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Blood components in laboratory medicine

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There are many groups of patients who share common needs of extensive blood transfusions the risks of which have been clearly illustrated. In this review, the author briefly presents the details of important blood components in laboratory medicine.

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วิโรจน์ ไววานิชกิจ. ส่วนประกอบของผลิตภัณฑ์เลือดทางเวชศาสตร์ชันสูตร. จุฬาลงกรณ์เวชสาร 2550 ก.ย. -ต.ค; 51(9): 451 - 8

มีผู้ป่วยมากมายที่ต้องได้รับเลือดและผลิตภัณฑ์ของเลือด ซึ่งความเสี่ยงของการกระทำดังกล่าวนั้นเป็นที่ยอมรับกันดี ในบทความนี้ผู้นิพนธ์ได้ทบทวนรายละเอียดเกี่ยวกับส่วนประกอบของเลือดที่สำคัญทางเวชศาสตร์ชันสูตร

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Introduction to used of donated blood

There are many groups of patients who share common needs to receive extensive blood transfusions including those in intensive care unit, thalassemic and traumatic patients. Approximately, 80 % of these groups of patients receive multiple transfusions. At present donor exposure is an issue because transfusion risk is still apparent.[1] Donated blood should be used for the treatment of the patients and handled with the same respect and ethical standards as when it was donated by the donor. Accordingly, directed donors or purchased system should be discouraged. Anonymous donation should be used: blood is a gift with no reimbursement and should be given to an unknown patient with the intention to help and not to harm.[2] Donation shall be easy and secure for the donor. Therefore, donated blood shall be handled with respect and should be used with the intension to treat patients as previouly stated. Promotion of the blood donation is the topic. Due to a recent study, the main obstacle to blood donation is fear due to inadequate information. [3]

Donated blood must be used for treatments of patients via direct transfusion (directly) or indirect transfusion (not transfused). Direct help to the patient may be transfusion of single units or transfusion of units from a batch, platelets or plasma products. Indirect help to the patient includes the use of a few tubes for laboratory controls or several units for standardization with the intention to help patients to set normal values for a new test which is useful for laboratory medicine. The use of donated blood for other purposes other than transfusion must be no special information when the blood is used as laboratory quality controls but information for other kinds of use and need to be assured for no identification at the stage of informed consent, with which identification of donor is needed. [2]

Risk of transfusions

Acute hemolytic (immediate antibody-antigen reaction triggered by transfusion of ABO incompatible blood) and delayed hemolytic (sensitization to minor blood group antigens during a previous transfusion which results in a reaction within 3 to 10 days after a subsequent transfusion) are the two most common complications of blood transfusion.[4] The third type is febrile, non-hemolytic due to reaction between antibodies and WBC antigens or plasma proteins.[5] It should be noted that all three types are rare in the newborn because of a deficiency in isohemagglutins and poor antibody response to foreign antigens. In addition, blood transfusion also posed the risk of transmission of many blood borne pathogens[6] including syphilis, HIV 1, HIV 2, Human T-lymphotrophic virus 1 (HTLV-1), hepatitis B surface antigen (HbsAg),malaria, microfilaria and babesia. These pathogens should be screened in the routine blood transfusion screening test. Also, some new markers are introduced including hepatitis C virus (HCV), alanine aminotransferase (ALT), a surrogate marker for HIV infection, and hepatitis B core antibody (Anti HBc), a surrogate marker for non-A, non-B hepatitis. According to the standard of the Thai National Blood Bank, the donor screening tests include ABO grouping, Rh, HBsAg, Anti HIV, Anti HCV, VDRL and malaria.

