

## **BLOOD COMPONENT THERAPY 2003**

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Puget Sound Blood Center and Program

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## **TRANSFUSION CONSULTATIONS**

The Blood Center Transfusion Services Laboratories operate 24 hours a day. Questions about samples, procedures, blood component orders or delivery should be directed to the University District Laboratory (from UWMC, CHRMC & Northwest Hospital) or the Central Transfusion Laboratory (from other hospitals). A Blood Center physician with full responsibility for transfusion services is on call at all times to resolve problems or provide medical consultation. The Blood Center physician on call may be paged by contacting any of the Transfusion Service Laboratories.

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## **IMPORTANT PHONE NUMBERS**

### **Puget Sound Blood Center**

- Transfusion service and Director on call for consultation, (206) 292-6525
- University District Lab, (206) 522-2462
- East Side Laboratory, (425) 453-4560

### **Hospital Blood/Transfusion Services**

- Children's Hospital and Regional Med Center, (206) 528-5151
- Evergreen Hospital, (425) 899-2730
- Group Health Coop, Central Hospital, (206) 326-3366
- Group Health Coop, East Side, (425) 883-5141
- Harborview Medical Center, (206) 731-3088
- Northwest Hospital, (206) 368-1344
- Overlake Medical Center, (425) 688-5107
- Seattle Cancer Care Alliance, (206)288-1095
- Swedish Medical Center, First Hill, (206) 386-2212
- Swedish Medical Center, Ballard, (206) 781-6360
- Swedish Medical Center, Providence Campus, (206) 320-3738
- University of Washington Medical Center, (206) 598-6240
- Valley Medical Center, (425) 228-3450, Ext. 5945
- Veterans Affairs Medical Center, (206) 764-2234
- Virginia Mason Medical Center, (206) 625-7257

## **RED BLOOD CELLS**

### **Description**

One unit of "packed" red blood cells (RBC) contains approximately 200mL red blood cells, 100 mL Optisol AS-5® (a solution added to extend storage life) and ~30mL plasma. All red blood cell transfusions must be ABO/Rh compatible with the recipient, so, in dire emergency, type O negative can be used for all patients. RBC do not provide viable platelets, nor do they provide clinically significant amounts of coagulation factors. RBC must be stored between 1-6° C and have a shelf life of 42 days.

### **Indications**

RBC are indicated for patients with symptomatic anemia who are not treatable, within a reasonable amount of time considering their symptoms, with specific therapy such as iron, vitamin B12 or folic acid.

### **Therapeutic Effect**

In a 70 kilogram adult, each unit should increase the hematocrit by 3-4%.

## **EMERGENCY BLOOD USAGE**

Many hospitals in the Puget Sound area have a small supply of uncrossmatched type O RBC's to be used for a bleeding patient in dire emergency. Type O, Rh-negative RBC's can be transfused to people of any type with only a slight risk of hemolysis. This risk increases in patients who have previously been transfused or pregnant and may have formed antibodies. At Harborview Medical Center a supply of uncrossmatched type O, Rh-positive RBC's is also available. Type O, Rh-positive RBC's can be used for women who are beyond childbearing age and in males. When Rh-positive RBC's are used in an Rh-negative patient, there is a chance of a D immunization, and they, therefore, should be used only in life-threatening emergencies. When type O, Rh positive RBC's are available, the following algorithm should be followed:

1. For all patients under 16, use type O, Rh negative RBC's
2. For females under 50, use type O, Rh negative RBC's
3. For males older than 18 and women beyond childbearing, use type O, Rh-positive RBC's
4. If the supply of the appropriate Rh type has been exhausted, RBC's of the other type should be used.

Rhogam® should be given within 48 hours of giving Rh positive blood to an Rh negative woman of childbearing age. If no uncrossmatched blood is available, type O RBC's of the appropriate Rh type that is being held for another patient may be used in life-threatening emergency. The Puget Sound Blood Center must be informed immediately that this has occurred so that these units can be replaced. A signed justification is needed for all use of uncrossmatched blood.

## SPECIAL CONSIDERATIONS IN PEDIATRIC TRANSFUSIONS

### Additive Solutions

There have been no reports of toxicity with transfusion of large volumes of red blood cells stored with additive, anticoagulant-preservative solutions (e.g. Optisol AS5\*). However, because of the theoretic risk of toxicity secondary to manitol and adenine contained in standard additive solutions, a limited number of red blood cells are stored in CPD (citrate/phosphate/dextrose), which contains neither manitol nor adenine. These CPD RBC's are primarily given to infants receiving large volume or rapid transfusion; all units are < 5 days of age and leukoreduced.

