**CONTRAINDICATIONS TO PLATELET TRANSFUSIONS**

- If bleeding is unrelated to decreased platelet numbers or abnormally functioning platelets.
- Activation or autoimmune destruction of endogenous platelets such as in ITP, TTP, HIT, HUS, or DIC, unless the patient has a life-threatening hemorrhage.

**SIDE EFFECTS AND HAZARDS OF PLATELET TRANSFUSIONS**

Hazards that pertain to all transfusions are applicable to platelet transfusions. Selected topics are discussed in this section.

**Bacterial Contamination**

- Platelet products are the most likely of all blood components to be contaminated with bacteria. Storage conditions contribute to the growth of bacteria in platelets as well as the fact that the platelets themselves serve as an excellent growth medium.
- Symptoms caused by bacterially contaminated platelets may include high fever (>2.0 C rise), shock, severe chills, vomiting, tachycardia, hypotension, or circulatory collapse during or immediately after transfusion.
- AABB Standards requires all platelets be checked for bacterial contamination.
- Management should include administration of antibiotics to the patient and cultures of the patient’s blood, platelet bag and administration set.
Platelet alloimmunization
- The most common cause of platelet refractoriness is antibodies to HLA.
- If caused by human platelet antigens (HPA), the most frequently identified is anti-HPA-1a.
- Platelet survival may be markedly shortened, leading to refractoriness. Alloimmunization can be reduced by the use of leukocyte-reduced blood products. UVB irradiation is equally effective.

Red cell alloimmunization
- Red cell alloimmunization may occur because of the presence of red cells in the platelets.
- Immunization can result when Rh-positive platelets containing red cells are transfused to an Rh-negative patient. The main concern is the transfusion of Rh-positive platelets to an Rh-negative female of childbearing age. Rh immune globulin (RhIG) should be administered if Rh-negative platelets are not available when a transfusion of Rh-positive platelets is necessary. A single dose should provide protection for at least 15-30 random donor platelet units, providing bloody platelets are not administered.

Hemolysis
See document: ABO/Rh in platelet transfusion

TRALI
Transfusion-related acute lung injury (TRALI) may result from an immunologic reaction between the donor's white cell antibodies and the recipient's white cells.

Transfusion-associated Graft-versus-host Disease (TA-GVHD)
Irradiation of the donor platelets can inactivate the accompanying lymphocytes thus reducing the likelihood of TA-GVHD.