Rare complications include graft versus host disease (GVHD)[7-8] which usually occurs in 4 to 30 days after transfusion and associated with high mortality. Concerning the pathophysiology,

T-lymphocytes in a transfusion product engraft in the recipient and react to the recipients tissues. The clinical pictures include liver dysfunction, watery diarrhea, erythroderma and pancytopenia. This condition is firstly described in immunocompromised children and most recently noticed in patients who received blood donated by their relatives. The new recommendation for the prevention of graft versus host disease is irradiation.[9-10] Irradiation is indicated in known suspected immunodeficiency case receiving blood from biologic relative as a part of directed donor program. It is also indicated in cases of *in utero* or exchange transfusion, bone marrow transplant recipients, infants with malignancies (leukemia, neuroblastomas), very low birth weight infants, infants receiving blood components with large amounts of leukocytes (platelets, granulocyte transfusions), cases with absolute lymphopenia (lymphocytes < 500). It should also be noted that removal of lymphocytes by white blood cell (WBC) filter is not a replacement for irradiation. Irradiated red blood cells can be stored up to 28 days or equal to the age of the main irradiated blood components based on which date is the earlier. Irradiated blood should be washed prior to administration to remove excessive potassium leaking out of the red blood cell. However, it should be mentioned that both irradiation and WBC filtering are not the method to prevent all transfusion reactions since there are other causes of transfusion reactions.

Indications for transfusions

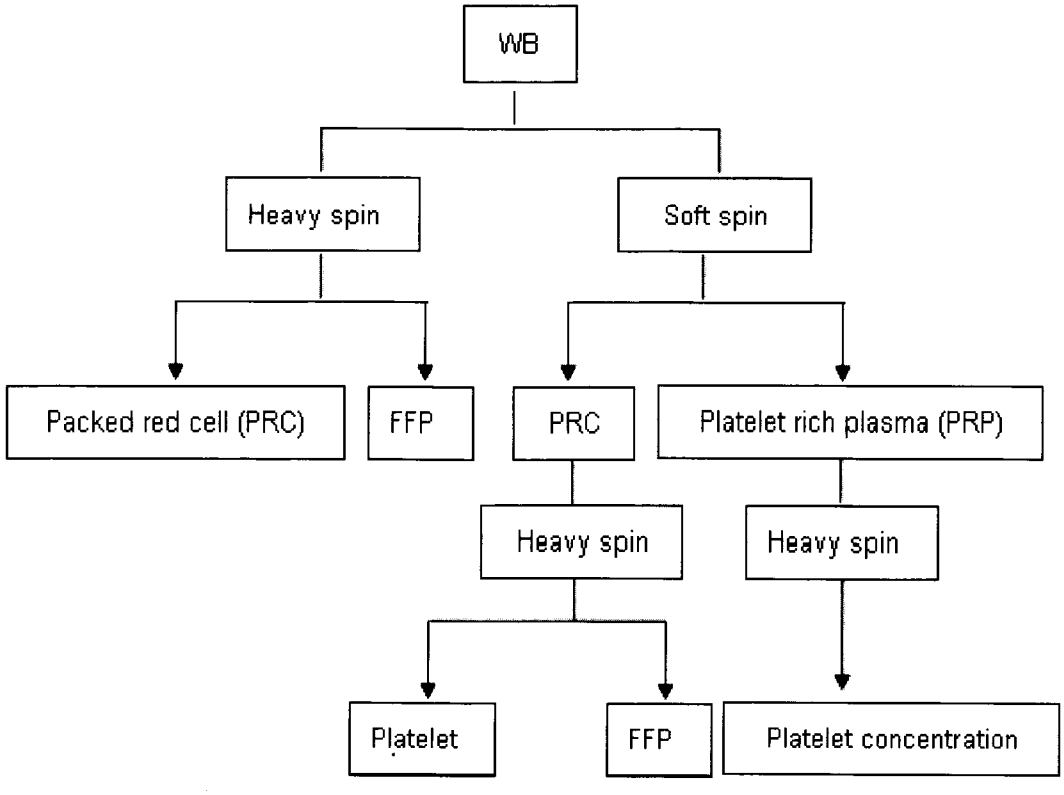
There are many indications[11] including replacing phlebotomy losses, treatment of symptomatic cardiac disease, treatment of severe respiratory distressed syndrome, surgical management, replacement of acute blood loss and exchange transfusion (in some diseases such as malaria and leptospirosis). Concerning the administration issues, cardiovascular system can only handle acute increases of 10 to 15 % without any compromise. Most units use single transfusion volumes of 10 to 20 % over 2 to 6 hours and dose of blood given are determined by hematocrit of the donor's blood. Freshness of the blood is also important. During the storage of blood 2,3 DPG decreases, pH decreases, extracellular potassium increases, and free HgB increases. Most blood banks use blood that is less than 7 days old. Preservation of donated blood by anticoagulation is suggested. Anticoagulants usually contain anticoagulant, buffer and energy sources for RBCs (citrate, sodium phosphate, dextrose). Citrate phosphate dextrose (CPD) is the most common preservative used in transfusions. One unit of whole blood contains 450 ml of donor's blood plus 60 ml of CPD. Other additives are not widely used due to their possible toxicities (adenine – renal toxicity, mannitol – osmotic diuretic effects and dextrose – hyperglycemia).