The following guidelines have been adopted by the CHRMC Blood Usage Committee for RBC transfusion:

#### Infants <4 months of age\*

ECMO, Liver Transplant	CPD RBC's, leukoreduced
Rapid or Large volume	
Exchange Transfusion	Reconstituted Whole Blood(CPD Oneg RBC's, AB FFP) leukoreduced RBC's

#### Children <2years of age\*

Priming cardiopulmonary bypass	CPD Whole Blood, leukoreduced**
Intraoperative cardiopulmonary bypass	CPD RBC's, leukoreduced
Routine transfusions*	Standard Additive (Optisol AS5*)

\* See pages 9-10 for recommendations on blood component modification.

\*\* It should be noted that there are no viable platelets in Whole Blood because of refrigerated storage. Factor VIII activity decreases rapidly in storage and will not be present in therapeutic levels. Other coagulation factors, including fibrinogen, in whole blood are at essentially normal levels at 5 days.

### Therapeutic Effect

In children receiving CPD RBC's, 1mL/kg should raise the hct 1%. In children receiving RBC's in standard additive, 1mL/kg should raise the hct .5 - .7%.

## **PLATELETS**

### **Description**

Platelets are essential for the initial phase of hemostasis. Platelet concentrates also contain about 60mL of plasma (coagulation factors) and small numbers of red blood cells and leukocytes. Platelet units must be maintained at room temperature and agitated during storage.

Pooled random donor platelet concentrates are prepared from platelets that have been harvested by centrifuging units of whole blood. Up to 8 units of platelets, each from a separate donor, can be pooled into a single bag for transfusion. Platelets expire 4 hours after pooling. All units are from the same ABO type. If ABO compatible platelets are unavailable, ABO incompatible platelets can be substituted with very little risk. The usual adult dose is 4-6 units of pooled random donor platelets.

Apheresis platelets, collected from a single donor, are prepared in standard (equivalent to ~4 pooled units) and "large" (equivalent to ~6 pooled units) sizes. An apheresis platelet concentrate contains 200-400mL of plasma. They may be collected as a random unit (random apheresis platelets or "RAP") or be obtained for a specific recipient from a family member or a volunteer HLA compatible "community" donor. Apheresis platelets expire 4 hours after processing for release from the blood center.

### **Indications**

1. To prevent bleeding due to thrombocytopenia. The threshold of thrombocytopenia at which bleeding may occur will vary depending on the patient's clinical condition. In general, spontaneous bleeding does not occur until the platelet count falls below 5,000 - 10,000/ $\mu$ L. The recommended "trigger" for prophylactic platelet transfusions in patients undergoing chemotherapy or hematopoietic stem cell transplantation is  $<10,000/\mu$ L.
2. In a bleeding patient a platelet count above 50,000 should be maintained. In a surgical patient, the necessary platelet count varies depending on the procedure. For most surgeries 50,000/ $\mu$ L will be adequate. For high risk procedures, such as neurologic or ophthalmologic surgeries, 100,000/ $\mu$ L is recommended.
3. Abnormal platelet function may be congenital, or due to medications, sepsis, malignancy, tissue trauma, obstetrical complications, extra corporeal circulation, or organ failure such as liver or kidney disease. Spontaneous bleeding may then occur at higher platelet counts. If platelet dysfunction is present, the patient with a disrupted vascular system (e.g. trauma or surgery) will require a higher platelet count to achieve hemostasis.
4. Family donor or HLA matched platelets are indicated when patients have become refractory to random donor platelet transfusions due to alloimmunization.
5. In several situations platelet transfusions may not be indicated unless there is significant bleeding. In autoimmune thrombocytopenias (e.g. ITP) transfusion increments are usually poor and platelet survival is short. Platelet transfusions are contraindicated in patients with thrombotic thrombocytopenic purpura (TTP) unless there is clinically significant threatening bleeding.

## Therapeutic Effect

Expected Platelet Increment			
	1 unit	4 units	6 units
	$1.0 \times 10^{11}$	$4.0 \times 10^{11}$	$6.0 \times 10^{11}$
50 lb/23 kg	22,000/ul	88,000/ul	132,000/ul
100 lb/45 kg	11,000	45,000	66,000
150 lb/68 kg	7,400	30,000	44,000
200 lb/91 kg	5,500	22,000	33,000

\* In a patient with a normal sized spleen and without platelet antibodies.

