

**BLOOD COMPONENT THERAPY**  
**2010**

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**University District Laboratory (206) 522-2462**

**East Side Laboratory (425) 453-4560**

**South Center Laboratory (425) 656-7900**

## **TRANSFUSION CONSULTATIONS**

The Puget Sound 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, Seattle Children's Hospital, Northwest Hospital, & Swedish Ballard) 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.

## RED BLOOD CELLS

### Description

One unit of 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 B<sup>12</sup>, folic acid or erythropoietin.

### Therapeutic Effect

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

## EMERGENCY RED BLOOD CELL USAGE

Many hospitals in the Puget Sound area have a limited 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. Type O, Rh-positive RBC's can be used for women who are beyond childbearing age and in males over the age of 16. When Rh-positive RBC's are used in an Rh-negative patient, there is a chance of D immunization, and 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 16 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 large amounts of Rh positive blood has been given red cell exchange may be necessary. 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 Red Cell Transfusions

There is concern for toxicity of red cell additive solutions containing adenine & mannitol to cause liver & renal dysfunction if given in large doses. The storage age of the red cell unit can affect extracellular potassium in the unit; too much potassium can cause cardiac toxicity. For these reasons, the choice of red cell products is based on the dose.

#### Definitions

- Routine or small volume transfusion: typically 10 mL/kg  
(Indications: Routine transfusion, anemic NICU patient from blood draws)
- Large volume transfusion: 20-25 mL/kg  
(Indications: IUT, cardiac surgery with bypass, ECMO, trauma)
- Infant blood protocol: 1 sample from baby <4m used until baby is 4m, to prevent excess phlebotomy.

#### Products

(1) Pedi-pack = RBC CPD Divided Unit

- Volume: ~70mL (1/4 of a regular sized rbc unit plus preservative)
- Preservative: CPD (contains anticoagulant citrate, phosphate, dextrose, does not contain mannitol or adenine)
- Shelf-life: <7 days "fresh", expires on day 8
- Attributes: Leukoreduced, HbS negative, Irradiated (if child <4m or if indicated otherwise)
- HCT of unit: 65%
- Indications: Used for small or large volume transfusions
- Dose: 10 – 15 mL/Kg will increase Hb ~2-3g/dL or Hct 7-9%

(2) Assigned aliquots = RBC AS-5 Divided Unit

- Volume: ~40mL (1/8 of a regular sized rbc unit plus preservative)
- Preservative/Additive: Optisol = AS-5 (similar as CPD, plus mannitol & adenine)
- Shelf-life: 42 days, one set of 8 units assigned to one patient
- Attributes: Leukoreduced, HbS negative, Irradiated (if child <4m or if indicated otherwise)
- HCT of unit: 57%
- Indications: Used for small volume transfusions, reduces donor exposure because all 8 aliquots are kept for one patient.
- Dose: 10-15mL/kg will increase Hb ~1.6 g/dL

(3) Reconstituted Whole Blood: Used for manual exchange transfusions. AS-5 leukocyte reduced, HbS negative, irradiated red cells and AB FFP. Platelets are not supplied in this product; post-procedure platelet count should be obtained.

### PLATELETS

#### Description

Platelets are essential for the initial phase of hemostasis. Platelet concentrates also contain about 60mL of plasma 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** are collected from a single donor and are equivalent to ~4-6 pooled units. An apheresis platelet concentrate contains 200-400mL of plasma. They may be collected as a random unit (random apheresis platelets) or be obtained for a specific recipient from a family member or a volunteer HLA compatible "directed" donor. Apheresis platelets expire 4 hours after processing for release from the blood center unless incubated storage is available at the local hospital.

## 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. Other coexisting clinical conditions may increase this "threshold".

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 30,000-50,000/ $\mu$ 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 may be contraindicated in patients with **thrombotic thrombocytopenic purpura** (TTP) unless there is clinically significant bleeding.

6. In **pediatric patients**, the usual platelet dose is 1 unit whole blood platelet per 10 kg child, or 5 mL/kg. A 50,000/  $\mu$ L rise is expected.

## Therapeutic Effect

### **Expected Platelet Increment\***

	1 unit $1.0 \times 10^{11}$	4 units $4.0 \times 10^{11}$	6 units $6.0 \times 10^{11}$
50 lb/ 23 kg	22,000/ $\mu$ l	88,000/ $\mu$ l	132,000/ $\mu$ l
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., antiplatelet agents, uremia).

## FRESH FROZEN PLASMA (FFP) AND THAWED PLASMA

### Description

One unit of FFP or thawed plasma is the plasma taken from a unit of whole blood. FFP is frozen within eight hours of collection. FFP contains all coagulation factors in normal concentrations. Thawed plasma may be transfused up to 5 days after thawing and contains slightly decreased levels of Factor V (66+9%) and decreased Factor VIII levels (41+8%). Plasma 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, plasma does not carry a risk of CMV transmission or Graft Vs. Host Disease (GVHD).

### Indications

Plasma 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. FFP, but not thawed plasma, can be used for Factor V deficiency. Recombinant or Factor VIII concentrates should be used to replace Factor VIII.

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

**Reversal of warfarin anticoagulation** with plasma 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 or holding warfarin two to three days prior to a planned procedure. Rapid reversal for life threatening bleeding may be achieved with recombinant Factor VIIa (Novo7®).

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

Plasma should not be used for volume expansion unless the patient also has a significant coagulopathy and is bleeding. **Pediatric patients** dosing is 10-15mL/kg, to provide ~15-20% rise in factor levels.

