

## 1. UCSD MEDICAL CENTER BLOOD BANK

The physicians and technologists of the UCSD Medical Center Blood Banks (Hillcrest and Thornton) want to assist you in meeting the transfusion needs of your patients. If problems arise, please call the Blood Bank Resident 3-5640/1 or the Blood Bank Medical Director, Dr. Thomas A. Lane at Hillcrest or Dr. Rearden at Thornton. Call the UCSD telephone operator (619 543-3767) to contact the covering Resident or Attending on nights and weekends. Problems should be referred to physician staff whenever possible.

The Blood Bank has strict requirements for patient identification on blood specimens that are to be used for obtaining blood products in order to assure patient safety. These requirements, or very similar ones are universally accepted and nearly all are mandated by Federal Law (FDA), CA State Law (DHS), or accrediting agencies (AABB, CAP, JCAHO). On rare occasions, the blood bank physician may waive some portion of a specimen requirement, if it is deemed to be in the best interest of the patient, but the lab technologists are not permitted to do this without physician approval.

Except to order autologous blood from the American Red Cross (ARC; 760 737-7921), or San Diego Blood Bank (619 296-6393) all requests for blood products must go through the UCSD Blood Bank.

## 2. STATE LAW & UCSD POLICY RE: INFORMED CONSENT

California State Law requires physicians to provide *all* patients who may require blood transfusion with specific information regarding the risks, benefits, and alternatives to blood transfusion, including the use of regular donor blood, autologous blood, or directed (donor specific) blood, and the availability of intraoperative or postoperative blood salvage, except in life threatening emergency (CA Health & Safety Code, Sec. 1645). If eligible, the patient must be given the option to pre-donate autologous blood prior to elective surgery, or the patient must waive this option in writing. It is UCSD Medical Staff policy (MCP 350.1B) that, except in life-threatening emergencies, all patients who are transfusion candidates are to receive "A Patient's Guide to Blood Transfusion" pamphlet from the State of CA regarding the risks, benefits, alternatives, and/or options concerning blood transfusion. The physician is responsible for educating the patient sufficiently in advance of scheduled procedures to ensure the above requirements are met and should document the discussion of these issues with eligible patients by completing the "Physician's Statement and Patient Consent for Blood Transfusion" form 151-132 and also ideally by making an entry in the progress record. The relevant forms are available for this purpose in inpatient and outpatient locations. Complete information regarding the Informed Consent requirement is available online in the UCSD Medical Center Policies website (<http://www-ucsdhealthcare.ucsd.edu/mcpweb/docs/350.1/doc.htm>). It is acceptable to obtain informed consent for blood transfusion only once every six months from patients who have ongoing transfusion requirements for chronic, stable medical conditions, such as Thalassemia, cancer or sickle cell anemia. In addition, it is unnecessary to obtain informed consent more than once in the event the patient requires

subsequent transfusions during the same hospitalization. Whenever there has been a change in the risks, benefits or alternatives to transfusion the physician must re-consent the patient for the blood transfusion.

Before ordering the transfusion of a blood product, consider the indication for the product, the dose, and whether an equally effective, but less risky therapeutic modality is available, eg DDAVP instead of cryoprecipitate for mild von Willebrand disease; or transfusion of crystalloid or colloids instead of FFP when only blood volume expansion is required. This manual will provide additional suggestions regarding alternatives to blood transfusion, where appropriate. The VA Medical Center has somewhat different policies and procedures, eg UCSD employs 100% leukocyte-reduced blood, but the VA does not.

### **3. HOW TO ORDER BLOOD PRODUCTS**

You may order:

#### **3.a Type and Screen (T & S)**

Typing involves determination of ABO and Rh types, and takes 5 minutes to perform under ideal conditions. Note that all turnaround times given in this book refer to the time required to perform the test. Additional time is required for the required blood specimen drawn from the patient and sent to the Blood Bank. In the near future, a second blood specimen for ABO/Rh typing will be required on all patients, to diminish the chance of a mistyping due to a blood draw mix-up (this occurs about 1/2000 blood draws by staff). The antibody screen tests recipient's plasma for the presence of blood group antibodies other than ABO antibodies using an indirect antiglobulin (Coombs) reaction, and takes about 30 minutes. Packed red blood cells can be provided within 15 minutes if the antibody screen is negative. If the T & S is negative, it is safe to give type specific blood without a classical "crossmatch" (see below), as <1/50,000 patients whose plasma tests negative by antibody screen will have a rbc antibody that might cause a significant hemolytic reaction. The T & S is appropriate for many surgical patients who are unlikely to need blood. Refer to the Surgical Blood Order Schedule in this booklet for recommended blood orders on surgery patients.

#### **3.b Type and Crossmatch**

This procedure, in addition to performing the type and screen, ensures the availability of the requested number of donor blood units for the recipient using a donor unit of the same or compatible ABO and Rh type as the recipient. Patients with a negative antibody screen will have either an abbreviated or "electronic" crossmatch to confirm ABO compatibility and up to 4 units can be made available in about 30 minutes. "Routine" blood orders are available within 8 hours; "ASAP" orders are available within 4 hours and "STAT" orders are available within 1 hour. Emergency (uncrossmatched) blood orders are described below. Do not specify STAT crossmatch unless blood is urgently

needed. Indiscriminate use of stat requests may jeopardize the speed of blood delivery to other patients who need blood quickly. The Blood Bank staff will call the nursing unit when the units that have been ordered STAT are ready. Patients who have unexpected anti-red blood cell antibodies (ie, a positive antibody screen) will require additional lab work and time to have the red cell alloantibodies identified, in order to provide compatible blood. In these patients, a classic antiglobulin crossmatch (anti-IgG) will be carried out before releasing the blood. In addition to the time required to identify antibodies, the antiglobulin crossmatch takes 60-90 minutes for up to 6 units. Blood held for surgical patients is released for use by other patients following surgery unless ordered otherwise.

### **3.c Recrossmatch**

A new blood compatibility specimen (recrossmatch) is required every 3 days (expiring at midnight of the 3<sup>rd</sup> day), since significant new antibodies may arise within 72h if the patient has been transfused within the last 3 months. A slip with the recrossmatch time is provided with the first unit issued and will indicate when a new specimen is required (Hillcrest). In the near future you may also ascertain the recrossmatch time from the Blood Bank Menu in the Lab Section of PCIS. The specimen drawn for a recrossmatch should be drawn no earlier than 2 hours before the recrossmatch time, to limit unnecessary blood draws from the patient.

### **3.d Hold Blood Specimen**

Obstetrics and Trauma Services only. No type or crossmatch done. Useful when blood use is unlikely, *e.g.*, normal delivery. Specimens are reserved for 3 days.

### **3.e Patients with Red Cell Antibodies (Positive Antibody Screen)**

Patients whose plasma gives a positive red cell antibody screen (also referred to as an indirect Coombs test) require extra time to obtain compatible blood. About 1/100 transfusions or pregnancies will result in the formation of an antibody to a foreign red cell antigen. Many of these antibodies can cause a severe hemolytic reaction, while others are clinically insignificant and can be ignored. The Blood Bank must first identify the antibody to ascertain its clinical relevance. This may take from several hours to several days. Clinically significant antibodies usually require a search for red cell units that lack the sensitizing antigen. This too, may take from hours to days. Try to give the Blood Bank extra lead time in these cases. ***If a patient with a positive antibody screen requires transfusion before the antibody can be identified and appropriate blood can be obtained, the Blood Bank will supply the safest blood available, consistent with the patient's needs. This may consist of uncrossmatched blood (see below) or crossmatch compatible blood, or possibly even blood that is incompatible by crossmatch.*** In the above cases, the physician must signify his/her understanding of the added risk of transfusion reaction in such cases by signing a "waiver" letter.

### **3.f Patients with a Positive Direct Coombs (Antiglobulin) Test (DAT)**

Direct Coombs testing is not performed as part of red cell compatibility testing, but only on specific request by the physician or as part of an antibody identification procedure in a patient with a positive indirect Coombs test, ie a positive antibody screen. A positive DAT indicates an immune reaction has taken place on the patient's rbc (either patient's own or transfused rbc). A patient with a positive DAT should be evaluated for hemolysis (blood smear, LDH, indirect bilirubin, reticulocytes, haptoglobin, etc) due to autoimmune antibody or a drug-induced auto-antibody. The use of 2nd and 3rd generation cephalosporins (eg cefotetan, cefotaxime et al; check with Pharmacy) is the most common cause of serious or fatal drug-induced hemolytic anemias; consequently the previous and current drug therapy of patients with a positive DAT should be carefully evaluated and consideration should be given to substituting antibiotics other than these when possible. Many other drugs, eg penicillin, quinidine, can cause immune red cell hemolysis, but rarely with the same severity as 2nd and 3rd generation cephalosporins. Autoimmune antibodies may be idiopathic, associated with B-cell malignancies, autoimmune diseases, infections, or due to drugs, eg procainamide, alpmethyl dopa. The DAT is frequently positive in patients with HIV infection. Autoimmune IgG antibodies are usually benign, but occasionally cause mild to severe hemolytic anemia requiring urgent red cell transfusions despite plasma incompatibility with all red cells. In general, patients with warm reacting autoantibodies will not destroy transfused rbc faster than their own rbc and transfusion is safe (there are reports of thrombotic episodes in the rare cases of HIV patients with severe autoimmune hemolytic anemia who are transfused). In contrast, patients with high titer cold reactive autoantibodies (see below) may have severe acute hemolysis upon transfusion. Early steroid treatment (eg Prednisone 1 mg/kg/d or equivalent) usually ameliorates hemolysis sufficiently in patients with warm reactive autoantibodies to permit transfusion of "least incompatible" red cells without significant hemolytic reactions. More difficult from the transfusion perspective in such cases, however, is that the presence of the *autoantibody* may make it difficult or impossible for the Blood Bank to identify or rule out the coexistence of significant red cell *alloantibodies* in the patient's plasma. Up to 40% of patients who have autoantibodies also have coexisting alloantibodies. In contrast with autoantibodies, alloantibodies to rbc may cause severe hemolysis of transfused red cells. Consequently, when a patient has an autoantibody that may mask an alloantibody, transfusion should be undertaken only with careful monitoring and the full cooperation of the Blood Bank (see below, Incompatible Crossmatch). Autoimmune IgM antibodies (typically cold-reactive), if present in sufficiently high titer, are associated with severe hemolysis of the patient's own red cells and transfused red cells, despite steroid treatment. There are also rare cases of red cell agglutination in coronary arteries and hemolysis during surgery that employs cold cardioplegia in patients with symptomatic cold agglutinin disease or high titer cold agglutinins. Apart from the use of steroids, warmed blood and a warm room (for patients with cold reactive autoantibody), the management of these patients is beyond the scope of this manual, but may include IVIG and plasmapheresis. Other diagnostic possibilities to consider in a patient with a positive DAT include a delayed hemolytic transfusion reaction associated with recent blood transfusion or transfusion of ABO incompatible plasma, eg due platelet transfusion.

### **3.g Extended Antigen Matching for Sickle Cell Anemia Patients**

Patients who have Sickle Cell Anemia (SCA) may require repeated or long term transfusion support. Since red cell antibody formation is transfusion dose-dependent and may cause repeated delayed hemolytic transfusion reactions, it is UCSD policy to try to prevent red cell antibody formation in SCA patients by extended matching of donor blood with the patient's blood type. To accomplish this, the patient's red cells must be extensively typed, only once, but before the first transfusion (or > 2 months following the last transfusion) in order to obtain an accurate phenotype. The UCSD Blood Bank will then arrange to obtain optimally matched blood (ABO/Rh, C, E, K, depending on patient phenotype). Patients who have made antibodies will be additionally matched for the specific antibody as indicated. Patients should carry a card indicating their phenotype to facilitate extended antigen matching if they are transfused elsewhere. Note that SCA patients should also receive leukocyte-reduced blood to prevent febrile reactions. Since SCA patients are not at increased risk for either graft vs host disease or CMV, neither irradiation nor CMV-negative blood is required for SCA patients unless there are established indications (see below in this manual).

## **4. EMERGENCY TRANSFUSION**

Depending on the urgency of the clinical situation, you may order:

### **4.a Uncrossmatched O, Rho (D) Negative Blood**

Up to 4 units of O Rho (D) negative blood (or Rh-pos if Rh-neg is unavailable) will be issued provided the patient's physician agrees to sign the appropriate release and provides the Blood Bank with a properly labeled EDTA sample of blood from the patient. This sample is essential for determination of the patient's ABO and Rho (D) type so that subsequent units may be type specific, and to determine if significant red cell antibodies are present. The OB hemorrhage protocol is similar to the above, but 2 units of type AB FFP will also be thawed. The neonatal emergency protocol calls for the Blood Bank tech to attempt to find a unit of CMV-negative, less than 5 day old blood, and irradiate the unit, but only if time permits. If not, the freshest O-neg (or possibly O-pos) unit is used.

Experience at UCSD indicates that about 1 in 50 patients who require uncrossmatched blood, mostly Trauma patients, will have a clinically significant antibody. If you are SURE your patient has never been transfused, pregnant, or been exposed to blood via IV drugs, then the chances of a significant antibody are very low, perhaps 1 in 2,500, but if the patient has been exposed to blood, the chance of an antibody is increased by about 1-2% for each exposure. Thus, a person who has had 2 transfusions would have about a 2-4% chance of being sensitized to foreign red cells. Sharing needles may also expose the individual to allogeneic blood and carries a small risk of alloimmunization.

#### **4.b Uncrossmatched Type-Specific Blood**

Uncrossmatched type-specific blood can be issued to patients whose ABO/Rh type has been confirmed, provided the release is signed by the physician. Compatibility testing will be completed as soon as possible (retrospectively). The risk of a hemolytic transfusion reaction with type-specific is no less than that for uncrossmatched type O blood (and may even be greater, since a blood draw mix-up might result in an ABO incompatible unit being given), but early switching to type-specific blood will preserve resources of rare type O-neg blood for other patients who may need it.

### **5. MASSIVE TRANSFUSION PROTOCOL**

Upon identification of a massive transfusion requirement, typically by the Trauma Service Attending (designated as "Massive Protocol") the Blood Bank will mobilize 45 units of blood ASAP. The initial 4 units may be O Rh negative (see Emergency Transfusions, Section 4 above). Following this, type-specific blood will be used to the extent possible. If necessary in order to provide sufficient blood without delay, the decision to switch blood types (to O for type B; A or O for type AB) will be made by the Blood Bank. It is almost always necessary to use Rh positive blood in Rh negative individuals. To prevent confusion, a single individual on the trauma team should be designated to communicate with the Blood Bank. Following the immediate resuscitation period, standard procedures for blood ordering will be followed. FFP and platelets are supplied as needed. Note: The massive transfusion protocol should be invoked judiciously. Responding to a massive transfusion may impair service to other patients. Also, the patient is charged for each crossmatch whether or not the unit is transfused.