The survival of transfused platelets averages 3 to 5 days but will decrease if a consumptive process is present. Correction of a prolonged bleeding time in platelet dysfunction will depend on whether a condition exists that will affect the transfused platelets as well (e.g., aspirin, uremia).

## **FRESH FROZEN PLASMA (FFP)**

### **Description**

One unit of FFP is the plasma taken from a unit of whole blood. It is frozen within eight hours of collection. FFP contains all coagulation factors in normal concentrations. It is free of red blood cells, leukocytes and platelets. One unit is approximately 250mL and must be ABO compatible. Rh factor need not be considered. Since there are no viable leukocytes, FFP does not carry a risk of CMV transmission or Graft Vs. Host Disease (GVHD).

### **Indications**

FFP transfusion is indicated in patients with documented coagulation factor deficiencies and active bleeding, or who are about to undergo an invasive procedure.

Deficiencies may be congenital or acquired secondary to liver disease, warfarin anticoagulation, disseminated intravascular coagulation, or massive replacement with red blood cells and crystalloid/colloid solutions. FFP should not be used for Hemophilia B (Factor IX) deficiency unless Factor IX concentrate is not available.

Usually, there is an increase of at least 1.5 times the normal PT or PTT or an INR \* 1.6 before clinically important factor deficiency exists. This corresponds to factor levels <30% of normal.

Reversal of warfarin anticoagulation with FFP is indicated only if significant bleeding or risk is present. Often it will require recurrent transfusion to maintain normal factor levels. Otherwise, reversal can be achieved by giving Vitamin K two to three days prior to a planned procedure.

FFP is indicated in the treatment of thrombotic thrombocytopenic purpura (TTP), usually in conjunction with plasma exchange.

FFP should not be used for volume expansion unless the patient also has a significant coagulopathy and is bleeding.

### **Fresh Frozen Plasma Dosage**

- Volume of 1 Unit FFP: 200-250 ml
- 1 mL plasma contains 1 u coagulation factors
- 1 Unit FFP contains 220 u coagulation factors
- Factor recovery with transfusion = 40%
- 1 Unit FFP provides ~80 u coagulation factors
- 70 kg X .05 = plasma volume of 35 dL (3.5 L)
- $\frac{80 \text{ u}}{35 \text{ dL}} = 2.3 \text{ u/dL} = 2.3\%$  (of normal 100 u/dL)

### **In a 70 kg Patient**

- 1 Unit FFP increases most factors ~2.5%
- 4 Units FFP increase most factors ~10%

## Therapeutic Effect

Usually an increase in factor levels of at least 10% will be needed for any significant change in coagulation status, so the usual dose is four units, but the amount will vary depending on the patient's size and clotting factor levels. Hematology consultation is advised concerning the dose of plasma.

<b>Recommended Coagulation Parameters for Common Procedures</b>		
	<b>Platelet Count*</b>	<b>INR</b>
Lumbar Puncture	=50,000	=1.5
Paracentesis	=30,000	=2.0
Thoracentesis	=50,000	=1.5
Transbronchial Lung Biopsy	=50,000	=1.5
Subclav/IJ Line	=30,000	=1.5
Renal Biopsy	=50,000	=1.5
Liver Biopsy	=50,000	=1.5
Hickmann, Groshong Catheters	=50,000	=1.5

\*These numbers assume normal platelet function. Conditions that may affect platelet function include renal failure, medications, leukemias and myelodysplasias, and congenital disorders. Bleeding Time is a poor predictor of surgical bleeding. The Usefulness of Platelet Function Analysis (PFA) in predicting surgical bleeding is unknown.

## **CRYOPRECIPITATE (CRYO)**

### **Description**

Cryoprecipitate is prepared from plasma and contains fibrinogen, von Willebrand factor, factor VIII, factor XIII and fibronectin. Cryoprecipitate is the only adequate fibrinogen concentrate available for intravenous use.

Cryoprecipitate is available in pre-pooled concentrates of six units. Each unit from a separate donor is suspended in 15 mL plasma prior to pooling. For use in small children, up to 4 single units can be pooled. Each unit provides 350 mg of fibrinogen.

### **Indications for Cryoprecipitate**

Cryoprecipitate is indicated for bleeding or immediately prior to an invasive procedure in patients with significant hypofibrinogenemia (<100 mg/dL). Cryoprecipitate should not be used for patients with von Willebrand disease or Hemophilia A (Factor VIII deficiency) unless they do not (or are not known to) respond to DDAVP and recombinant and/or virally inactivated preparations are not available. It is not usually given for Factor XIII deficiency, as there are virus-inactivated concentrates of this protein available. Cryoprecipitate is sometimes useful if platelet dysfunction associated with renal failure does not respond to dialysis or DDAVP.

