Platelets and their significance for the nurse anesthetist
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The author explores the function of platelets, a major component of the blood's clotting mechanism, and provides nurse anesthetists with a basic understanding of the hemostatic capabilities of platelets.

Today, as more and more critically ill patients undergo surgery, it is important for the anesthetist to be totally familiar with the body's physiological responses to disease. Disturbance of the blood and blood components is one example of these responses. When faced with a coagulation abnormality, the anesthetist should be able to recognize the possible causes and anticipate any treatment the physician may want to initiate.

This article is intended to give the anesthetist a basic understanding of platelet function and dysfunction. It attempts to explain some of the processes behind collection, storage, and the effects on survival and hemostatic capabilities of platelets. A short discussion of the drugs which most commonly disturb platelet function and indications for platelet transfusions are also included.

The physiology of platelets
Numerous investigators in the early part of the 19th century observed blood platelets. Zimmermann in 1860, Schultz in 1865 and Osler in 1874 realized that these corpuscles were not artifacts; however, they failed to recognize the true importance of these cells. They thought that platelets developed into red blood cells. In 1882, Bizzozero described platelets as they appeared, demonstrating their adhesive qualities, their participation in the formation of thrombi, and their role in coagulation of the blood. But until 1906, no one was able to prove where platelets originated. At that time, Wright concluded that platelets were detached portions of the cytoplasm of megakaryocytes.

It is generally believed that platelet production occurs in the bone marrow, but studies done by Howell and Donahue challenged this view. They concluded that 20-25% of mature megakaryocytes may enter the blood, ultimately reaching the lungs, and that 7-17% of the body's platelets are released from the lungs.

Platelets are composed of most of the common cellular materials and components, with the exception of DNA (deoxyribonucleic acid). Platelets are small (2-4 microns), colorless, and round, oval or rod shaped. Under electron microscopy, platelets have a cell membrane of approximately 60A (Angstrom units) thick. They contain golgi apparatus, endoplasmic reticulum, 50-100 oval granules of varying density, very few mitochondria, microvesicles and microtubuli.

Platelets are composed chiefly of protein, totaling approximately 60% by dry weight. Of this total protein, 15% is an enzyme known as atpase thrombosthenin, which is similar to the proteins actin and myosin found in muscle tissue. It is
thought that this protein aids in clot retraction during the coagulation process. Another 13.5% of the platelet is fibrinogen. Platelet albumin amounts to 2%.

The coagulation factor, factor XIII, is present in platelets and accounts for 30-50% of the total factor XIII found in the blood. Other clotting factors are: factor V (also known as platelet factor I or PF-1), factor VIII, (PF-2) which is a fibrinogen to fibrin activating factor and PF-4 which is the antithrombin factor.

Carbohydrates comprise about 9% of platelets by dry weight; lipids comprise about 13%. Phospholipids make up 75% of the total lipid content of blood. Not all phospholipids play an active role in blood coagulation, however. The remainder of the platelet is made up of aminoacids, nucleotides such as adenosine triphosphate (ATP), adenosine 5'-diphosphate (ADP) and adenosine monophosphate (AMP), minerals and vitamins such as sodium, potassium, calcium, magnesium, zinc, folic acid, vitamin B-12 and ascorbic acid.

The powerful, smooth muscle vasoconstrictor substance serotonin is normally present in platelets but is absent in plasma. Following coagulation or platelet aggregation, 20-25% of the total platelet serotonin is released into the plasma. Platelets acquire serotonin from cells which secrete this substance; the platelets then concentrate it by an active transport mechanism.

**Platelet function**

The function of platelets can be considered under several categories, such as hemostasis, participation in coagulation, storage and transport, and miscellaneous activities. The platelet is the first and most important element seen at a break in the vascular lining. Within 1-3 seconds after injury of a small vessel, platelets start to adhere to the damaged endothelial cells and to tissue fibers, particularly to collagen. More platelets adhere to those already fixed and to each other, forming a loose platelet aggregate. The platelets become transformed from their natural shapes to structures which protrude long, sticky processus. Finally, the platelets interlock, fitting together like the pieces of a puzzle.

As the bleeding slows and stops, fibrin strands appear to reinforce the plug and the clot retracts. Platelets may also accumulate within a vessel which is damaged without being severed; such accumulations form the white head and part of the mixed body of a thrombus. Platelets not only arrest bleeding from injured blood vessels, they also prevent formation of petechial hemorrhages when the walls of minute blood vessels are subjected to abnormal tension, as in the capillary fragility test.

The aggregation process is divided into two steps, reversible and irreversible. The reversible step can be triggered by ADP, or by thrombin and epinephrine, which then triggers the release of ADP, causing aggregation. However, if a critical amount of thrombin is present, irreversible aggregation can occur. The breakdown of ATP to ADP releases the energy necessary for aggregation. Again, thrombin is necessary for irreversible aggregation.