Hemostatic defects are common in massive transfusion and are most often related to dilution and consumption of platelets and coagulation factors. In the absence of trauma, DIC, or preexisting coagulopathy, patients who bleed up to 1.5 blood volumes (in a 70 kg male approximately 15 units of PRBC and 3-5L crystalloid) generally do not have clinically relevant hemostatic defects that require transfusion with platelets, FFP, or cryo. Consequently, prophylactic transfusion of platelets or plasma should not be given to stable patients whose bleeding has ceased simply because they have received 10-15 units of PRBC. The presence of a preexisting coagulopathy, trauma with extensive tissue damage, or DIC increases the likelihood that hemostatic support will be required at any level of bleeding. Such patients or those whose blood loss is >1.5 blood volume should be carefully monitored for clinical signs of microvascular bleeding, i.e., from IV sites or wounds, and by laboratory monitoring for significant coagulopathy, eg PT >18 sec, PTT >55 sec; fibrinogen <100 mg/dl, platelets <75,000. Hemostatic supportive therapy should be individualized, based on all available clinical and laboratory information and the patient's status should be frequently reassessed to determine ongoing hemostatic needs. Massively transfused patients who have microvascular bleeding are more likely to require platelet transfusion than FFP (note that a platelet transfusion supplies the amount of plasma in 1U FFP), but both are frequently needed. If FFP is required, an adequate dose should be given, i.e., 1U/10 Kg. Following initial therapy, it is important to

evaluate clinical and laboratory parameters of response. There is no, universal formula to guide hemostatic replacement therapy, however, in patients who bleed in excess of two blood volumes (>20 units of PRBC) it is usually necessary to transfuse sufficient platelets to keep the platelet count >75,000, and sufficient FFP to maintain fibrinogen > 150 mg/dl and/or the PT<18 sec; PTT<55 sec (corresponds to a hemostatic level of coagulation factors >30%). It is generally not necessary to give cryo unless there is a disproportionate decrease in fibrinogen or factor VIII, (e.g., as occurs with DIC), since a unit of FFP supplies about twice as much fibrinogen and factor VIII as a unit of cryo. The most common error in massively bleeding patients is to apply outdated, rote formulae which may result in inadequate FFP or platelet replacement therapy in some, while others are treated unnecessarily.

## 6. BLOOD SPECIMEN REQUIREMENTS

The blood drawing team collects blood specimens on a 7/24 basis at Hillcrest. The team draws blood in the morning (5 – 7 AM) on hospitalized patients at Thornton and from 7:30 AM to 6 PM, M-F at Perlman.

Correct patient identification and blood sample labeling at the time of blood drawing is **ESSENTIAL**. It is the single most important way a physician can ensure blood safety. Most fatal transfusion reactions are due to errors in patient identification at the time the blood specimen is drawn or the blood unit is given. Patients' identity should be confirmed using the patient's armband ID. When drawing a blood specimen, labels with the patient's ID should be checked against the armband and affixed to blood specimen tubes **at the bedside** immediately after the blood is drawn. Blood specimen labels should contain the patient's first and last names, hospital number, date of birth, the date and time specimen was drawn, and the legible signature of the person who drew the blood.

No specimen will be accepted if the patient's first and last name or the hospital number on the blood sample request forms or labels do not agree. In case of discrepancy or doubt, another specimen will be obtained. Mislabeled or unlabeled blood samples will not be released from the Blood Bank. Blood Bank tech may not make exceptions. In the near future it will be a requirement to type a 2<sup>nd</sup> blood specimen, drawn at a different time, before type-specific blood may be administered.

Draw a 7-10 mL EDTA blood (purple top) for compatibility testing; more blood may be needed if extensive antibody identification is necessary. Do not use red top (clot), heparinized or Corvac tubes.

Blood specimens should be accompanied by the completed Blood Bank order form (151-104) or computer-generated Blood Bank Request; one for total order). Blood orders that do not require a new specimen (eg additional units of blood within 3 days, platelets, FFP) may be transmitted to the Blood Bank using the Hospital Computer under the Lab section, and a Blood Products Request will be generated in the Blood Bank. Neonatal Blood orders have special requirements, to prevent excessive donor exposure and to

ensure that infants who require rapid transfusions do not receive blood with high K<sup>+</sup> levels. For neonates, the physician must indicate whether the blood order is for a transfusion to be administered slowly (2-4 h) or rapidly, eg in an emergency, surgery, exchange, bleeding, and the volume required (usually 15 mL/kg), and the clerk must indicate the infant's gestational age and weight. See Neonatal and Pediatric Transfusion for details.

**Elective Same-Day Surgery:** Specimens for blood type and antibody screen should be sent to the Blood Bank within three weeks if possible and no less than three working days prior to surgery. Patients with no history of transfusions or pregnancy within 3 months before scheduled surgery may have blood specimens drawn up to 28 days before surgery by specially certified Nursing staff in the surgery "Pre-evaluation" clinics at Thornton and Hillcrest. Some "same day" surgery patients will have blood specimens drawn only a few hours before surgery. This practice is hazardous, because about 8% of them will have a positive antibody screen that will delay obtaining compatible blood. When this happens in surgery, prior to the workup of the antibody and acquisition of compatible blood, then uncrossmatched or if necessary, the most compatible blood available on short notice may be requested with a "waiver" form under the physician's signature, acknowledging that there is a greater risk of hemolytic transfusion reaction.

## **7. ISSUE OF BLOOD COMPONENTS**

A physician's blood order is required to administer blood. To obtain blood from the transfusion service, a qualified individual must present a blood pickup form containing the patient's identification (ID) which must include at least name, date of birth and medical record number, also containing the number and type of unit requested and any specific additional instructions, eg irradiation. Except for the Operating Room or in cases where the patient's condition is serious enough to have two IVs going, only one unit of blood is released to the unit at a time. No blood can be issued without appropriate documentation.

The courier picking up the blood will sign the pickup form with the patient's ID, which remains in the Blood Bank after the technologist records the unit numbers, ward, time, and date on the form. The technologist will issue the blood with Blood Transfusion Record, which should be placed into the patient's chart following completion of the transfusion. The empty blood bag should be disposed of on the ward; except if there is a transfusion reaction, in which case the bag (and associated tubing) is aseptically returned to the Blood Bank (along with the completed Transfusion Reaction section of the Transfusion Record).

Blood will not be released from the Blood Bank if there is any discrepancy between the patient's ID stamped on the EDTA blood specimen submitted for type and crossmatch and the ID stamped on the blood pickup form.

Blood should be transfused within 4 hours after issue. Blood leaving the Blood Bank should be returned within 30 minutes after leaving the Blood Bank if it is not to be used immediately. Otherwise it cannot be used by another patient and will be wasted. Do not pickup blood unless you plan to transfuse it. Do not put blood or blood products in the ward refrigerator since they are not certified and the blood stored in them may be damaged and cannot be re-issued.

## 8. ADMINISTRATION OF BLOOD

Most fatal transfusion reactions are due to improper patient identification. Before a transfusion is started, it is **ESSENTIAL** to properly identify the patient as the intended recipient. **Two appropriately trained UCSD employees must positively identify that unit belongs to the patient by checking the PATIENT'S ARMBAND against the name, MRN, AND unit number on BOTH the blood bag and the Transfusion Record** (If the patient is conscious, s/he should be asked to state his/her name). They will then sign Blood Transfusion Record and write in the date and time the unit was started. At the end of the transfusion, the physician or nurse completes the post-transfusion section by writing in the volume of blood given and time transfusion is completed.

Routinely, it should not take more than about 1.5 to 2 hours to transfuse a unit of blood (about 60 drops or 3 mL /minute) and should be complete within 4 hours. A unit of packed red blood cells may be expected to raise the hemoglobin 1 gm per 100 mL, or the hematocrit about 3 percentage points. Only intravenous solutions that are known not to damage the blood or react with the anticoagulant solution, such as isotonic saline, may be transfused with blood, to avoid hemolysis or clotting. Dextrose in water, hypotonic or hypertonic saline or Ringer's lactate should not be used. Medications are not to be added to blood.

All blood components are transfused through a filter. The standard blood filter has a 170–210 micron pore size and is indicated for most transfusions. Microembolic filters (20–40 micron pore size) have only limited applications and will not remove leukocytes effectively. Since 2001, blood and platelets supplied to UCSD have been leukocyte reduced by the American Red Cross. Exception: autologous and directed donor blood is leukocyte reduced only on special order (see below for indications). Directed donor blood should be ordered as leukocyte-reduced from the blood supplier. In the unlikely event that pre-storage leukocyte reduced blood is unavailable at UCSD, blood may be administered through leukocyte-reduction filters at the bedside.

Complete details on UCSD policy for Blood Administration are found in the UCSD Blood Administration Medical Center Policy, (MCP 617.1) that is available online (<http://www-ucsdhealthcare.ucsd.edu/mcpweb/docs/617.1/doc.htm>).

## 9. INCOMPATIBLE CROSSMATCH

Blood that is incompatible in the crossmatch will not be released by the technologist without the Blood Bank physician's approval. A Blood Bank physician is always available for consultation with the clinician on management of difficult transfusion problems. In some emergencies in which no compatible blood can be found (e.g. autoimmune hemolytic anemia), and the Blood Bank workup shows that there is no rbc alloantibody, a small volume (100 mL) of blood may be given slowly (0.5 hr) with continuous monitoring of the patient's condition. If the patient remains asymptomatic and there is no evidence of hemolysis in a sample of blood obtained after 0.5 hr, experience indicates that the risk of a severe hemolytic reaction is low, and the remainder of the unit may be given under careful observation. The preceding type of transfusion trial should be undertaken **ONLY** with the full participation of the Blood Bank physician. Rarely, an *in vivo* crossmatch using radio-labeled red cells may be performed to aid in the selection of compatible blood (principally to rule out alloantibodies).

Except in emergencies, the Blood Bank will not release blood that may be compatible in the crossmatch when the patient has an unidentified antibody. The crossmatch procedure may not be sufficiently sensitive to detect some weak antibodies, and an apparently compatible unit may result in hemolysis or shortened red cell survival following transfusion. Identifying antibodies can take from as little as 2 hours to several days in those cases where rare blood is needed. If the patient requires blood before the antibody investigation can be completed, the Blood Bank will approve provision of the most compatible blood available after the clinician indicates his/her understanding of the increased risk of a hemolytic reaction by signing a release or "waiver". The availability of single patient, compassionate-use approval for an artificial oxygen carrier (stroma-free Hb, Polyheme<sup>tm</sup>) may be investigated in appropriate circumstances (life-threatening anemia despite optimal therapy, no compatible blood, short-term need with plan to wean), by calling Northfield Labs (pager 800 423-8517 or website) who will provide instructions regarding obtaining rapid FDA and IRB approval. This product may be FDA approved in the near future.

## 10. RED BLOOD CELLS

### 10.a Packed Red Blood Cells (RBC) \*

(CPDA1; 250-275 mL; Hct-70-80%; Shelf Life = 35 days)

(AS1,3, or 5; 250-350 mL; Hct-57-62%; Shelf Life = 42 days)

**Indications:** RBC are transfused to support blood oxygen-carrying capacity. A physiologically stable medical or surgical patient whose hemoglobin is greater than 7-8 g/dl generally does not require a red cell transfusion. Exceptions may be made based on compromised cardiovascular or cerebrovascular status, blood volume, or anticipated blood requirements. One unit of RBC should raise the Hb of a 70 kg patient by approximately 1 gm/dl (3% increase in Hct). RBC may be preserved in a variety of different anticoagulant/preservatives. They will all have the same relative red cell mass (about 190 mL of rbc at a Hct of 90%, but will have different volumes of plasma, Hcts, and shelf lives. For neonates or small infants RBC may be concentrated by

centrifugation and/or re-suspended in FFP in the Blood Bank, upon specific request.

RBC is the component of choice in the great majority of clinical situations requiring transfusion therapy. It is generally recognized that >90% of all transfusions should be packed red cells. The therapeutic advantages of RBC over whole blood include minimizing circulatory overload, and reduction of Na<sup>+</sup>, K<sup>+</sup>, and citrate administered to the patient, reduction of reactions associated with plasma components and more efficient utilization of the available blood resources. The use of RBC facilitates the production of other blood components, such as platelets, cryoprecipitate, etc., so that one donated unit can meet the needs of many patients. Newer “adenine-saline” blood preservative solutions, eg AS1, -3, or -5 may have advantages over CPDA1 RBC in a lower incidence of allergic reactions and/or TRALI, due to the lower plasma volume, and a faster rate of administration, due to the lower Hct. Nearly all blood supplied to UCSD Medical Center as of 2006 is preserved in one of the AS solutions.

\* Note that all allogeneic RBC supplied to UCSD are pre-storage leukocyte-reduced. At the VA, this component requires a special order.

#### **10.b Leukocyte-reduced RBC (LRC)**

(same as RBC but < 5 x 10<sup>6</sup> WBC)

Whole Blood, Red Cells, and Platelets also contain large numbers of leukocytes (eg 2 to 5 x 10<sup>9</sup> per unit). Patients who have received transfusions of standard blood products and women who have been pregnant may become sensitized (alloimmunized) to leukocyte and sometimes platelet antigens. Sensitization to leukocyte or platelet antigens may be manifest as febrile transfusion reactions, as refractoriness to platelet transfusion or rarely, as transfusion-related acute lung injury (TRALI). Leukocyte-reduced red cells (and platelets) contain < 5 x 10<sup>6</sup> WBC/unit and are indicated to prevent febrile, non-hemolytic transfusion reactions, or sensitization to leukocyte antigens, they prevent some cases of TRALI, and also to prevent Cytomegalovirus (CMV) transmission in selected susceptible patients. Leukocytes are most effectively removed from the red cells (or platelets) within 72 hours after they are collected by the American Red Cross and are referred to as “pre-storage leukocyte-reduced” red cells or platelets. Use of pre-storage leukocyte-reduced red cells or platelets assures that the level of leukocyte removal and quality control thereof is sufficient to reliably prevent the above leukocyte-associated complications. Pre-storage leukocyte-reduced units are transfused using only the standard 170 micron filter, which assures removal of residual clots, etc. To ensure that you obtain pre-storage leukocyte-reduced red cells (eg in the rare case of a supply problem), you should specify in the blood order "Leukocyte-reduced" RBC. In the event that pre-storage leukocyte-reduced blood is unavailable, blood may also be leukocyte-reduced at the bedside by transfusion using a "3rd generation" leukocyte-reduction filter available from the Blood Bank. Such bedside filtration methods remove fewer leukocytes than the pre-storage filtration methods noted above and may have a failure rate of 5-10%, but if used properly will usually be adequate for prevention of recurrent febrile reactions. In order to assure success with this method, one bedside leukocyte reduction filter designed for use with *two* units of red blood cells should be used to filter only *one* unit of red blood cells.