It should also be noted that no data suggest that parents' or relatives' donated blood is safer than banked blood. Indeed, parents should not donate blood to their children because it decreases the future chance that a parent can provide organs to their children for transplant and maternal plasma in postpartum period usually contains numerous allpantibodies against paternal red blood cells, white blood cells, platelets, and HLA antigens.

Blood component from donation

One unit of blood is consisted of several components. The main components included red cells, platelets, plasma and white cells (normally not used). [12] Before making a transfusion, the physician in charge must consider that the blood can be or cannot be transfused. Transfusion should be cancelled in cases of failures during the production which do not pass quality control, outdated and delivered to the department within more than ½ hour. The preparation of blood component has many steps passing many spinning as shown in Figure 1.

A. Spinning.



B. Plasma fractionation pathway.

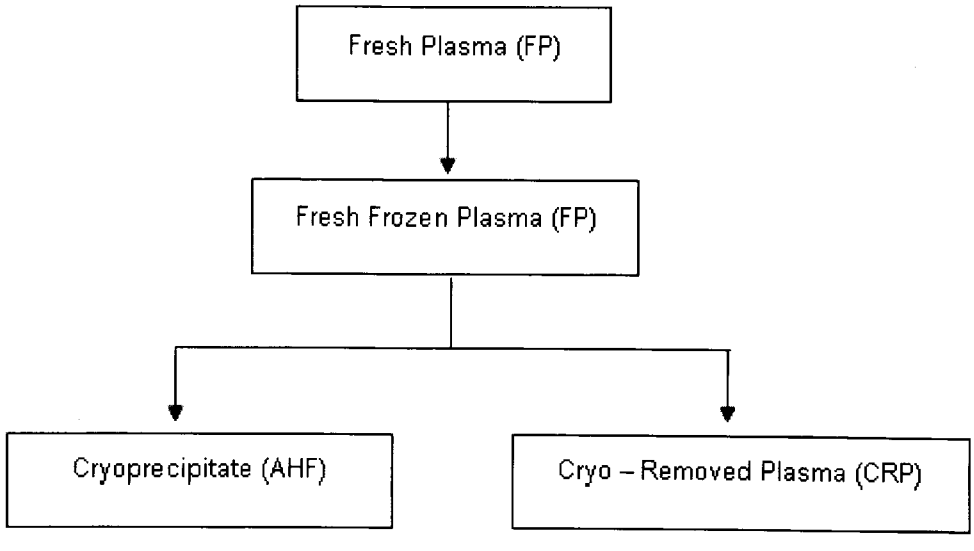


Figure 1. Steps for blood component preparations.

Important blood components include

1. Red blood cells

Red blood cells must be filtered. Increased hemolysis with small needles for administration can be seen. It should be noted that fresh blood is less prone to hemolyze and pumps do not damage the red cells. Also, blood warmers do not damage the cells. The main indications include acuted severe anemia and chronic anemia with heart and lung disease. The dosage depends on the patient's age, diseases, symptoms. The usefulness of red cell transfusion is the increase of red cell that helps increase oxygen transportation. Klein *et al.* said that laboratory assays that indicated failing tissue oxygenation would be ideal to guide the need of transfusion, but none had been proved easy, reproducible, and sensitive to regional tissue hypoxia. [13]

2. Leukocyte depleted (poor) blood (LPB) [14]

Preparation of LPB is by refrigerated Centrifugation or specific leukocyte filter (Sepacell R500, Imugard IG500, Pall RC100). The indication include use for the prevention of transfusion reaction, alloimmunization to leukocyte antigen, platelet refractoriness and CMV infection.