### **Cryoprecipitate Dosage**

- 1 bag contains ~350 mg Fibrinogen
- 6 bags (1pool) contains 2100 mg Fibrinogen
- Recovery with transfusion = 75%
- 6 bag pool cryoprecipitate provides 1560 mg Fibrinogen
- $70 \text{ kg} \times .05 = \text{plasma volume of } 35 \text{ dL (3.5 L)}$
- $\frac{1560 \text{ mg}}{35 \text{ dL}} = 45 \text{ mg/dL}$  provided by 6 bag pool of cryoprecipitate

### **In a 70 kg Patient**

- 6 bags (1pool) of cryo raises Fibrinogen 45 mg/dL

Fibrinogen replacement: Effect can be monitored by fibrinogen level assay and clinical response.

**To replace factor VIII or von Willebrand factor:** When specific factor concentrates are unavailable, the usual adult dose is a pool of 6 - 12 bags. Approximately 150 units of factor VIII and von Willebrand factor are provided per bag. A single donor may be used repeatedly for a young or mildly affected patient to limit donor exposures.

**Fibrin glue:** Although single units of cryoprecipitate are available for use in the preparation of locally applied for surgery, commercially available, virally inactivated concentrates have a higher fibrinogen concentration and are preferred for this

purpose (Tisseel®). A patient may donate autologous plasma for processing into cryoprecipitate prior to a planned surgical procedure.

## TRANSFUSION RELATED RISKS

### Infectious Risk/Unit

Blood Centers began clinical trials in April 1999 to screen blood with a PCR test for HCV RNA and HIV DNA. Although confirmed data are not available, the current estimated risks/unit are:

- HIV 1:1,900,000
- Hepatitis C 1:1,000,000

The most recent estimated risks/unit for other viral transmissions are:

- Hepatitis B 1:137,000
- HTLV I & II 1:641,000

West Nile Virus (WNV) can be transmitted by blood transfusions but the risk is extremely low. PCR testing for WNV will begin in July 2003.

In CMV negative, immunosuppressed transplant and HIV positive patients, the risk of CMV infection is high. In the King County area the CMV sero-positive incidence in the donor population is about 50%. Leukocyte depletion of blood is equivalent to CMV seronegative blood in preventing CMV infection through transfusion, but is more expensive and indicated only if CMV negative blood is not available. It is unnecessary to order both. In some organ transplant recipients CMV negative blood is transfused to prevent infection with secondary strains.

Bacterial contamination is estimated to occur in  $\leq 1:542$  six unit platelet pools,  $\leq 1:777$  apheresis platelets and  $\leq 1:38,565$  rbc units.

### Transfusion Reactions

A transfusion should be stopped immediately whenever a transfusion reaction is suspected.

A **hemolytic transfusion reaction** occurs following transfusion of an incompatible blood component. Most are due to naturally occurring antibodies in the ABO antigen system. An acute hemolytic transfusion reaction may cause hemoglobin induced renal failure and a consumptive coagulopathy (DIC). Signs and symptoms include fever, hypotension, tachycardia, dyspnea, chest or back pain, flushing and severe anxiety. Hemoglobinuria may be noted and, in the anesthetized patient, may be the first sign of hemolysis. The diagnosis can be quickly made by centrifuging a tube of blood and examining the plasma for a reddish discoloration. A fresh sample of blood should be sent to the Blood Center for testing and all paper work and the patient's identification checked. Treatment involves fluids, diuresis and transfusion support for bleeding. A fatal hemolytic transfusion reaction occurs about once in 600,000 transfusions. Most errors are clerical or due to misidentification of a patient at the bedside.

**Delayed hemolytic transfusion reactions** usually occur in patients who have been previously sensitized to an antigen through transfusion or pregnancy. They can

result in symptomatic or asymptomatic hemolysis several days after a subsequent transfusion with recall of the antibody.

Transfusion of Rh positive red blood cells to an Rh negative woman of childbearing age can result in sensitization and hemolytic disease of the newborn in future pregnancies.

**Febrile transfusion reactions** usually occur due to sensitization to antigens on cell components, particularly leukocytes. Leukocyte depletion of red blood cells by filtration may be helpful in patients for whom this is a problem. Leukocyte reduced single donor pheresed platelets are a possible alternative to leukocyte depletion by filtration of pooled random donor platelets and are comparable in cost. Occasionally, removal of most of the plasma (volume reduction) may be necessary to remove cytokines in platelet preparations for patient with persistent febrile reactions.