Bedside filtration is less reliable for the purpose of preventing CMV transmission or alloimmunization to HLA/leukocyte antigens; consequently bedside filters should be used only if pre-storage leukocyte-reduced units are unavailable. Neither the standard 170 micron blood filter nor "microaggregate" (20-40 micron) blood filters remove leukocytes. The dose of leukocyte-reduced red cells is the same as RBC. Call the Blood Bank Resident or Attending for additional information.

**Indications:** Patients who have severe or recurrent febrile nonhemolytic transfusion reactions (FNHTR) should receive leukocyte-reduced blood components. Before concluding that an individual febrile transfusion reaction is due to anti-leukocyte antibodies, you must first rule out a hemolytic or other serious reaction. Most patients who have one febrile transfusion reaction will not have a second one. This is because most fevers occurring during transfusion are unrelated to the blood itself and are due to the patient's underlying condition. A positive test for anti-leukocyte antibodies supports the diagnosis of FNHTR due to anti-leukocyte antibodies and should be obtained on all patients with recurrent FNHTR. The UCSD HLA lab can perform a rapid test for anti-HLA antibodies (HLA ELISA screen). Leukocyte-reduced blood is also indicated in some patients who are destined to have long-term blood requirements (eg leukemia, malignancy, refractory anemia), since the risk of alloimmunization to leukocyte antigens can be diminished by the routine prophylactic use of leukocyte-reduced red blood cells and platelets. Pre-storage leukocyte reduced red cells and platelets are as effective as blood from CMV-seronegative donors in preventing CMV transmission; consequently, at UCSD pre-storage leukocyte-reduced red cells (and platelets) are used interchangeably with blood from CMV-seronegative donors to prevent CMV infection. NOTE: Leukocyte-reduced blood will NOT prevent transfusion associated graft vs. host disease in patients who are susceptible to this condition (see section on Blood Irradiation).

### **10.c Frozen (Deglycerolized) Red Blood Cells**

(180 mL; Hct=60-70%; Expire 24 h post thaw)

Frozen RBC are indicated as a method to store blood units that have special or rare antigen types for patients who have unusual or multiple red cell antibodies and rarely for storage of autologous blood. Frozen RBC have low plasma and leukocyte content but should not be ordered specifically for the purpose of avoiding allergic reactions (see saline washed RBC) or febrile reactions (see leukocyte-reduced RBC). Frozen RBC outdate 24 hours after thawing due to the possibility of bacterial contamination. Once the component arrives in the Blood Bank, the patient will be charged whether used or not. Frozen red blood cells are reconstituted in saline to a final hematocrit of 60-70% for transfusion. Frozen RBC are not stocked at UCSD, but must be ordered from the American Red Cross. Consequently frozen RBC should be ordered at least 24 hours in advance of anticipated need, since several hours are required to thaw and wash them prior to use. Frozen RBC should only be ordered if they are certain to be used since they outdate 24 hours after thawing. Since the freeze-thaw process destroys 20% or more of the rbc, patients who receive this product usually require a greater number of units to achieve the same Hct than patients given liquid RBC.

### **10.d Saline Washed RBC**

(180 mL; Hct=60-90%, Shelf Life = 24 h)

Washed Red Cells are indicated in patients who have had repeated allergic reactions to transfusion (almost always due to plasma proteins) and sometimes for patients who have paroxysmal nocturnal hemoglobinuria. Washed RBC are **not** considered leukocyte-reduced by today's standards (see leukocyte-reduced RBC) and will **not** prevent CMV transmission or immunization to leukocyte antigens. Washed RBC are not stocked at UCSD, but must be ordered from the American Red Cross. Consequently saline washed RBC should be ordered at least 24 hours in advance of anticipated need, since several hours are required to prepare them. Saline washed RBC should be ordered only if they are definitely to be used, since they outdate in 24 hours after preparation. Since the washing process destroys up to 20% of the rbc, patients who receive washed red cells usually require a greater number of units to achieve the same Hct than patients given RBC.

### **10.e Whole Blood**

(500 mL; Hct=36-44%; Shelf Life = 35 days)

Whole blood is only indicated for massive blood loss associated with hypovolemic shock and is not offered by most blood suppliers. Packed red blood cells combined with balanced salt solutions are as effective as whole blood for blood loss in surgery. The platelets in whole blood are nonfunctional and the plasma coagulation factors V and VIII decrease progressively during storage. Circulatory volume overload should be carefully monitored during therapy with whole blood. The dose is same as for RBC. Neonates who require low amounts of potassium, ammonia, and hydrogen ion can be transfused with RBC that have been stored less than one week prior to transfusion or older units that have been centrifuged, the plasma removed, and resuspended in AB FFP. Red cell 2,3 DPG levels are normal after 7 days storage and decrease to 40% after 14 days storage (CPD-A) while ATP levels remain at 100% for approximately 2 days. Blood less than 5 days of age is usually not available from the American Red Cross because of processing requirements for infectious diseases testing.

## **11. PLATELETS**

### **11.a Apheresis Platelets (Plateletpheresis)**

(200-400 mL; Hct=0%; Shelf Life=5 d)

The UCSD Medical Center Blood Bank attempts to maintain a stock of apheresis platelets in anticipation of use, but cannot always guarantee having platelets available. Platelet concentrates (PC) derived from single units of whole blood are not used at UCSD and should not be confused with apheresis platelets, which are equivalent to 6 units of PC. ABO and Rh matching of platelets is ideal, but it is frequently necessary to give platelets that are a different blood type than the patient (see Matching, below). Apheresis platelets are collected from an individual donor during a 2-3 hour apheresis procedure

and contain about  $3 \times 10^{11}$  platelets (equivalent of 6-8 units of platelet concentrate; a therapeutic dose for an adult). Apheresis platelets are preferable to platelet concentrate since their use results in diminished donor exposure and therefore lower risk of side effects. Since 11/1/98 UCSD has employed only pre-storage leukocyte-reduced apheresis platelets ( $< 5 \times 10^6$  WBC/unit) from the Red Cross. In the unlikely event that leukocyte-reduced units are unavailable the platelets must be passed through a leukocyte-reduction filter (see 11.c) in order to ensure that they are leukocyte reduced. Platelet concentrate contain about  $5.5 \times 10^{10}$  platelets in 50 ml plasma are procured from a unit of whole blood shortly after collection using centrifugation. Platelets are stored at room temperature with continuous gentle agitation for up to 5 days. Since 2005, all platelets are cultured prior to delivery to UCSD in order to prevent bacterial sepsis, but this is not 100% effective, hence sepsis should still be considered in patients who have fever shortly after platelet transfusion.

### **11.b Indications for Platelets:**

Platelets are indicated for bleeding in thrombocytopenic patients (usually  $< 50,000/\text{microL}$ ), typically due to leukemia or other infiltrative disease of the bone marrow, chemotherapy, aplastic anemia, massive transfusions, or congenital or acquired platelet dysfunction with normal platelet levels. Surgical patients or those scheduled for invasive procedures in whom bleeding is of concern, may require platelet transfusion with counts  $< 50,000-75,000$ . Platelets are not indicated in patients who have immune thrombocytopenia (ITP) and "hypersplenic" thrombocytopenia, except if life threatening bleeding exists (then use larger doses). Platelets are not effective in uncontrolled DIC prior to heparinization and may even be harmful in uncontrolled Thrombotic Thrombocytopenic Purpura (TTP), except to control life-threatening bleeding.

Platelets may also be administered for prophylaxis against bleeding in patients who have chemotherapy-induced bone marrow failure and a platelet count  $< 10,000-20,000$ . The benefits of prophylactic platelet transfusion in stable, afebrile, non-bleeding adult patients with counts  $> 10,000-15,000$  should be weighed against the risks associated with multiple donor exposures (see **Transfusion Risks**).

### **11.c Platelet Matching:**

ABO matching of platelets is desirable, but not required in adult patients. Rh negative recipients receiving platelets from Rh positive donors are at risk for Rh (D antigen) immunization because platelets may contain a small amount of red cells (typically less than 0.1 mL RBC per unit of apheresis platelets). Rh negative females with the future prospect of childbearing who receive platelets obtained from Rh positive donors should be treated with Rh Immune Globulin (RhIg), 50 or 300 micrograms (mcg) per dose or preferably the IV preparation, WinRho available from the Pharmacy (120 mcg per dose) to prevent immunization to Rh. One dose of either of these products should be sufficient to prevent Rh sensitization from > 25 units of Rh positive apheresis platelets (assuming a maximum of 0.1 mL of rbc per unit and a dose of 20 mcg RhIg per mL rbc). In view of this, we recommend that treatment may be administered only once per month, unless the patient receives >25 units of Rh-positive apheresis platelets. If the product for IM injection is used, then in order to avoid an IM hemorrhage, it should be given immediately after platelet transfusion, if at all. If IM injections must be strictly avoided, the IM product may also be given SQ, but the efficacy of SQ dosing has not been extensively studied. Treatment of Rh negative males or post-menopausal females is considered optional, but recommended. Red blood cell compatibility testing of platelets is not required in view of the minimal number of rbc therein. Preferably, the donor plasma should be ABO compatible with the recipient's rbc if the platelets are not type specific. Apheresis platelets contain up to 300 mL plasma; consequently if incompatible plasma must be administered with ABO mismatched platelets, only units that are non-reactive for anti-A or -B at a 1/100 dilution will be selected for transfusion (UCSD-Hillcrest).

### **11.d Platelet Administration:**

Platelets (including pre-storage leukocyte-reduced platelets) must be administered through a filter set, usually the standard 170 micron screen filter; the only exception being that in the rare event that a "bedside" leukocyte reduction filter must be used, it takes the place of the 170 micron filter. There is no advantage in routine use of 20-40 micron screen filters. Upon request, platelets may be volume reduced for neonates in the Blood Bank prior to issue. This requires about 60 min. extra time. Platelets must not be administered through a microaggregate filter or a filter designed to be used for leukocyte reduction of red cells, since such filters will remove platelets. Call the Blood Bank Resident if you are unsure of which filter to use.

### **11.e Platelet Dosage and Platelet Count Increment:**

The standard adult dose is 1 Unit of apheresis platelets (equivalent to 1 platelet concentrate per 10 kg patient wgt). This dose should temporarily raise platelet levels approximately by 30,000 to 60,000/uL in a hematologically stable adult with 1.8m<sup>2</sup> body surface area (or 30,000/mm<sup>3</sup>/m<sup>2</sup>). Smaller increments commonly occur, however, depending upon the patient's clinical condition. The equivalent pediatric dose is 5-10 mL of apheresis platelets per kg. Small aliquots are aseptically removed from a unit of

apheresis platelets to supply platelets to neonates. Such units may still be employed for adults if no longer needed for the neonate and if they still contain  $> 3 \times 10^{11}$  platelets.

### 11.f Platelet Refractoriness:

This refers to failure of platelet transfusion to satisfactorily increase the 1 hour post transfusion platelet count. Platelet refractoriness is usually accompanied by failure to achieve hemostasis and frequently by a febrile transfusion reaction. The objective definition of the platelet refractory state requires at least 2 transfusion failures and may be documented by calculation of the Corrected Count Increment (CCI) as follows:

$$\text{CCI} = \frac{(\text{post trf plt ct}) - (\text{pre trf plt ct})}{\# \text{ platelets transfused (x } 10^{11})} \times \text{BSA} \quad \text{where,}$$

BSA = body surface area in  $\text{m}^2$ . For apheresis platelets, assume  $3.5 \times 10^{11}$  platelets/transfusion (and for platelet concentrate [not used at UCSD] assume  $0.6 \times 10^{11}$  platelets/unit). A CCI of  $< 7.5 \times 10^9/\text{L}$  from a blood sample drawn 10-60 minutes post transfusion, or a CCI  $< 4.5 \times 10^9/\text{L}$  from a sample drawn 18-24 hours post transfusion are considered indicative of refractoriness.

Platelet survival is shortened and the post transfusion incremental platelet count is reduced when the patient has fever, infection, disseminated intravascular coagulation, active bleeding, splenomegaly, TTP, platelet antibodies (alloimmunization, drug-induced or ITP), a very low starting platelet count, major organ failure, and after ABO incompatible platelets. Response to platelet transfusion is also diminished in patients who have had recent bone marrow transplant and frequently after highly myelotoxic chemotherapy for cancer.

Prior transfusion or, less commonly, pregnancy may provoke alloantibodies to platelet-specific or HLA antigens. Platelets collected from unselected donors have shortened survival in patients with alloantibodies and may not be effective in preventing or controlling bleeding. Likewise, in patients with platelet auto-antibodies, such as autoimmune or drug-induced thrombocytopenic purpura, survival of transfused platelets may be extremely brief, sometimes only a matter of minutes. A platelet count performed 10 min to 1 hour after platelet transfusion detects impaired platelet recovery, and identifies those patients who have become refractory to random-donor platelets (see CCI above).

### 11.g Leukocyte-Reduced Platelets

UCSD Medical Center stocks only pre-storage leukocyte-reduced apheresis platelets ( $< 5 \times 10^6$  WBC/unit). The indications for leukocyte-reduction of platelets are the same as for leukocyte-reduced red cells, i.e., to prevent alloimmunization to HLA antigens in selected patients, to prevent febrile reactions in patients who are alloimmunized, and to prevent CMV. Note that patients who have repeated febrile reactions after platelet transfusion are almost always alloimmunized to HLA and are refractory to random donor platelet transfusion. These patients should therefore be given crossmatched or HLA matched or antigen-negative apheresis platelets after documentation of alloimmunization (see above). Like red cells, apheresis platelets are preferably rendered leukocyte-reduced at the time they are collected ("pre-storage" leukocyte-reduced). In the unlikely event that pre-storage leukocyte-reduced platelets are not available and your patient requires this product, you must use the type of "bedside" filter specifically designed for removal of leukocytes from platelets. Use of the wrong type of filter will either result in no leuko-depletion or loss of all platelets. One filter can be used for one apheresis unit.