The biochemical events of hemostasis start with the stimulation of the platelet's energy metabolism. This can be from the three factors mentioned earlier, ADP, thrombin and epinephrine. At the same time, various substances are released. PF-3 becomes available and, with collagen and ADP, initiates the *intrinsic clotting mechanism*. Tissue thromboplastin initiates the *extrinsic clotting mechanism* and the resultant intrinsic clotting mechanism, both release thrombin. Thrombin, in turn, initiates clot retraction through its combined action on platelets and fibrinogen. In the hours which follow, the platelet plug disintegrates and is replaced by fibrin.

**Platelet production**

When platelet transfusions are given, there is a reduction or suppression of megakaryocytes, indicating a clear feedback mechanism capable of regulating platelet production. The consistency of platelet production over a period of years indicates a finely tuned control mechanism. No hormone has yet to be identified with platelet production. However, in individuals born with thrombocytopenic disease, there is an increase in the level of mature megakaryocytes when fresh, normal plasma is given.

Although the spleen has not been linked to the production of platelets, it is known that splenectomies affect an increase in platelets by decreasing the rate of destruction (but not the life span). Platelets have a normal life span of 8-12 days, with a normal concentration of around 200,000-400,000 per cubic millimeter.

**Platelet collection and storage**

There are several methods for collecting and storing platelets; each has specific effects on the life span and the viability of platelet aggregates. Each method can also be used to prepare supplemental batches of platelets for use in arresting a bleeding episode (initially caused by an acute loss...
of the body's own platelets) or for preventing a bleeding tendency, as found in thrombocytopenia. Presenting each is beyond the scope of this article; therefore, only the general process will be discussed.

Platelets can be administered in three forms, depending upon the needs of the patient. They can be given in fresh whole blood in circumstances when a low platelet count is associated with acute or chronic blood loss. Secondly, they can be given in plasma-rich-platelet (PRP) concentrations when the patient needs volume expansion or when a source of active clotting factors are needed along with platelets. Thirdly, they can be given as a platelet concentrate where the platelets from a unit of whole blood are suspended in 25-50 ml plasma.

The practice of storing whole blood for platelet replacement in either acid-citrate-dextrose (ACD) or citrate-phosphate-dextrose (CPD) at 4°C for up to three weeks before transfusion is no longer considered an acceptable method by many. Although post-transfusion survival values of red blood cells, albumin, gamma globulin and fibrinogen are adequately maintained, significant deterioration of factors V and VIII and platelets occurs. Less than 25% of the transfused platelets are present before the end of the second day and none by the third day.

Blood collected in either heparin, ACD or CPD and stored at room temperature (22°C) for not more than four hours is considered to be fresh and is the best replacement for blood loss and coagulation deficiencies. During this storage time there is only minimal damage to red blood cells, platelets and plasma proteins. Platelets can be separated from whole blood within four hours of collection and prepared for liquid preservation at 22°C or at 4°C. For freezing preservation, they should be stored at -80°C or -150°C.

Procedure. Fresh blood is drawn into the ADC-containing bag of a triple bag pack. The blood is centrifuged and the plasma, which contains 90% of the platelets, is expressed into the second bag. Centrifuging the plasma in the second bag drives the platelets into the bottom, leaving a platelet-poor plasma. The platelet-poor plasma is expressed off into the third bag, leaving the platelet concentrate suspended in 25-50 ml of plasma in the second bag. Preparation of concentrates may produce platelet clumps which have poor platelet recovery and survival. Acidification of the platelet-rich plasma to lower the pH to 6.4-6.8 prior to concentrating the platelets will decrease platelet clumping.

Platelets may also be obtained by means of plasmapheresis. Donors undergoing plasmapheresis may donate up to 1.5 L. of plasma per week. This may be accomplished in one or more sessions with little depletion of formed elements and only a slight decrease in serum protein.

When stored at 22°C and transfused within 24 hours, the platelets will survive as long as eight days in contrast to a normal life span of 9-11 days. While storage at 4°C decreases survival to 2-3 days, platelets stored at 4°C are reported to be more capable of shortening the bleeding time in thrombocytopenic patients. Platelets stored at 22°C develop a "storage lesion" that prevents effective hemostasis during the first 8-24 hours following infusion. Therefore, it would seem that platelets stored at 4°C should be used to treat active bleeding secondary to thrombocytopenia, and platelets stored at 22°C should be used for prophylaxis in thrombocytopenic patients with risk of hemorrhage.

Hemostatic effectiveness
The survival of platelets preserved at different temperatures can be measured by the increase in platelet count in thrombocytopenic recipients or by labeling the preserved platelets with 51 chromium (CR). Hemostatic effectiveness can be determined by the ability of platelets to correct bleeding from an incision of the skin or surgical wound and the aggregation of platelets to ADP, epinephrine and collagen.