3. Platelets

The main indication for platelet transfusion is the treatment or prevention of bleeding in profoundly thrombocytopenic patients with bone marrow failure due to malignancy and/or myelosuppressive therapy.[15] The satisfied post transfusion platelet level has to be judged in each individual patient. It is usually done with a single transfusion and can be transfused as rapidly as the patient's condition permits (1 to 2 hours). It should be noted that storage at room temperature is requested but it can increase bacterial risk. At room temperature, platelet can be stored for 5 days. The effect of platelet concentrate storage temperature (4 ^{o}C versus room temperature) on platelet adenine nucleotide metabolism was studied by Filip *et al.* [16] The results of concentrates stored at room temperature, with a final pH above 6.0, were not inferior to the results for those stored at 4 ^{o}C. Filip *et al.* proposed that storage at both temperatures were associated with conversion of ATP in the metabolic adenine nucleotide pool to hypoxanthine. [16]

Fresh Frozen Plasma (FFP) [17-18]

FFP is separated from whole blood (WB) within 8 hours and immediately frozen in ethanol bath at -4 ^{o}C or freezer at -18 ^{o}C. The derived FFP should be stored at the temperature of -25 ^{o}C or lower.[19] One unit consists of factor VIII > 0.7 I.U. /ml, red blood cells < 0.6 x 10^9 cells/L, white blood cells < 0.1 x 10^9cells/L, platelets < 50 x 10^9 cells/L. The thawing can, for example, appear in a package, i.e. a plastic bag in a water bath (refresh/clean daily) of 37 ^{o}C (with temperature monitoring).[19] The indication of FFP transfusion includes single or multiple coagulation factors deficiency, reversal of warfarin therapy, plasma exchange therapy for thrombotic thrombocytopenic purpura. [20]

Cryoprecipitate (Anti-Hemophilia Factor, AHF) [15]

One unit of cryoprecipitate contains factor VIII: C 80 -100 I.U., factor VIII : vWF 40 -70 %, fibrinogen 150 - 300 mg, factor XIII 20 -30 % and plasma 5 -10 ml. The main indication of cryoprecipitate transfusion

includes hemophilia A, von Willebrand's disease, obstetric complication, congenital or acquired fibrinogen deficiency, factor XIII deficiency and DIC.[20] However, an important risk of cryoprecipitate is virus contamination. Evatt *et al.* noted that over a lifetime of treatment (60 years), the cumulative risk of HIV exposure for a person with haemophilia who received monthly infusion of cryoprecipitate prepared from plasma was estimated as 2 % in the USA and 40 % in Venezuela.[21] Considering the cumulative risk for transmitting HIV to patients with haemophilia through cryoprecipitate treatment, medical care providers should carefully evaluate the use of cryoprecipitate and reserve it for emergency conditions or when no virally inactivated products are available. The present trend is changing from cryoprecipitate to virus-safe high-purity concentrate. [22]

Cryo - removed plasma (CRP) [15]

One unit of CRP contains plasma volume 200 ml, all stable coagulation factors and proteins. The main indication of CRP transfusion includes hemophilia B, replacement of prothrombin complex (Factor II, VII, IX, X) and volume expansion.[20] A summary of important indications for transfusions of blood components[23] is given in Table 1.

Conclusion

There are many groups of patients who share common needs to receive extensive blood transfusions. Details of important blood components are summarized in this article.

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Table 1. Indication of blood component transfusion.

Components	Indications
Whole blood	acute massive blood loss
PRC	severe anemia
platelet	profound thrombocytopenia
FFP	coagulation factor deficiency, severe coagulopathy
Cryoprecipitate	hypofibrinogenemia, hemophilia A
Cryo – removed plasma	hemophilia B, volume expansion

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