### **11.h HLA matched, Antigen-negative, and Crossmatched platelets:**

Apheresis platelets that have been HLA-matched or are antigen-negative or Crossmatched with the recipient are indicated for patients who are unresponsive (refractory) to random donor platelets due to alloimmunization (most frequently due to anti-HLA antibodies). Before ordering HLA-matched platelets, alloimmunization should be documented by a test for HLA and platelet-specific antibodies. This can be most quickly accomplished by sending a sample of patient's plasma to the American Red Cross Platelet Immunology Lab. They will first perform a screen for anti-HLA and anti-platelet-specific antibodies using platelet membranes bound to plastic. If positive for HLA antibodies it may be possible to identify their specificity (similar to identifying anti-rbc antibodies) by extensive lymphocytotoxicity testing. If platelet-specific (non-HLA) antibodies are present, platelet crossmatching must be used to identify compatible platelets. If the clinical picture is consistent with post-transfusion purpura (PTP) the lab should also be directed to test for antibodies to HPA-1A.. (Note: A stat "HLA antibody screen" by ELISA may also be ordered through the UCSD HLA Lab (or ITL; 642-4774) using a 5 mL EDTA or red-top tube, but this lab does not perform a test for platelet-specific antibodies.) Call the Blood Bank physician for additional information about platelet antibody testing.

There are several ways for the Blood Bank to obtain compatible platelets for a patient who is refractory to platelets due to alloimmunization. 1) If the patient's HLA type is already known, it may be possible to quickly obtain HLA matched platelets by communicating the type to the Red Cross Platelet Immunology Lab who will search for the most compatible donors. Sometimes a matched HLA apheresis platelets is already available and can be shipped within 24 h. Otherwise, the patient must be HLA typed, either at the LA ARC or the UCSD ITL. Specimen requirements include at least one 5 mL yellow-top (heparin) tube; more if the patient is lymphopenic ( $< 1000 \times 10^9/L$ ). 2) If the patient's HLA type is not already known, or no HLA compatible platelets are in stock, the quickest method to obtain compatible platelets is to send an EDTA blood sample to the Red Cross Platelet lab to test for "crossmatch compatible" platelets. The lab will test

the patient's plasma against 5-10 apheresis platelets that are available for use and select the ones that are compatible for immediate shipment to UCSD (usually requires at least 24-48h). This method will be necessary if platelet-specific antibodies are identified. 3) The Platelet lab may be able to determine a limited array of HLA antibody specificity (similar to testing for rbc antibodies) and supply "antigen-negative" platelets. This broadens the pool of "HLA matched" donors available. In the most difficult cases, a combination of antigen-negative, HLA-matched, and crossmatch compatible platelets may be required, but it is very difficult to provide platelet support under these conditions. 4) Finally, if family members are readily available and are acceptable donors, one in four may be HLA matched with the patient. The management of each patient must be individualized to achieve the best result, and in any event, this process requires close coordination with the UCSD Blood Bank Resident. HLA-matched or crossmatched platelets should be irradiated to prevent transfusion associated GVHD. An adequate trial of HLA matched or crossmatched platelets generally consists of at least 3 transfusions of matched apheresis platelets, ideally on the same or consecutive days. The platelet count increment should be checked after each transfusion and the units giving successful increments noted, since it may be possible to employ the same donor repeatedly. Advance consideration should be given to weekend coverage with HLA-matched or crossmatched platelets. If 3-4 well matched or crossmatch compatible plateletpheresis units are unsuccessful, then the patient is unlikely to respond to matched platelets. In this event non-immune factors and drug therapy should be re-evaluated and a trial of IVIG (2 gm/kg) should be considered. If the patient is actively bleeding, human recombinant factor VIIa may be tried, if there are no contraindications. There is no advantage in using HLA-matched platelets in patients whose refractory state is not due to alloimmunization. In such patients, HLA-matched platelets would not survive longer *in vivo* than would the random donor PLT. Physicians treating patients refractory to platelet transfusion should consult with the Blood Bank Resident to determine the best therapeutic alternatives.

## 12. APHERESIS GRANULOCYTE CONCENTRATE

(50-300 mL; Hct = 5-10%; Shelf Life = 24 h)

Granulocytes are indicated for patients who have granulocytopenia,  $< 500/\text{mm}^3$ , due to marrow failure *e.g.*, leukemia, chemotherapy, agranulocytosis, or who have a congenital granulocyte function defect, and sepsis or infection unresponsive, after 24-48 hours, to adequate antibiotic therapy, and are expected to recover bone marrow function (if granulocytopenic). At least 24 hours advance notice is required to obtain granulocytes, which are prepared by the American Red Cross from unrelated, ABO-matched donors by leukapheresis. Since the patient frequently is also thrombocytopenic, platelets are also collected (leukoplateletpheresis). Granulocytes should be obtained from HLA matched donors if the patient is immunized to HLA antigens. This is likely if the patient is having febrile reactions to blood products or is refractory to platelet transfusion. Family members may donate if they are ABO compatible and are not candidates for marrow donation. CMV seronegative donors must be chosen for susceptible individuals. Donors may be treated with G-CSF, 5-10 mcg/kg SC and dexamethasone, 0.1-0.15 mg/kg PO, 8-12 h before apheresis to increase the WBC. This increases the yield of PMN by 3-5 fold

and may permit alternate day infusion of granulocytes in small patients. Side effects of G-CSF include bone pain and headaches, but are generally mild and responsive to acetaminophen. G-CSF must not be used in potentially pregnant females. ARC currently has no G-CSF protocol but will administer dexamethasone. Each unit of granulocytes should contain at least  $10^{10}$  PMN (approximately  $1.5 \times 10^9/10$  Kg) in 50 - 300 mL. Irradiation of granulocytes is indicated in most patients and does not significantly alter their function. Granulocytes contain red cells and must be ABO compatible with the recipient, therefore a T & S must be sent to the UCSD Blood Bank. Granulocytes are stored at room temperature without agitation for up to 24 hours. NOTE: Granulocytes have a limited shelf life and must be administered as soon as possible after they are obtained. Since granulocytes are used rarely, the Nursing staff are frequently unaware of the short shelf life and must be reminded to infuse them promptly. Granulocytes should be transfused through a standard blood filter (170 $\mu$ ) slowly in 0.5-1 hour. A microaggregate or leukocyte reduction filter must **NOT** be used for granulocytes. Reactions to granulocytes are common, consisting of chills, fever, and occasionally dyspnea and chest pain. It may be advantageous to premedicate patients with acetaminophen and benadryl. Some reactions respond to parenteral Demerol. Patients who are receiving amphotericin B have rarely been reported to have severe pulmonary reactions when granulocytes are coadministered and should have doses of amphotericin spaced as far apart from the granulocytes as possible. Only G-CSF stimulated donor granulocytes produce an increment in the patient's WBC. 1 to 2 units of granulocytes (from donors without G-CSF) should be given daily for at least 4 days (daily or alternate day for G-CSF stimulated donors), or until either 72 h after a clinical response is noted, or the granulocyte count increases spontaneously above 1000/microL. If there is no response after 10-14 days of therapy, it is unlikely that additional transfusions will be beneficial. Note: since there is little time to complete donor infectious disease testing before the granulocytes must be administered, the physician must ordinarily sign a waiver indicating that the product is to be transfused despite incomplete testing and the patient should be so informed. To lessen the risk of infectious disease transmission, only donors who have recently tested negative are typically employed.

### **13. PLASMA PREPARATIONS:**

#### **13.a Fresh Frozen Plasma (FFP), Frozen Plasma (FP) and Thawed Plasma**

(200 mL; Hct=0%; Expires 24 h post-thaw)

FFP and Frozen Plasma are made by centrifuging a unit of whole blood and freezing the supernatant, cell free plasma within 8 (FFP) or 24 (FP) hours of collection. Each unit contains approximately 400-800 mg fibrinogen and 200 U (1 U/mL) of other coagulation factors, except that FP is not indicated as a source of factors VIII and V. It takes about 25 min to thaw FFP/FP under ideal conditions. FFP/FP contains no rbc and insignificant numbers leukocytes. FFP is also available in single donor 400-600 mL bags and is equal to 2-3U FFP ("jumbo FFP"). This has the advantage of few donor exposures, but takes longer to thaw and bag breakage is a problem. FFP/FP may be stored frozen (-18 C) for 12 months, and may be used for up to 24 hours after thawing, if kept at 4 C. Virus-inactivated FFP is in clinical trials. Thawed FFP/FP may be stored up to 5 days at 4 C

(“Thawed Plasma”) and used as a readily available emergency plasma replacement for patients who do not require factors V and VIII, eg trauma, burn, coumadin overdose, some liver disease patients.

### **13.b Cryo-poor FFP supernate**

Cryo-poor FFP supernate is made by refreezing the FFP removed from units of cryoprecipitate (see Cryo below). Cryo-poor FFP supernate contains low levels of the high mol wgt von Willebrand multimers implicated in the pathogenesis of TTP, and may be efficacious in patients with this disease who have failed to respond to apheresis with FFP replacement. Cryo-poor FFP supernate is neither pooled nor virus-inactivated. It is indicated only for patients with TTP who have failed FFP therapy or are deemed at very high risk.

### **13.c Indications:**

FFP or FP is indicated for replacement of multiple clotting factor deficiencies in bleeding patients who have significant coagulopathy due to multiple factor deficiencies, e.g. massive transfusion, DIC, Vitamin K deficiency. A significant coagulopathy is defined as PT > 18 sec, or PTT > 55 sec and usually occurs after replacement of > 1.5 blood volumes (15 U rbc and crystalloid/colloid), but may occur with lower replacement volumes in patients with trauma, DIC, or pre-existing coagulopathy. Generally, FFP/FP are neither required nor indicated for mild deficiencies in coagulation factors, eg PT < 16 sec or PTT < 45 sec, except for selected patients who have multiple defects in hemostasis, eg liver disease and thrombocytopenia. FFP/FP contain more fibrinogen per unit than Cryoprecipitate and is superior to Cryo for patients who are both volume deficient and fibrinogen deficient, eg a massively bleeding trauma patient with DIC. FFP/FP are also used with or without plasmapheresis in TTP or HUS, and in congenital clotting protein deficiencies for which no concentrate exists, eg Factor XI or XIII deficiency. FFP/FP are NOT indicated for blood volume expansion or protein supplement. FFP/FP are acellular and do not cause graft vs host disease, Rh immunization, nor do they transmit CMV or HTLV-I/II.

### **13.d Dose, Preparation & Administration:**

Each unit of FFP/FP provides the equivalent of all coagulation factors and plasma proteins found in the plasma of a single unit of freshly drawn blood (FP has 10-20% lower factor V and VIII), and more fibrinogen than in a single unit of cryoprecipitate. It takes 25 minutes to thaw each unit and a few minutes extra to issue. FFP/FP should be ABO compatible with recipient and are transfused via standard (170 $\mu$ ) blood filters. One unit of FFP/FP would be expected to raise the level of a given coagulation factor by 7-10%, and the usual dose is 0.5-1 U per 10 kg or 10-20 mL/kg (4-8 units in an average adult). Factor VII has a half life of only 6 hours, so if FFP/FP is given to correct a coagulopathy prior to a procedure, it should be given in as close proximity to the procedure as possible. For prophylaxis in Factor XIII deficiency 2-3 ml/kg, eg 1 unit

may be administered every 3-4 days. FFP/FP, once thawed, should be stored at 4°C and infused as soon as possible, ideally within 2-4 hours. If unused, it should be returned to the Blood Bank, since it can be used, for up to 24 hours if maintained at 4°C. Thawed Plasma is FFP or FP that has been thawed and maintained at 4°C in the Blood Bank for up to 5 days and therefore should not be considered adequate replacement for Factor V or VIII. This product may not always be available, but if so, it can be issued within 15 minutes of order and serves as a source of coagulation factor and/or protein for patients who have suffered trauma, burn, for coumadin overdose or in some patients with liver disease. Cryo-poor supernate is used interchangeably with FFP/FP in patients who have failed FFP/FP therapy for TTP.

#### **14. CRYOPRECIPITATE (Cryo)**

(10-15 mL/bag; Expires 24 h post-thaw)

Cryoprecipitate is made by slowly thawing units of FFP and saving the Factor VIII-rich precipitate that remains. Each bag or "unit" contains 80-100U Factor VIII, 200-300 mg fibrinogen, 80U von Willebrand Factor, and 40-60U Factor XIII in a volume of about 15 ml. Commercially available coagulation factor concentrates which are non-infectious for HIV and hepatitis are available to treat VIII deficiency, and some contain effective quantities of von Willebrand Factor (Humate P and Alphanate), and are therefore the drugs of choice for these conditions. Cryo contains insignificant amounts of other coagulation factors. Cryo (sometime autologous) has also been employed as a topical adhesive or hemostatic agent, but this use requires bovine thrombin for activation, which has been associated with anti-factor V antibodies in nearly ½ of all patients. An FDA-approved, virus-inactivated topical fibrin adhesive product containing only human proteins and made from plasma pools (eg Johnson & Johnson's Crosseal™) is commercially available for use as a fibrin sealant. Therefore the use of either commercial or home-grown fibrin sealant products that employ bovine thrombin are to be avoided, since they may induce anti-factor V antibodies and cause severe coagulopathy.