### **Plasma - Dosage**

Volume of 1 Unit Plasma: 200-250 mL

1 mL plasma contains 1 u coagulation factors

**1 Unit contains 220 u coagulation factors**

Factor recovery with transfusion = 40%

**1 Unit 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)

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**In a 70 kg Patient:**

**1 Unit Plasma increases most factors ~2.5%**

**4 Units Plasma increase most factors ~10%**

### Initial dose of FFP

$\frac{10\text{cc/Kg (round up to nearest 200cc)}}{200 \text{ cc/unit FFP}} = \text{\#units FFP}$

### 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.

### **Recommended Coagulation Parameters for Common Procedures**

	<u>Plt Count*</u>	<u>INR</u>
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 ordered. Each unit provides about 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 kg X .05 = plasma volume of 35 dL (3.5 L)  
1560 mg = 45 mg/dL provided by 6 bag pool of cryoprecipitate  
35 dL

**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.

**Pediatric** dosing for cryoprecipitate is 1 unit per 10kg child, which should increase fibrinogen by 60 - 100 mg/dL.

**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 fibrin glue to be applied locally 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: 1,000,000
HTLV I & II	1: 641,000

West Nile Virus (WNV) can be transmitted by blood transfusions but the risk is extremely low. PCR testing is performed to detect WNV. At the current time no cases of WNV in humans has been reported in Washington State. Rarely, Chagas disease (*Trypanosoma cruzi*) has been transmitted through transfusion. Testing is done on donors who have lived in or were born in endemic areas (Central & South America).

In **CMV sero-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 sero-negative blood in preventing CMV infection through transfusion, but is more expensive and indicated only if CMV sero-negative blood or platelets are not available. In some organ transplant recipients CMV sero-negative blood is transfused to prevent infection with secondary strains.

Bacterial contamination was previously estimated to occur in <1:2000 platelet concentrates and  $\leq$  1:38,565 rbc units. Bacterial testing of platelet concentrates has significantly decreased this risk from platelet transfusions.

### 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, nausea, vomiting, 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 due to an anamnestic 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. Generally these reactions are quite severe with high fever, rigors and/or other systemic symptoms such as hypotension, nausea or vomiting. If a bacterially contaminated component is suspected, the transfusion should be stopped and the bag sent for gram stain and culture. The Blood Center should be notified. 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 30 minutes to 6 hours after transfusion and the chest x-ray shows diffuse non-specific infiltrates. Ventilatory support may be required for several days before resolution. Therapy is primarily supportive. 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, 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. IgA deficiency should be considered in the case of anaphylactic reactions.

### 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 family members. HLA alloimmunization also decreases the likelihood of finding a compatible donor for heart or renal transplant.

Removal of donor leukocytes has been shown to decrease the immunomodulatory effects of blood transfusions but the clinical usefulness is clear only in the prevention of alloimmunization in patients undergoing chemotherapy for AML.

### BLOOD COMPONENT MODIFICATION

#### CMV Sero-negative

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

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

Leukocyte depletion of blood is equivalent to CMV screening but is more expensive and indicated only if CMV sero-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-reduction (“leukopoor”)

Removal of leukocytes by filtration of platelets and red blood cell concentrates is indicated for febrile transfusion reactions and when CMV sero-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.

#### Washed Red Blood Cells and Platelets

Patients with severe life threatening plasma allergies uncontrolled by medications or volume reduction may require red blood cells or platelets to be resuspended in saline. Washed red blood cells must be transfused within 24 hours or be wasted. The recovery and function of platelets after washing are severely impaired.

Recommendations:

	<u>CMV</u> <u>Neg.</u> <sup>1,2</sup>	<u>Irradiation</u> <sup>3</sup>	<u>Leukocyte</u> <u>Reduced</u>
<b>BM/ Stem Cell Transplant Candidate</b>	√	4	5
<b>Organ Transplant Candidate</b>	√		Candidates for heart and kidney transplant
<b>Chemo Rx Only</b>		6	7
<b>AIDS/HIV+</b>	√		
<b>Febrile Rxn's</b>			√8
<b>Neonate</b>	√	√	
<b>Hematopoietic or Lymphoproliferative Malignancy</b>		√	

1 - For patients with negative or unknown CMV serology.

2 - Leukocyte depletion may be used if CMV sero-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 - Gamma irradiation is required pre-transplant for patients who may receive non-myeloablative ("mini") transplants.

5 - Required to prevent alloimmunization pre-transplant only.

6 - Irradiation may be indicated in severely immunosuppressive chemotherapy, such as is used to treat patients with acute leukemia, or with fludarabine rx.

7 - Leukocyte reduced blood is recommended for patients who will undergo multiple cycles of chemotherapy that will require platelet transfusion support.

8 - If uncontrolled by leukocyte depletion, volume depletion of platelets prior to transfusion may decrease febrile reactions.

## **IMPORTANT PHONE NUMBERS**

Puget Sound Blood Center Transfusion Service  
and Physician on Call for Consultation (206) 292-6525

Puget Sound Blood Center -  
University District Lab (206) 522-2462  
East Side Laboratory (425) 453-4560  
South Center Laboratory (425) 656-7900  
HLA Matched Platelet Program (425) 453-5098

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

Seattle Children's Hospital (206) 987-5151

Evergreen Hospital Medical Center (425) 899-3900

Group Health Coop  
Central Hospital (206) 326-3366  
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  
Ballard (206) 781-6360  
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

**Puget Sound Blood Center**

*Printed February, 2010*