In his studies, Ellison indicated that the hemostatic effectiveness of platelets rapidly decays over a period of 48-72 hours. He showed that platelet concentrates or fresh whole blood, both of which contain viable platelets, will correct bleeding due to dilutional thrombocytopenia.

The most common cause of bleeding related to platelets is a reduction in the platelet count. Reductions in the platelet count may be due to decreased production, as found in patients receiving cancer chemotherapy; increased utilization as in disseminated intravascular coagulation (DIC); and increased destruction, as in idiopathic thrombocytopenic purpura, and hypersplenism. These situations are secondary to massive transfusions with bank blood, which contains little or no viable platelets. In cases of decreased production or massive transfusions, the use of platelet concentrates will increase the platelet count and correct the hemostatic defect.

The development of antibodies to react against platelets following repeated transfusions
is not uncommon. There is an associated decrease in response to platelet function. Complement-fixing antibodies against platelets have been detected frequently in the serum of recipients when a decreased response or a shortened platelet survival period was shown. However, the presence of complement-fixing antibodies was not necessarily associated with a decreased hemostatic response to transfusion.

Repeated platelet transfusions can be associated with an increased incidence of fever-chill reactions as high as 20%. There is a direct relationship between this and A-B-O and RH incompatibility to the plasma of plasma-rich-platelets or platelet concentrates.

**Indications for platelet transfusions**

Platelets are given for abnormal bleeding in severe leukemia with marked thrombocytopenia, and bleeding associated with severe idiopathic thrombocytopenic purpura. Platelet transfusions for thrombocytopenic patients or those with severe aplastic anemia (where the bone marrow production of megakaryocytes in depressed) is a very important treatment for patients about to undergo surgery. This is because platelet transfusions prevent excessive hemorrhaging during surgery, or bleeding secondary to massive transfusions of bank blood, sepsis or hemorrhagic fever. Platelet transfusion is not indicated in cases of patients who have an increased destruction of platelets on an autoimmune basis when hypersplenism is the cause, rather, splenectomy is the treatment of choice.

**Impairment of platelet production and function from drugs**

Aspirin ingestion in man results in a variety of platelet abnormalities, most of which may be attributed to aspirin's inhibitory effect on the release of intrinsic platelet ADP. Platelet aggregation by collagen, connective tissue or epinephrine are all abnormal. The mechanism by which aspirin does this is unknown. A single dose can be detected for 4-7 days after administration, a period roughly matching the life-span of platelets.

The infusion of plasma expanders, such as dextran and hydroxyethyl starch, are associated with an increase in bleeding time which cannot be explained. The effect is dose related and occurs with a dextran which has a molecular weight over 65,000. Dextran interferes with PF-3 activity. Platelet adhesion decreases following the administration of 1-2 L. of dextran. Dextran coats the surface of platelets altering the surface charge, an effect which can last up to 4-8 hours. This proves to be a beneficial effect for patients who require intra-aortic balloon pumping for heart surgery, in that dextran decreases the mechanical destruction caused by inflating and deflating of the balloon.

Phenybutazone (Butazolidin®), sulfinpyrazone (Anturane®) and other anti-inflammatory drugs, some antihistamines and a variety of psychotropic agents of the phenothiazine class appear to suppress collagen-induced aggregation. Decreased platelet adhesiveness has been associated with Atromid-S® (clofibrate) and local anesthetics. In some cases with the anti-inflammatory and psychotropic agents, platelet reduction has been caused by direct suppression of bone marrow.

The effects of heparin and dicumarol on platelet function is not clear. Both normal and decreased platelet adhesiveness have been reported. No side effects from the commonly used anesthetic agents have been reported in relation to platelet production and function, with the exception of ethyl ether—there is a slight increase in the number of platelets seen following ethyl ether anesthesia, but this has not been proven to be significant.

Estrogens have the effect of reducing the number of active megakaryocytes. Finally, corticosteroids given for prolonged periods suppress platelet production in patients with ongoing idiopathic thrombocytopenic purpura (ITP).4

**REFERENCES**

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Randall L. Carter, CRNA, received his diploma in nursing from St. Anthony's Hospital School of Nursing in Oklahoma City, Oklahoma in 1976. He worked in the Coronary Care Unit and Open Heart Unit, and was a member of the nurse staffed and operated Mobile Coronary Care Unit at St. Anthony's Hospital from 1976 through 1977. He attended St. Catherine's Hospital School of Nurse Anesthesia in Garden City, Kansas, and graduated in September, 1979. Mr. Carter currently lives in Tulsa, Oklahoma, and is a staff anesthetist for Associated Anesthesiologists at St. Francis Hospital in Tulsa.

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