##### **14.a Indications:**

The indications for Cryo are quite limited since the advent of virus inactivated commercial concentrates to treat hemophilia A and von Willebrand disease. The chief clinical indication for Cryo is now treatment of bleeding due to fibrinogen deficiency (fibrinogen < 100-150 mg/dl) where fibrinogen is disproportionately lower than other coagulation factors, eg in the setting of DIC, or L-asparaginase therapy (note that a fibrinogen levels < 50 mg/dl after L-asp Rx in adult ALL has been associated with a 25% incidence of CNS thrombotic events, presumably due to AT and protein C/S deficiency, so prophylactic anticoagulation with heparin and/or AT therapy may be indicated [Am J Hematol 2004;77:331]). A virus inactivated fibrinogen concentrate is available in Canada, but has not yet been FDA approved. FFP, not Cryo is the component of first choice to correct the common form of coagulopathy associated with massive transfusion and hemodilution in which all coagulation factors are severely diminished. Cryo may be indicated in massive transfusion patients who also have fibrinolysis and/or DIC, *i.e.*,

cases in which there is a disproportionate decrease in fibrinogen and Factor VIII. Cryo may be used to treat hemophilia A, but only if commercial coagulation factor concentrates are not available (since the concentrates no longer transmit HIV or hepatitis) and the patient does not respond to DDAVP (0.3 mcg/kg IV or 300 mcg metered dose by nasal spray q 8-12 h). Cryo is third-line treatment for von Willebrand disease, for the same reasons. Cryo may be used to treat bleeding in patients who have platelet dysfunction due to uremia and who fail to respond to DDAVP (0.3 mcg/kg IV q 6-12 h). Other important therapeutic measures for uremic bleeding, before using Cryo include adequate dialysis (BUN < 40), an Hct >25%, a platelet count > 75,000, a trial of estrogen (0.6 mg/kg daily x 5) if time permits, and ruling out other causes of bleeding. Patients should be carefully monitored to determine dosage for follow-up therapy. Cryo may be beneficial as prophylaxis or therapy in patients with Factor XIII deficiency, but FFP may also be used. Cryo is also indicated for bleeding patients who have dysfibrinogenemia.

#### **14.b Dose, Preparation & Administration:**

The dose of Cryo varies with the specific indication. One bag of Cryo may be expected to increase the fibrinogen in an adult by 10 mg/dL. Since the critical level of fibrinogen for hemostasis is approximately 100 mg/dL, then a reasonable starting dose of Cryo to treat fibrinogen deficiency would be 10-15 bags of Cryo, or 1 bag/5 kg. Approximately 10 bags every 12-24 h are usually used to treat uremic bleeding. It is important to monitor the results of therapy in order to make intelligent estimates of additional doses of Cryo. Between 10-15 bags (1000-1500 U Factor VIII) are usually sufficient to treat a hemarthrosis in a patient with hemophilia A, or for initial treatment of bleeding in von Willebrand Disease (but see 14.a.). For Factor XIII deficiency 1 unit/10 kg may be administered every 3-4 days. Thawing and pooling require about 30-45 minutes. Cryo must be administered through a blood filter. Cryo may be administered without regard to ABO/Rh, except in infants, in whom the plasma should be compatible with infant's rbc. As with all pooled components, pooled cryo should be administered within 4 hours.

### **15. COAGULATION FACTOR CONCENTRATES**

Commercial coagulation concentrates are the drugs of first choice in the treatment of Hemophilia A and B, von Willebrand Disease, and isolated Antithrombin III deficiency, since these purified and virus inactivated or recombinant products have minimal or no risk of transmitting HIV and hepatitis. Several types and dosage forms of Factor VIII (Anti-Hemophilia A Factor, AHF) and Factor IX (Anti-Hemophilia B Factor) are stocked only in the UCSD Pharmacy (not in the Blood Bank) and may be ordered by calling the pharmacy (ext 3-6194). In view of frequent changes in the availability of increasingly purified products, questions regarding the use of these products should be addressed via the UCSD Pharmacy during normal working hours or to the Hematology Service at other times. Recombinant human Factor VIIa, (Novo-7) is indicated in patients with hemophilia who have inhibitors and is being investigated in a variety of other coagulopathies (dose for hemophilia A with inhibitors; 90 mcg/kg q 2 hours for bleeding). Recombinant human Protein C concentrate has been FDA approved for use in

severe sepsis. An Apha-1 proteinase inhibitor concentrate made of pooled plasma has been FDA approved for use in deficiency states.

## **16. Rh(D) IMMUNE GLOBULIN (RhIg)**

### **16.a Preparations and Administration**

RhIg is available as an IM preparation (eg, RhoGam <sup>TM</sup>) primarily used for prophylaxis against sensitization to the Rho(D) antigen in pregnant women, and as an IV/IM preparation (eg WinRho <sup>TM</sup>, or Rhophylactic <sup>TM</sup>); the former is primarily used IV in therapy of Autoimmune Thrombocytopenic Purpura (ITP) but may also be used IV or IM as above and the latter is primarily indicated for suppression of immunization to Rho(D) in pregnant women. These products are derived from limited pools of plasma from sensitized donors, are virus inactivated, and carry little or no risk of infectious disease. Each product is available in a variety of dosage forms, depending on the indication.

### **16.b Indications:**

Pregnant women who are candidates for RhIg should be identified by blood type (Rho(D)-neg) and antibody screen (no anti-D) at the first prenatal visit and should be informed of the need for RhIg administration, as follows: RhIg is administered IM to Rho(D) negative mothers at the 28th week of pregnancy and within 72 hours post-delivery of an Rho(D) positive infant, and post-abortion, trauma, external fetal manipulation, invasive procedures involving the fetus or amniotic cavity, e.g. amniocentesis, chorionic villus sampling, or ruptured tubal pregnancy. At term, an assessment of the need for additional RhIg dosing should be made by testing for fetal-maternal bleeding on a maternal blood specimen drawn on the day after delivery.

RhIg may also be given to nonpregnant Rho(D) negative individuals after transfusion of a Rho(D) positive blood product which contains small numbers of red cells, such as platelets. Treatment of Rh-neg males or Rh-neg patients being treated with high dose chemotherapy for malignancy, after exposure to Rh-pos platelets, is optional but recommended, since the latter may still be sensitized to anti-D (albeit with low frequency). The IV preparations have advantages in this setting by eliminating the risk of hematoma from IM injection.

It is not necessary to give RhIg after transfusion of acellular blood components, e.g. FFP or Cryo and it is impractical to attempt to treat an individual who has received an entire unit of Rh positive PRBC, except in extraordinary circumstances. RhIg is not indicated in persons who are already immunized to the Rho(D) antigen. IM RhIg is available through the UCSD Blood Bank.

WinRho (IV anti-D) is indicated for treatment of ITP in non-splenectomized, Rho(D)-positive patients. Recent results suggest that WinRho has as rapid an onset of action in ITP therapy as IVIg and it is far less costly than IVIg. IV RhIg is available through the UCSD Pharmacy Service.

### 16.c Dose:

The recommended dose of RhIg at 26-28 weeks of pregnancy, at term, and for other sensitization risks noted above is 300 ug of RhIg (IM). Since 20 ug of IM RhIg suppresses immunization from one mL of rbc the 300 ug dose of IM RhIg will protect against immunization by up to 15 mL packed red cells (approximately 25-30 cc of whole blood). The greatest risk for fetal-maternal hemorrhage (FMH) in an uncomplicated pregnancy occurs at delivery, and less than 3 births in 1,000 will be associated with FMH > 30 mL. However, studies show that “high risk” factors for FMH fail to predict which births will be associated with FMH > 30 mL, nor does the presence of circulating anti-D (from the 28 wk dose) protect against a large FMH. Consequently, a test for excessive FMH (at UCSD, the Kleihauer-Betke or fetal screen; 5 mL EDTA tube) should be performed by the Blood Bank in **ALL** Rho(D) negative women who give birth to Rho(D) positive infants, to determine if a single dose of RhIg is sufficient to prevent immunization. The number of vials of RhIg (300 ug, IM) to administer post-partum is calculated by dividing the mL of fetal-maternal bleed (whole blood) by 30 and a safety margin is added to the calculated dose of RhIg due to the wide error in calculating FMH. Thus, if the resultant fraction is < 0.5, drop the fraction and add one vial. If the fraction is 0.5 or more round up to the next dose and add one vial. For example, if the result is 0.4, the dose is 1 vial; if the result is 0.5 the dose is two vials; if the result is 1.4 the dose is two vials, if the result is 1.5 the dose is three vials. While RhIg should be administered within 72 h post partum, this limit is arbitrary and treatment should not be withheld even if more than 72 hours have elapsed. If RhIg is administered earlier than 28 wk, additional doses should be given every 12 wk during pregnancy. Mini-dose Rh(D) immune globulin contains about 50 ug RhIg (1/6 the quantity of a standard dose) and is indicated for prophylaxis after termination of pregnancy or miscarriage occurring prior to 12 weeks of pregnancy and will protect against immunization to Rh(D) by up to 2.5 mL of RBC (approximately 5 cc of whole blood). If WinRho is used for suppression of immunization during pregnancy, the recommended dose at 28 weeks is 300 ug and at term is 120 ug. RhIg is indicated to prevent sensitization to anti-D in Rh-negative females of childbearing potential who are recipients of Rh-positive platelets. RhIg may also be indicated after invasive procedures in Rh-neg pregnant women, eg ACOG guidelines call for RhIg to be administered after amniocentesis. If RhIg is administered within 21 days prior to delivery and the post-partum fetal blood screen on the mother fails to show excess bleeding, RhIg need not be re-administered post-partum (AABB guideline).

RhIg should suppress alloimmunization to Rh(D) in Rh-negative persons exposed to small amounts of Rh-positive blood, eg after platelet transfusion. Apheresis platelets produced by modern methods contain < 0.1 ml rbc each; consequently a small dose of RhIg is sufficient. IV RhIg (WinRho, 120 ug/dose) has the advantage of avoiding an IM injection in thrombocytopenic patients. If an IM RhIg is used it should be administered soon after determining that the patient’s platelet count is adequate to avoid bleeding. Administration of one dose of RhIg per month should be sufficient to cover the small amount of rbc in platelets, unless the patient is known to have received > 25 units during

the month or platelets that have heavier rbc contamination. For patients given repeated doses of platelets over a period of time, it will be necessary to give additional doses monthly, since the half life of IgG is approximately 21 days. If an Rh-negative patient has been exposed to larger amounts of Rh-positive rbc, the suppressive dose is 20 mcg/mL packed rbc, but it is generally considered impracticable to attempt to suppress anti-D formation in persons who have received a full unit (250 mL) of Rh-positive RBC.

WinRho is indicated in ITP therapy. The usual starting dose is 50 ug/kg IV (rounded to the nearest vial), unless the patient's hemoglobin is < 10 gm/dl (then 25-40 ug/kg). Expected side effects include a 1-2 gm/dL reduction in Hb. Patients should be monitored for hemolysis, since cases of severe or fatal hemolysis have been reported. The duration of beneficial effect of anti-D on platelet count (about 3-6 wk) may be longer than that typically associated with IVIg (about 1-3 wk), and repeated dosing is usually required.

## 17. AUTOLOGOUS TRANSFUSIONS

California State Law requires that all patients who are scheduled for surgery, invasive procedure, or other therapy in which there is a reasonable possibility of blood use are to be given the opportunity to donate their own blood. Many patients will be able to pre-deposit 2-4 units of their blood between 35-3 days prior to surgery. Eligibility requirements are few, but include the absence of active bacterial infection or potential for bacteremia, severe hypertension, aortic stenosis, recent myocardial infarction, angina or significant cardiovascular or cerebrovascular disease and a hematocrit >33% (ideally >40% prior to the first donation). Autologous donation during pregnancy is possible, but not generally necessary unless there is a compelling reason, eg high-risk pregnancy or unusual antibody. The use of erythropoietin may increase the number of patients who can donate autologous blood, and the number of units drawn/patient. Patients who are known to be carriers for Hepatitis B or have positive tests for HIV are not encouraged, due to the possibility of infecting others through mishaps. Patients who are HCV positive are eligible upon written request by the physician. The autologous donor will be bled by the American Red Cross (760 737-7921). This requires a physician's verification of patient health status, eligibility, and an order requesting that blood be drawn for autologous transfusion (Red Cross has special forms). A blood specimen from the recipient as well as the usual request slips must be sent to the UCSD Blood Bank before anticipated usage. The order must indicate **AUTOLOGOUS BLOOD**. Further information may be obtained from the Blood Bank.

## **18. DIRECTED DONATIONS**

Directed donor (donor-specific) blood is not recommended due to clinical studies showing that it is no safer than the normal blood pool and may be less safe, presumably because of social pressure on the donor to withhold information which might prohibit their eligibility. Fatal graft vs host (GVHD) reactions after transfusion of directed donor blood have been reported as a result of HLA similarities in donations between close relatives. Directed donor blood from all blood relatives must be type-compatible with the recipient and must be irradiated to prevent GVHD. Unless the Blood Bank can be sure which Directed Donor units come from blood relatives, all Directed Donor units will be irradiated. Directed donations are more complicated for patients who may require CMV-negative blood, since arrangements must be made to assure that the donor is CMV negative or that the blood is pre-storage leukocyte-reduced. In view of this, and to prevent a double standard of care, all directed donor blood should be ordered as leukocyte-reduced. Although efforts should be made to discourage directed donations, the American Red Cross will comply when this is requested. Donors will be bled and the units labeled for the prospective recipient will be sent to the UCSD Blood Bank. Units will be held only a week beyond the date of expected surgery or transfusion, unless the physician notifies the Blood Bank to extend the storage time beyond a week. Further information may be obtained from the UCSD Blood Bank. Do not arrange for blood components of donors from distant locations to be sent directly to UCSD. All such donations must first go to the American Red Cross (760 737-7921).

## **19. THERAPEUTIC HEMAPHERESIS AND PHOTOPHERESIS**

These procedures may be scheduled through the UCSD Nephrology Division. The physician supervising therapeutic pheresis will be responsible for ordering replacement components. Saline and 5% albumin for volume replacement will be provided by the pheresis team. Any other product (RBC, plasma, etc.) for replacing components should be ordered by the physician supervising the therapeutic pheresis from the UCSD Blood Bank in the usual manner using routine Blood Bank forms, and indicating that it is for therapeutic apheresis.

## **20 TRANSFUSION REACTIONS & HAZARDS**

The immediate work-up of all transfusion reactions is outlined below and is also found on the Blood Transfusion Record. For all reactions, the Transfusion Reaction section of the Transfusion Record must be completed and returned to the Blood Bank, along with the remainder of the unit and the post-transfusion specimens. The only exception is that allergic reactions require reporting but do not require laboratory work-up.

Transfusion reactions can be immediate (*e.g.*, allergic, febrile, circulatory overload, transfusion-related acute lung injury, gram-negative sepsis, hemolytic, etc.), or delayed (*e.g.*, hemolytic, HIV, hepatitis, Graft vs Host disease, iron overload, etc.). All suspected transfusion reactions must be immediately reported to the UCSD Medical Center Blood

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Bank (Hillcrest 3-5640; Thornton 7-6162) and should be immediately worked-up by the patient's physician and laboratory staff.

It has been estimated that 3/10,000 transfusion recipients will develop a severe or fatal transfusion transmitted disease (NEJM 327:420, 1992). In view of the risks of transfusion (and California State law), it is essential to obtain informed consent before using blood products in nonemergency situations. The patient should be made aware of the risks and benefits of transfusion, and alternatives to transfusion, and this should be documented in the medical record.