Rarely, a febrile episode during a transfusion, particularly with platelets, is due to bacterial contamination (estimated in 1:500 to 1:2,000 platelet transfusions). If a bacterially contaminated component is suspected, the transfusion should be stopped and the bag returned to the Blood Center for culture. The patient should have blood cultures obtained and, if appropriate, IV antibiotic therapy begun.

**Transfusion Related Acute Lung Injury (TRALI)** occurs when donor plasma contains an antibody, usually against the patient's HLA or leukocyte specific antigens. Less often, the patient may have antibodies against donor leukocytes in the component. Symptoms of dyspnea, hypotension and fever typically begin 1-2 hours after transfusion and the chest x-ray shows diffuse non-specific infiltrates. Ventilatory support may be required for several days before resolution. The Blood Center should be notified so that the donor may be tested for antibodies against the patient.

**Urticarial and allergic type reactions** are the most common and usually due to allergies to specific proteins in the donor's plasma and can be avoided with future transfusions by pretreatment with antihistamines or steroids. Only if severe (anaphylaxis), are washed RBC's and platelets to remove all plasma indicated.

### **Immune Modulation**

Transfusions have been known to induce immune tolerance following the observation made more than 20 years ago that multiply transfused kidney transplant recipients had an increased graft survival rate. In addition, some studies suggest that transfusion may increase the rate of post-operative bacterial infection. There is also evidence from animal studies that transfusion increases the risk of metastatic disease, although data in humans are inconclusive.

Sensitization to foreign donor HLA antigens, or alloimmunization, can lead to poor platelet transfusion increments. Patients may respond to pheresed platelets from HLA-matched donors or close family members.

Removal of donor leukocytes has been shown to decrease the immunomodulatory effects of blood transfusions but the clinical usefulness is clear only with alloimmunization.

## BLOOD COMPONENT MODIFICATION

### Recommendations

	<b>CMV Neg.</b> <sup>1,2</sup>	<b>Irradiation</b> <sup>3</sup>	<b>Leukocyte Reduced</b>
<b>BM/Stem Cell Transplant Candidate</b>	X	7	X
<b>Organ Transplant Candidate</b>	X		Candidates for heart and kidney transplant.
<b>Chemo Rx Only</b>		4	5
<b>AIDS/HIV+</b>	X		
<b>Febrile Rxn's 6</b>			X
<b>Neonate</b>	X	X	
<b>Any Lymphoproliferative Malignancy</b>		X	

1. For patients with negative or unknown CMV serology.
2. Leukocyte depletion may be used if CMV negative blood components are not available.
3. All components for stem cell transplant patients require irradiation. All directed donations from family members or HLA matched donors require gamma irradiation.
4. Irradiation may be indicated in severely immunosuppressive chemotherapy, such as is used to treat patients with acute leukemia.
5. Leukocyte reduced blood is recommended for patients who will undergo multiple cycles of chemotherapy that will require platelet transfusion support.
6. If uncontrolled by leukocyte depletion, volume depletion of platelets prior to transfusion may decrease febrile reactions.
7. Gamma irradiation is required pre-transplant for patients who may receive non-myeloablative ("mini") transplants.

### CMV Negative

CMV negative patients who are, or will be, severely immunosuppressed due to transplantation should receive only CMV negative platelets, whole blood and red blood cells to prevent primary CMV infection.

Premature infants and low birth weight neonates should receive CMV negative blood components regardless of serology.

Leukocyte depletion of blood is equivalent to CMV screening but is more expensive and indicated only if CMV negative blood is not available.

### Irradiation (gamma)

Inactivation of lymphocytes prevents transfusion induced GVHD due to engraftment of donor cells in an immunosuppressed patient.

### Leukocyte-depletion (leukopoor)

Removal of leukocytes by filtration of platelets and red blood cell concentrates is indicated for febrile transfusion reactions and when CMV negative components are indicated but not available.

Leukocyte depletion may prevent alloimmunization to platelets and should be used in patients who are expected to need platelet transfusions during multiple courses of chemotherapy and do not have pre-existing HLA antibodies.

### **Volume Reduced Platelets**

Removal of excess donor plasma is indicated in patients who cannot tolerate the full volume or when ABO incompatible single donor platelets are transfused. Volume reduction may be helpful in patients with febrile transfusion reactions that persist despite leukocyte reduction. Approximately 10% of the platelets are lost in this process and the extra centrifugation step may cause some platelet activation and loss of function.