The following tables represent an attempt to summarize the hazards of transfusion and may be helpful in communicating with the patient. The risk estimates shown are approximations which will vary with the donor population, procedures used in the blood bank laboratory, types of components administered, recipient population and possibly other factors. Recent experience shows that new transfusion risks emerge continuously; hence the following list is likely to become outdated within 6 – 12 months. It thus behooves the physician to keep up with recent developments. Call the Blood Bank for additional information.

### Estimates of the Frequency of Adverse Effects of Blood Transfusion

Infectious Risk	Risk/Unit	Comments
Viral hepatitis:		
HAV	rare	Donors screened for recent HAV by history
HBV	1 in 140,000 - 200,000	HBV (HBsAg) tested since 1971, HBcAb in 1989
HCV	1 in 1.3 – 1.9 million	HCV since 5/90; improved assays 3/92, 5/96, 1/01 NAT (PCR); FDA approved 5/02
HDV	rare	HDV occurs only in HBV carriers.
HGV	1 in 100	HGV (GBVc) Not clearly associated with disease
HIV-1/2	1 in 1.5-2.4 million	Donor blood screened for HIV antibody since 4/85, p24 antigen from 3/96-7/03, NAT in 1/02.
HTLV-I/II	1 in 2.9 million	Donor blood tested since 1/89. Cases of HTLV- associated myelopathy (HAM) reported.
CMV	~ 7/100 (non leukocyte-reduced blood)  1-2/100 (leukocyte- reduced blood or CMV seronegative blood)	Clinically insignificant in most patients, but may be a serious problem in some seronegative pts, eg, neonates (& pregnant women), pts with immune deficiency, seronegative HIV+, and transplant pts. UCSD employs only leukocyte-reduced blood, which is equivalent to CMV seronegative.
Epstein-Barr virus	1 in 200 (seroconversion)	Mononucleosis picture 2-5 weeks after transfusion. Historically with open heart surgery.
Bacterial sepsis or endotoxin reaction	RBC - 1 in 30,000 PLT - 1 in 100,000 transfusions	Approx 1 death / 1-6 million units transfused. Previously higher incidence in PLT due to storage at RT, but ARC cultures PLTs before release as of 4/04
Malaria, Chaga's and other parasitic diseases	Rare (<1 in 1,000,000)	Donors from endemic regions, returning servicemen, third world students, etc. Test for Chaga's disease may be used regionally.
Lyme disease	Rare	Primarily limited to Eastern USA
Syphilis	Rare	Donors tested (RPR, VDRL) since 1940s. Spirochetes do not survive 4 C for 3 days.
B 19 parvovirus	Unknown	Clinically insignificant in most pts, (5 <sup>th</sup> disease), but may cause transient red cell aplasia in pts with chronic hemolysis, or prolonged aplasia in pts with HIV or immune suppression, or fetal demise
West Nile Virus	Unknown	NAT testing to begin in 2003

#### Window period to seroconversion or positive test after infection.

Virus	Days
HIV	11 - 16
HTLV	36 - 72
HCV	10 – 70

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HBV	45 - 59
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### Non Infectious Risks of Transfusion

Adverse Effect	Risk/Unit	Comments
Acute hemolytic reaction	1 in 25,000 – 50,000	Majority of cases due to patient identification error in drawing blood specimen or giving blood, and involve ABO mismatch; 10-30% are fatal.
Delayed hemolytic reaction	1 in 2,500	Occurs 4-14 days after transfusion. Usually clinically silent, evident from dropping Hct and serological findings.
Platelet alloimmunization to HLA	1 in 10 transfusions (non-leukocyte reduced)	Refractory state to platelet transfusion; usually due to anti-HLA antibodies. Minimize or prevent by leukocyte-reduced platelets.
Febrile, non-hemolytic reaction	1 in 200	Leukocytes are major cause; previous donor history of multiple transfusions or pregnancy. Minimize and/or prevent by leukocyte-reduced blood components.
Transfusion Related Acute lung injury (TRALI)	1 in 5,000 - 10,000	Non-cardiogenic pulmonary edema due to high-titer leukocyte antibody in donor (or rarely recipient) plasma. 5 to 10% are fatal.
Allergic reactions	1 in 200	Urticaria, usually with plasma containing components.
Anaphylactic hypotensive reaction	1 in 50,000 – 150,000	Most are due to antibody to unidentified foreign plasma protein, but some due to anti- haptoglobin, -complement, or -IgA, eg in IgA-deficient pt (1 in 600). Use washed RBC; pre-Rx with steroid.
Red cell alloimmunization	1 in 100	Problem in multiple RBC recipient, Sickle-cell anemia, thalassemia, etc.
Graft vs Host disease	Rare	Problem in patients with severe immunodeficiency (not reported in HIV), marrow transplant, and recipients of blood from family members. Prevent by blood irradiation
Circulatory overload	1 in 10,000	Infants and patients over 60 usually involved. Prevention depends on clinical judgment. Use RBC and controlled rates of infusion.
Hyperkalemia	Unknown	Premature hyperkalemic newborns & anhepatic phase of liver transplant surgery
Hypothermia	Unknown	Premature newborns & occasionally other massively transfused patients. Use blood warmer.
Citrate toxicity	Unknown	Massive transfusion, eg more than 1 unit q 5 min.

Data sources include:

Walker, RH, Am J Clin Path 1987; 88:374,  
Morrow, JF, JAMA 1991; 266:555,  
Dodd, RY, N Engl J Med 1992; 326:419,  
Nelson KE, Ann Int Med 1992, 117:554,  
Chiu, ET, Transfusion 1995; 34:950,

Schreiber GB, N Engl J Med 1996;334:1685  
Jacobs MR Transfusion 2001;41:1331  
Busch, MP JAMA 2003;289:959-962  
Kleinman SH Vox Sang 2002;83:106  
Dodd RY Transfusion 2002;42:975

## 20.a Hemolytic Transfusion Reactions

Hemolytic reactions may be immediate or delayed. Most serious, or life threatening hemolytic reactions involve ABO incompatibility and are due to human error (mislabelled or mixed-up crossmatch specimens, blood unit given to the wrong patient, etc.).

1. **MONITOR** all patients shortly after the start of transfusion. In the conscious patient, symptoms of hemolytic reaction usually develop with the first 50-100 mL of blood. Immediate reactions may include fever, chills, nausea, restlessness, chest or abdominal pain, etc. In the unconscious patient the only signs may be alteration in the vital signs or hemoglobinuria. Symptoms are often nonspecific (chills, fever, back pain, dyspnea, etc.), and there may be no correlation between severity of symptoms and degree of hemolysis.
2. **STOP TRANSFUSION IMMEDIATELY** if a reaction develops, but keep the IV open with saline. Severity of the complications resulting from a hemolytic reaction is dose-dependent. Recheck the patient's ID armband with the recipient ID tag/label attached to the unit.
3. Immediately notify the Blood Bank (Hillcrest; 3-5640/3-5641; Thornton 7-6162). Follow instructions on Transfusion Record.
4. Transfusion Record gives specific instructions regarding initial management and work-up. The form must be filled out, signed by physician, and sent to the Blood Bank ASAP.
5. Specimens: Return blood container and all tubing to the Blood Bank immediately. Maintain sterility of the system for cultures. After stopping transfusion, carefully draw a 7 mL blood specimen in a tube with EDTA, avoiding hemolysis. Be sure to label the tube correctly, including the time and date, and send it to Blood Bank stat. The specimen will be used to confirm the patient's ABO/Rh type, perform a direct antiglobulin test (DAT), and will be examined for plasma hemoglobin. A significant reaction will be accompanied by hemolysis, visible as a pink or red color in the plasma (>25 mg Hb/dL; after intravascular destruction of <25 mL PRBC and/or a positive DAT. If indicated, antibody screen, repeat crossmatches, and other studies will be performed.
6. Have patient void and send first post-transfusion urine for urinalysis and tests for hemoglobin.
7. Do not administer any additional units without confirmation from the Blood Bank that it is safe to do so. The Blood Bank Resident is notified of any transfusion reaction and can advise you.

8. **If a hemolytic reaction strongly suspected:** Give a saline volume load; 1000 mL over 1-2 hours (if not contraindicated by cardiac status) and furosemide 20-80 mg IV stat, prn to keep urine flow at 100 mL/hr. Give dopamine, 1-4 ug/min for pressor support (< 4 ug/min may permit renal arteriolar vasodilatation). Obtain baseline renal function (Cr, BUN); test for DIC (PT, aPTT, Ddimer, fibrinogen, 3P) and treat prn. Supportive care; eg colloids for volume, coagulation components prn. Role of steroids (1 mg/kg prednisone IM or IV), exchange transfusion to remove remaining incompatible rbc, or bicarbonate to diminish renal Hb toxicity is unclear.
9. Recall that hemolysis accompanying transfusion may be due not only to blood incompatibility, but also to hemolytic drug reaction (eg administration of 2<sup>nd</sup> generation cephalosporins), administration of hemolyzed blood (excessive heating, cooling, incompatible IV solutions), mechanical trauma, (eg bypass machine), infected blood, and/or infections, eg malaria, clostridia.
10. Delayed hemolytic reactions are due to the emergence of a new antibody and may occur from 1 to 14 days after transfusion. They are usually manifest by fever, icterus and a rapidly falling hematocrit. If a delayed reaction is suspected, it should be reported to the Blood Bank, since a serious hemolytic reaction may occur in 10% of cases and should be treated as above. The patient should be kept well hydrated to prevent renal failure and monitored for hemolysis.

## **20.b Non-Hemolytic Transfusion Reactions**

### **20.b.1 Febrile Reaction:**

All febrile reactions (> 1°C or 1.7°F rise in temperature; frequency 1/200 transfusions) occurring during blood transfusion must be reported to the Blood Bank. Most "febrile transfusion reactions" (fever during transfusion) are unrelated to blood administration, but are due to the patient's underlying condition. However, fever may also be the first sign of either a hemolytic reaction, an anti-leukocyte reaction (so-called "febrile non-hemolytic reaction", or FNHTR), or the harbinger of transfusion-related acute lung injury (see below), or rarely, may be due to bacterial sepsis due to blood unit contamination. Thus, when a patient develops fever in association with transfusion, red cell hemolysis must be excluded (see above) and bacterial contamination must also be considered (see below). The lab workup accomplishes these goals. If these serious reactions can be excluded, and the patient's underlying condition can be ruled out as causing the reaction, it is reasonable to suspect that a reaction associated with fever represents a FNHTR due to leukocyte antibodies. FNHTRs due to leukocyte antibodies are usually recurrent. However, this is ordinarily a diagnosis of exclusion, and is based upon a characteristic pattern of a >1°C rise in temperature during or after transfusion in a patient with a history of previous transfusion or pregnancy. Such patients usually have a positive test for anti-HLA antibodies (assessed by sending an EDTA specimen to the HLA lab for "HLA antibody screen by ELISA"). Such antibodies occur as a result of prior exposure to leukocyte-containing blood products or pregnancy. FNHTR are usually treated with

acetaminophen, 600 mg, PO and can be prevented by giving leukocyte-reduced components (see above). All rbc and platelets at UCSD are pre-storage leukocyte-reduced, so this type of reaction should be rare. Occasionally a mild elevation in temperature may also accompany an allergic reaction or may be due to infusion of cytokines that accumulate in stored platelets. Cytokine reactions are also minimized or prevented in pre-storage leukocyte reduced platelets and rbc.

### **20.b.2 Allergic Reactions:**

The spectrum of allergic reactions varies from hives (urticaria) to anaphylaxis. Mild allergic reactions occur during 1 in every 200 transfusions, their onset is rapid, and they are due to patient antibodies to donor plasma proteins. A mild urticarial reaction (hives localized to one small area, responsive to antihistamine treatment) is the only transfusion reaction in which the remains of the unit may be given, albeit slowly, after appropriate treatment. Most mild urticarial reactions are isolated episodes that rarely recur. Recurrent mild allergic reactions may be treated by premedication with antihistamine within one hour of giving the blood, (e.g., 25-50 mg diphenhydramine, [benadryl] PO or IM). Moderate reactions associated with bronchospasm may require antihistamine IM or IV and sub-Q epinephrine, 0.3-0.5 mL of 1 mg/mL (1/1000 USP) q 5-20' prn. Severe allergic reactions may occur in IgA deficient persons (1/600 incidence) or persons homozygous for an IgA immunotype, who develop antibodies to foreign IgA. However, the majority of severe allergic reactions occur in persons who are not IgA deficient or homozygous, and probably represent antibodies to other polymorphic plasma protein immunotypes, eg haptoglobin, complement components, IgG, etc. Severe allergic reactions are treated with IV fluids and vasopressors prn to support blood pressure, epinephrine Sub-Q as above or slowly IV (dilute 1 mL of 1/1000 epi in 10 mL saline and give over 5-10 min), antihistamine IM or IV, and steroids (1 mg/kg prednisone IM). After a single anaphylactic reaction, future transfusions should employ washed red cells, premedication with antihistamine one hour before transfusion and steroids (as above at 12, 6, and 1 h pre-transfusion), immediate availability of epinephrine, and careful patient observation. IgA levels, and anti-IgA antibody studies should be performed using a pretransfusion specimen, if indicated. Washed platelets are not generally available, and premedication with steroids and antihistamines is effective in preventing reactions.

### **20.b.3 Transfusion-related Acute Lung Injury (TRALI):**

This reaction is characterized by acute, non-cardiogenic pulmonary edema and respiratory failure, occurring in proximity with blood transfusion (< 6 h) and is fatal in 10%. The etiology in > 90% of cases is passive transmission of anti-leukocyte antibodies from the donor unit, usually derived from a multiparous woman who has a high-titer anti-leukocyte antibody from immunization during previous pregnancies. There is sufficient plasma to cause this reaction in PRBC and Platelet Concentrate as well as FFP. About 5% of TRALI is due to recipient antibodies reacting with donor leukocytes, and is prevented by use of pre-storage leukocyte-reduced blood. Initial diagnosis of TRALI

requires a high index of suspicion in a patient developing acute respiratory failure (non-cardiogenic pulmonary edema associated with a "white out" on chest film) within 0.5 - 4 hr after blood transfusion. Diagnostic criteria for TRALI and Possible TRALI have been proposed (Transfusion 2004;44:1774):

**TRALI:**

1. Acute Lung Injury (ALI; ASA criteria)
  - a. Acute onset
  - b. Hypoxemia -  $\text{PaO}_2/\text{FiO}_2 < 300$  or  $\text{SpO}_2 < 90\%$  on room air or other clinical evidence of hypoxemia (oximetry  $< 90\%$  sat [UCSD criteria])
  - c. Bilateral infiltrates on frontal chest radiograph
  - d. No evidence of left atrial hypertension (ie, circulatory overload)
2. No preexisting ALI before transfusion
3. During or  $< 6$  hr after transfusion
4. No temporal relationship to an alternative risk factor for ALI

**Possible TRALI**

1. Same as 1 – 3 above, **BUT**
2. Temporal relationship to an alternative risk factor for ALI, eg
  - a. Direct - aspiration, pneumonia, toxin inhalation, drowning
  - b. Indirect – sepsis, burn, trauma, drug, shock, CPB

A TRALI diagnosis requires evidence of acute hypoxia/desaturation, absence of left atrial hypertension (eg, a normal CVP, pulmonary capillary wedge pressure (less than 15-20), or BNP) and bilateral infiltrates on chest radiography, and is supported by testing the donor unit for anti-leukocyte antibodies, which should correspond with the patient's tissue type (see below). Milder cases of TRALI may also occur and this diagnosis should be considered in all patients who have transient respiratory distress that accompanies transfusion and other causes are ruled out. Antibody testing is most efficiently done by submitting a specimen from the unit or patient (post +/- pre-transfusion) for anti-HLA ELISA screen as 85% of cases are due to anti-HLA class I and/or class II antibodies. However, if this test is negative and there is a high index of suspicion, then additional testing should be done, since 15% of cases are due to anti-PMN antibodies and some may be due to monocyte antibodies. Additional testing may include the patient's HLA type. About 5% of TRALI cases occur in patients who are alloimmunized to HLA and/or leukocyte antigens and receive non-leukocyte-reduced blood, but this should not occur at UCSD since all rbc and platelets are pre-storage leukocyte-reduced. Treatment is supportive, and usually includes mechanical ventilation with positive end-expiratory pressure and oxygen supplement. The role of steroids and diuretics is unclear. The Transfusion Service must be immediately notified when TRALI is suspected, since additional patients are at risk for this reaction from a different blood component from the same donor. Thus, the Transfusion Service Resident must immediately 1) contact the American Red Cross to recall/quarantine any other components from the same donation of blood, 2) assure that a search is made of the UCSD inventory for any components from the same donation and order their quarantine if found. The patient should receive

leukocyte-reduced rbc and platelets (automatic at UCSD). The ARC is responsible to restrict the donations of such donors to non-plasma containing products.

#### **20.b.4 Transfusion-associated Graft vs Host Disease (TAGVHD):**

TAGVHD is a rare but nearly always fatal complication of transfusion of cellular blood components, occurring primarily in immunocompromized hosts. TAGVHD occurs when viable donor T-cells transfused with cellular blood components are not eliminated by normal immune mechanisms, but proliferate, recognize the host's tissues as foreign, and undertake to "reject" the host tissues. Skin, gut, liver, and bone marrow are the primary target organs. Persons at risk for TAGVHD include patients with congenital immunodeficiency, allogeneic and autologous bone marrow transplant recipients, fetuses given intrauterine transfusion, neonates, especially premature and those given exchange transfusion, patients with Hodgkin's disease, lymphoma, acute leukemia and selected other oncology patients given high dose chemotherapy, recipients of HLA matched blood products and directed donor blood from blood relatives, due to the possibility of HLA similarity. In addition, cases of TAGVHD have been reported in CLL patients who received fludarabine. UCSD policy is to irradiate all directed donor blood, since there is a risk that a blood relationship between a directed donor and the patient may not always be identified. The degree of risk for GVHD in term newborns, patients with hematologic malignancy or solid tumors, and organ transplant recipients other than bone marrow are less well defined. There is no defined risk of GVHD in patients with AIDS. TAGVHD is easily prevented by blood irradiation, but TAGVHD is **not** prevented by using leukocyte-reduced blood. Since the Transfusion Service at UCSD is not aware of all potential indications for irradiated blood in a given patient, the physician who orders blood is responsible to ensure that irradiation is also ordered, if indicated.

#### **20.c Infectious Complications of Blood Transfusion**

The risk for a transfusion-transmitted infection requires a careful assessment of the need for transfusion, since new infectious diseases that may be transmitted by blood emerge with regularity (most recently, SARS and West Nile Virus). When possible, autologous blood transfusions should be considered as an alternative to homologous transfusions to reduce these risks. Autologous blood can prevent most of the serious adverse effects of homologous blood transfusions, including most disease transmission, immunological effects, etc., but will not prevent clerical errors or bacterial sepsis, and even anaphylactic reactions have rarely been reported. Note that albumin, plasma protein fraction, Rh Immune globulin, and gamma globulin do not transmit any infectious agents. Commercial Factor VIII and IX preparations and recombinant proteins are free of infectious risk from hepatitis, HIV, HTLV, HCV and CMV. Certain cell-dependent infectious agents, eg HTLV-I/II and CMV are not transmitted by acellular components, eg FFP, Cryoprecipitate. CMV transmission is also reliably prevented by pre-storage leukocyte-reduced red cells and platelets. The possibility that blood may transmit variant Creutzfeld-Jacob disease (vCJD) is of concern, but there have been < 5 potential cases of

vCJD transmission in humans by blood as of June, 2006. West Nile Virus has been transmitted by blood and is of concern in immunocompromized patients, but this risk has been mitigated by universal donor testing since 2004. SARS and other newly identified pathogenic microbes that have a pre-symptomatic blood phase and for which there is no effective donor test, serve as reminders to employ blood only when indicated.

### **20.c.1 Hepatitis:**

Hepatitis may be transmitted by all blood components, however the risk has diminished to the point that current risk estimates of the known viruses (see Table) are based on mathematical models, not direct measurement. With improvements in donor tests for HCV antibody, and nucleic acid testing, HBV (donors tested by HBsAg and HBcAb) is once again estimated to be the most common, albeit rare, hepatitis risk. Since cases of transfusion associated "Non-A, non-B, non-C, non-D, non-E, non-G" hepatitis continue to be reported, there are probably additional, as yet unidentified parenterally transmitted hepatitis viruses.

### **20.c.2 HIV (AIDS):**

Human Immunodeficiency Virus (HIV) may be transmitted by all blood products that can transmit other viruses. Efforts are made to exclude groups with a high incidence of HIV or other parenterally transmitted viruses and blood donors are tested for antibody to HIV-1/2 and the HIV p24 antigen. With the advent of nucleic acid testing (FDA approved 5/02) there is further improvement in safety from HIV and testing for p24 antigen will be discontinued in 2003. There is no risk of becoming infected with HIV from blood donation.

### **20.c.3 Human T cell Leukemia Virus (HTLV-I/II):**

HTLV-I/II may be transmitted by cellular blood components and donors are tested for HTLV-I/II antibody. There are several case reports of transfusion-transmitted cases of HTLV-I/II developing HTLV-associated myelopathy (HAM) within one year. HTLV-I may also cause T-cell leukemia (ATL), but the latent period is many years and it is estimated that individuals infected with HTLV-I have a 4% lifetime risk of ATL or HAM.

### **20.c.4 Cytomegalovirus (CMV)**

UCSD Medical Center Hospitals employ only leukocyte-reduced blood, in order to minimize the risk of transfusion-associated CMV infection. CMV may be transmitted by leukocytes in cellular blood components (red cells and platelets, not FFP). The likelihood of CMV transmission in non-leukocyte-reduced blood is dependent on whether the donor is CMV infected (about 50% of donors in the USA) and the dose of leukocytes. The severity of infection is related to host immune status. In normal persons, CMV infection is trivial. In severely immunocompromized individuals and low birthweight neonates born of CMV seronegative mothers, CMV infection may cause

hepatitis or pneumonia, and infection may become disseminated. In the fetus CMV may cause neurological damage. At UCSD, CMV-safe blood (either prestorage-leukocyte-reduced or from CMV-neg donors) is routinely provided for all neonates and infants less than 4 months of age, not because it is required in all, but to prevent omissions in ordering. In addition, CMV infection should be prevented in marrow transplant patients and in the other patient groups listed below. In CMV-seronegative bone marrow transplant recipients with CMV-seronegative donors it may be preferable to use CMV seronegative blood despite the fact that these patients receive pre-storage leukocyte-reduced blood, in order to prevent confusion regarding lab tests caused by passive administration of anti-CMV IgG. Transfusion-induced CMV is prevented equally well either by using pre-storage leukocyte-reduced red cells and platelets, or by obtaining red cells and platelets from CMV-seronegative donors. If neither of the above are available then red cells and platelets should be filtered through 3rd generation leukocyte-reduction filters at the bedside, paying careful attention to instructions and using one filter per unit. Neither saline-washing nor irradiation will prevent CMV. Acellular blood components (FFP, cryo) do not transmit CMV. Contact the Blood Bank Resident (3-5640) for further information. Accepted indications for CMV-safe blood components include:

- CMV-seronegative pregnant women
- Intrauterine (fetal) transfusion and exchange transfusions in newborns
- Low birth weight infants born of CMV seronegative mothers
- CMV-seronegative organ transplant candidates and transplant recipients from CMV-seronegative donors (includes autologous bone marrow)
- CMV-seronegative patients with congenital or acquired immune deficiency syndromes, including HIV infection
- CMV-seronegative adults undergoing splenectomy as a result of trauma

### **20.c.5 Bacterial Contamination**

It is estimated that 0.2 to 2% of donated blood may contain bacteria at the time of collection. This may be due to inadequate sterilization of the donor site, the incision of a skin core through the needle, or asymptomatic bacteremia in the donor. There is also a small risk that a unit left hanging for a prolonged period may become contaminated. Bacterial sepsis, while a rare complication of red blood cell transfusion, is more common with platelets (1 in 2000 transfusions) because they are stored at room temperature. Symptoms may vary from a "febrile reaction" to typical septic shock; consequently sepsis should be considered in all patients who have fever with transfusion and all units from patients who have a febrile reaction should be gram stained and cultured. Treatment is supportive and includes broad spectrum antibiotic coverage. The Transfusion Service must be notified immediately, since other components from the same blood draw will also be contaminated, thus placing other patients at risk. The Transfusion Service Resident must immediately 1) contact the American Red Cross to recall/quarantine any other components from the same donation of blood, 2) assure that a search is made of the UCSD inventory for any components from the same donation and order their quarantine if found.

### 20.c.6 Severe Acute Respiratory Syndrome (SARS)

SARS was identified in Asia in February, 2003 as a respiratory illness of unknown etiology, that is currently thought to be due to a lipid enveloped coronavirus and has a case fatality rate of approximately 3-5%. Viremia has been detected in persons with SARS. In an effort to protect the blood supply, blood donors are deferred 28 days for a history of SARS or 14 days for possible exposure to SARS by travel or close personal contact.

### 20.c.7 West Nile Virus (WNV)

WNV was identified in the US in 1999 and by 2003 is expected to have spread to the West Coast. It is spread by mosquitoes that feed on infected birds, and may be spread to humans, typically during the summer. Approximately 80% of infected persons are asymptomatic. Others may develop a mild to moderate febrile illness with myalgia, adenopathy, gastroenteritis, or rash, 3 to 15 days after the bite of an infected mosquito. Severe illness, including encephalitis or meningitis may occur in 1/150–200 cases, typically in the elderly and in organ transplant recipients and may be fatal in 10%. Viremia occurs 1-3 days after mosquito bite and may persist 1-11 days. WNV may be spread among humans by organ donation, blood administration, and possibly breast feeding from a viremic donor. The risk of WNV from blood is currently unknown. As of June, 2003 blood donors are deferred 28 days for fever and headache within the previous week, recipients will be contacted when post-donation risk factors are identified, and a NAT will be implemented on blood donors by July, 2003. Organ and tissue transplant donors should be screened likewise. Plasma derivatives are not thought to be infectious, since lipid enveloped viruses are destroyed during preparation.

Summary of some infectious risks of common blood components & derivatives:

Infectious Risk	Whole blood & RBC	Platelets	FFP & Cryo	Coag factor concentrates	Immune-globulin	Plasma protein fraction & albumin
HIV 1/2	yes	yes	yes	No	no	no
HTLV-1/II	yes	yes	no	No	no	no
Hepatitis	yes	yes	yes	No	no	no
CMV	yes <sup>1</sup>	yes <sup>1</sup>	no	No	no	no
Bacteria	yes	yes	no	No	no	no
Malaria	yes	yes	rare	No	no	no
Syphilis	yes	yes	no	No	no	no
B19	yes	yes	yes	Yes	no	no
WNV	yes	yes	yes	No	no	no

<sup>1</sup> prevented by pre-storage leukocyte-reduced blood components

## 21. NEONATAL AND PEDIATRIC TRANSFUSIONS

### 21.a Pediatric Packed Red Blood Cells

(100-125 mL; Hct = 70-80%; Shelf Life = 35 days)

Pediatric packed red blood cells contain about 100 mL of packed red cells. Transfusion criteria are the same as for adults. Pediatric RBC are not available for surgical procedures. Adult RBC may be substituted in such cases.

### **21.b Neonatal Red Cell Transfusions**

Neonates have special transfusion requirements due to their small blood volume, relative immune deficiency, and metabolic immaturity. In general, the lower the infant's birthweight and younger chronological age, the more complex are the transfusion requirements. Stable neonates are typically transfused when their Hct falls below 25% (Hb < 8 gm/dL). Infants < 24h old and sick neonates (eg, respiratory distress, cyanotic heart disease) are frequently transfused with Hct < 40% (Hb < 13 gm/dL). Blood loss or phlebotomy losses are replaced when they exceed 5-10% of blood volume. Transfusion criteria for infants older than 4 mo. are similar to adult. A standard 15 mL/kg transfusion of RBC should increase the Hct by 12% and the Hb by 4 gm/dL. The UCSD Medical Center Neonatology unit (ISCC) has a sophisticated transfusion program designed to limit donor exposure, provide safe blood, and minimize blood waste. The program requires the ordering physician to determine whether the infant 1) requires a transfusion of no more than 15 mL/kg that can be administered slowly (over 2-4 h), or 2) requires rapid infusion of blood, eg for surgery or hypovolemia, or a large volume of blood, eg exchange transfusion. For transfusions that can be administered slowly, infants < 28 days of age receive their initial transfusion using irradiated, group O Rh-negative, < 7 day old, CMV-safe RBC preserved in CPDA-1 or AS1. To limit donor exposure, blood for subsequent transfusions is obtained from the same unit until the unit outdates (35-42 days). Based upon predicted transfusion needs, the blood unit may be assigned to a single infant or up to 3 infants. Blood is ordered by volume, usually 15 mL/kg, up to two transfusions/day and delivered to the ISCC prefiltered, in a labeled syringe. Note: Blood older than 7 days develops increasing K<sup>+</sup> levels and decreased 2,3 DPG. It is safe for older infants who are not hyperkalemic and who require standard volume transfusions (15 mL/Kg) administered at controlled rates (ie over 2 - 4 hours). There is a risk for severe hyperkalemia if blood > 7 days old is given by bolus infusion. Blood for rapid or large volume transfusion (see above) is provided exclusively from < 5 day old O Rh-neg, CMV-safe, irradiated units or by centrifuging older units and resuspending in FFP. Irradiated units have a shelf life of only 28 days. Criteria for selecting blood are that donor's RBC are compatible with maternal or infant's plasma and donor's plasma is compatible with infant's RBC. Maternal plasma is ideal for crossmatching, and must be transported to UCSD along with the infant, if the infant was not born at UCSD. Crossmatch is never performed with cord blood because of Wharton's jelly (false positive reactions) and unreliability of its identity.

### **21.c Intrauterine Transfusion**

Intravascular or intraperitoneal fetal transfusions are administered for severe fetal anemia (Hct typically < 25%), usually in the setting of hemolytic disease of the newborn.

Irradiated, < 5 day old, CMV-safe, type O Rh-neg RBC (which lack the antigen corresponding to maternal antibody) are used.

#### **21.d. Neonatal Platelet Transfusion**

Transfusion guidelines for platelet transfusion to term infants and children > 4 months of age are similar to those for adults. Premature infants may be more susceptible to serious hemorrhage. Stable premature infants are frequently given prophylactic transfusions with counts < 50,000 /uL, and sick premature infants are frequently transfused with counts < 100,000 /uL. A standard dose of apheresis platelets, 5-10 mL/kg body wt. or 0.1-0.2 units platelet concentrate/kg, should increase the platelet count by 30,000 - 60,000 /uL. Irradiated, CMV-seronegative, or CMV-safe platelets are employed. In isoimmune neonatal thrombocytopenia, usually due to placental transfer of maternal anti-PI<sup>A1</sup> (HPA-1a) antibodies to a PI<sup>A1</sup> positive fetus (pathophysiology similar to hemolytic disease of the newborn), platelets from a PI<sup>A1</sup>-neg donor (1/50 donors), or washed, maternal platelets may be employed. The latter requires the mother to have a plateletpheresis at the American Red Cross, which will be arranged by the Blood Bank Resident.

#### **21.e Reduced Volume Platelet Concentrates for Neonates (20 mL)**

On request, the Blood Bank will reduce the volume of platelets by centrifugation. This component must be administered within 2 hours after concentration and is not available on stat basis, since it takes a minimum of 2.5 hours to prepare.

#### **21.f Cord Blood Testing**

All cord blood must be sent to the Blood Bank where it is stored for 1 week; ABO grouping, Rh typing and direct Coombs' are performed on selected patients deemed at risk for hemolytic disease of the newborn.

### **22. BLOOD IRRADIATION TO PREVENT GRAFT VS. HOST DISEASE (GVHD)**

The UCSD Medical Center Blood Bank will provide irradiated red blood cells and platelets (2500 rads or 25 Gy) on request to prevent post-transfusion GVHD in susceptible recipients (see Section 20.b.4). All directed donor units and HLA matched platelets are irradiated. The request for blood or blood products (Blood Bank Form I) should contain a handwritten notation "Irradiate." Thornton Hospital obtains irradiated blood from the Red Cross. Blood irradiation is available around the clock at Hillcrest and requires about 15 minutes. Irradiation at Hillcrest is typically performed just before blood issue, since irradiation decreases the storage life of red cells from 35 to 28 days.

### **23. OUTPATIENT TRANSFUSION**

Patients may be transfused on an outpatient basis by appointment at UCSD Medical Center (ER and Cancer Center). Check with the Blood Bank or UCSD infusion service for more information. The UCSD Medical Center Transfusion Service will also serve selected Out-of-Hospital Transfusion Agencies if their protocols and practices adhere strictly to UCSD standards. There are currently no Home Transfusions. All Home Care Agencies must be pre-approved before they will be allowed to obtain Transfusion Medicine Services through UCSD. For an up-to-date list of approved agencies, call the Transfusion Service Supervisor (4-5640 at Hillcrest or 7-6162 at Thornton). Out of hospital transfusion is safe and practical only for patients who have uncomplicated transfusion histories. All outpatients who receive transfusion must be wristbanded for proper identification.

#### **24. TRANSPORT OF BLOOD**

Patients sometimes inquire whether autologous units drawn at another location can be used at UCSD. Autologous or directed donor units should be drawn locally at the American Red Cross (760 737-7921). If that is not possible, arrangements should be made for the units to be sent directly to the American Red Cross, who will ascertain their acceptability, then send them to UCSD. As a last resort, units of blood (usually autologous or directed donor units) transported from referring hospitals within the state of California may be used at UCSD if the UCSD Blood Bank is first notified, and the units are drawn according to acceptable procedures at an accredited, FDA-registered facility, the units are maintained at 2-6°C during the transport, and they are taken directly to the UCSD Blood Bank (Federal regulation). ARC and SDBB no longer accept out of state autologous or directed donor products. Blood units drawn outside California must be from an FDA-licensed facility. Call the Blood Bank Resident for additional details.

#### **25. DONOR RECRUITMENT**

There continue to be serious shortages of blood and the staff should actively encourage blood donation by eligible donors, including family members and friends. Appointments can be made at the American Red Cross in San Diego (858 514-1608) which has multiple locations throughout the county.

**26. BLOOD ORDERING GUIDELINES FOR ELECTIVE SURGERY**

To ensure correct surgical blood orders and to reduce excessive crossmatch requests, the Medical Staff Executive Committee has adopted the use of blood order guidelines for elective surgery (see Table). These guidelines have been recommended and approved by each Division Chief or his/her designee.

The recommended order for crossmatched packed red blood cells (RBC) or for type and screen (T&S, no crossmatch) is listed below for each procedure. Requests differing from these recommendations should be approved by the responsible attending physician.

## Guidelines for Ordering Blood for Elective Surgery

### General Surgery

Procedure	Blood Order
Abdominal-perineal resection	3
Amputation AK, BK	1
Biopsy, breast	T & S
Cholecystectomy	T & S
Colon resection	
Total large colon	2
Hemi-colectomy	T & S
Sigmoidectomy	T & S
Anterior resection	2
Small bowel resection	T & S
Colostomy, revision and gastrotomy	T & S
Gastrectomy, with/without vagotomy	
Subtotal	T & S
Total	2
Hemorrhoidectomy	T & S
Hepatectomy	6
Hernias	
Inguinal	T & S
Incisional	T & S
Umbilical	T & S
Ventral	T & S
Ileo-jejunal bypass	T & S
Laparotomy, exploratory	T & S
Liver Transplant	Varies by risk category
Mastectomy	
Simple	T & S
Modified radical	T & S
Pancreatectomy	
Partial	4
Radical (Whipple's)	4
Parathyroidectomy	T & S
Pilonidal cyst	T & S
Portal caval shunt	6
Sympathectomy	T & S
Thyroidectomy, partial or total	T & S
Vein stripping	T & S

### Open Heart Surgery

<b>Procedure</b>	<b>Blood Order</b>
Adults (>13 years)	6 PRBC
Redos--add FFP & platelets	4 FFP
	1 unit, apheresis platelet
Pediatric (<12 years)	4 PRBC
	2 FFP
	2 platelet concentrates

### Thoracic Surgery

<b>Procedure</b>	<b>Blood Order</b>
Aneurysm, thoracic	6
Bronchopleural fistula	2
Embolectomy	T & S
Lung biopsy, open	T & S
Pectus excavatum	T & S
Thoracotomy	
Pneumonectomy/lobectomy	2
Segmental resection	T & S
With decortication	4
Tracheostomy	T & S
Vascular tumor	4

### Neurosurgery

<b>Procedure</b>	<b>Blood Order</b>
Cranioplasty	0
Craniotomy, aneurysm/A-V malformation	6
Craniotomy, tumor and/or hematoma	2
Decompressive laminectomy	T & S
Excision lumbar disc	0
Excision cervical disc	0
Fusion, anterior	0
Hypophysectomy, transphenoidal	T & S
Janetta procedure (Tic Doul.)	0
Nerve exploration	0
Stereotactic surgery	0
VP or LP shunt	0
VP or LP revision	0

### Plastic Surgery

<b>Procedure</b>	<b>Blood Order</b>
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Blood orders for plastic surgery should be made on a case-by-case basis.

### Vascular Surgery

<b>Procedure</b>	<b>Blood Order</b>
Aneurysm, abdominal aortic	4
Aorto-carotid bypass graft	2
Aorto-femoral bypass graft	4
Carotid body tumor resection	2
Enderterectomy, carotid or femoral	T & S
Femoral-distal bypass graft	2
Femoral-femoral bypass graft	2
Femoral-popliteal bypass graft	2
Renal art. repair	2
Sympathectomy	T & S
Vein stripping	0

### Otolaryngology

<b>Procedure</b>	<b>Blood Order</b>
Angiofibroma, dissection	4
Branchial cleft or thyroglossal duct cyst	T & S
Caldwell-Luc	T & S
Carotid body tumor resection	4
Ethmoidectomy	T & S
Glossectomy	T & S
Jaw, neck, tongue resection	4
Laryngectomy	2
with radical neck	4
Mandibulectomy	2
Mastoidectomy	T & S
Maxillectomy	2
Neck, radical dissection	3
Orbital exploration	1
Palate, tumor	T & S
Septoplasty	T & S
Temporal bone resection	6

### Orthopedics

<b>Procedure</b>	<b>Blood Order</b>
Amputation, mid thigh	2
Revision	2
Amputation, below knee	0
Revision, BKA	0
Arthroscopy	0
Arthrotomy, knee or shoulder	0
Hip	2
Bone graft	0
Dupuytren's contracture release	0
Femur fracture, open rodding	2
Harrington fusion and rod insertion	4
Hip, total replacement	4
Hip, nailing Richard's screw	2
AO screw	2
Hip pin removal	0
Menisectomy, medial	0
ORIF, forearm, ulna, tibia, patella	0
Osteotomy, biopsy	0
Shoulder, total	2

### Gynecology

<b>Procedure</b>	<b>Blood Order</b>
AP repair	1
Cervical cone biopsy	T & S
D & C	T & S
Hysterectomy	
Vaginal	1
Abdominal	1
Radical (Werrthelm)	4
Hysterotomy	2
Uterine suspension	T & S
Laparotomy with or without BTL	T & S
Laparotomy, exploration for lysis of adhesions and fimbrioplasty	T & S
Oophorectomy	T & S
Ovary, wedge resection	T & S
Pregnancy, ectopic	2
Tuboplasty	T & S
Urethral diverticulum	T & S

### Neonatal ECMO

<b>Procedure</b>	<b>Blood Order</b>
Initial priming	2 PRBC; O-neg or type-specific, < 5 day old, CMV-safe 2 platelet concentrates, type-specific, CMV-safe 2 FFP, type-specific or AB 1 cryo, type-specific or AB
ECMO emergency unit	1 PRBC; O-neg or type-specific, < 8 day old, CMV-safe (kept in Blood Bank but issued to ISCC)
Daily requirements	1 PRBC; O-neg or type-specific, < 8 day old, CMV-safe 1 platelet concentrate, type-specific, CMV-safe 1 FFP, type-specific or AB

### Urology

<b>Procedure</b>	<b>Blood Order</b>
Adrenalectomy	3
Bladder biopsy	T & S
Bladder tumor, transurethral resection	T & S
Bladder, bleeding tumor fulguration	T & S
Cystectomy, radical	4-6
Cystotomy	T & S
Ileal-conduit	T & S
Meatotomy	2
Orchiopexy	T & S
Prostate, open biopsy	T & S
Prostate, perineal biopsy	T & S
Prostatectomy	
Transurethral	T & S
Suprapubic	2
Perineal	2
Radical retropubic	2
Pyelolithotomy	T & S
Nephrectomy	2
Radical	4
Renal transplant	2
Renal biopsy, open	T & S
Ureteral reimplantation	T & S
Ureterolithotomy	T & S
Vesico-urethropexy	T & S

T & S = Type and Screen

## 27. CHARGES FOR BLOOD TESTS AND COMPONENTS

<b>Test</b>	<b>Charges*</b>
ABO/Rh type	\$ 112
Red Cell Antibody Screen	91
Type and (antibody) Screen (T&S)	203
Crossmatch, electronic, per unit	67
Crossmatch, antiglobulin, per unit	119
Antibody Identification	151
Coombs test, direct	47
Blood Irradiation	56
RhIg, 300 mcg vial	88
Neonatal aliquot preparation (+ blood cost)	125
Autologous blood fee per unit** (+ blood cost)	125
Directed donor fee per unit ** (+ blood cost)	125

\* Charges are subject to change

\*\* Blood Center Charge

Sample requirements: Adults 7 mL EDTA (Purple top tube) or 15 mL if antibody ID required. For patients < 10 years old - 3 mL EDTA.

<b>Item</b>	<b>Patient Cost for Blood Components</b>
Red Blood Cells Leukocyte-reduced (LR) (pre-storage)	\$ 291
Neonatal aliquot preparation	125 (+ 75 / aliquot)
Autologous Blood fee / unit *	125 (+ 291 / unit)
Directed Donor Blood fee / unit*	125 (+ 291 / unit)
Saline-washed red cells	254 (+ 291 / unit)
Frozen, thawed red blood cells	297 (+ 291 / unit)
Leukocyte-reduced (LR) apheresis platelets (pre-storage)	631
HLA-matched LR apheresis platelets	345 (+ 631 / unit)
HLA antigen neg LR platelets set-up fee	255 (+ 746 / unit)
Crossmatched LR platelets set-up fee	230 (+ 746 / unit)
Fresh Frozen Plasma / Frozen Plasma	88
Cryoprecipitate (one unit)	78
Cryosupernate (TTP only)	101
CMV negative blood (additional charge/unit)	56
Apheresis granulocytes	2100

\* American Red Cross fee, 7/30/06; call 760 737-7921 to arrange for blood donation