1. UCSD MEDICAL CENTER BLOOD BANK & TRANSFUSION SERVICES

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 (pager 290-2418) or Associate Directors, Dr. Dzung Le (pager 290-5652) and Dr. Patricia Kopko (pager 290-3177). Call the UCSD telephone operator (Hillcrest-619 543-3767; Thornton-858 657-7000) or consult the on-line schedule under "Pathology" to contact the covering Resident or Attending on nights, holidays and weekends. Problems should be referred to physician staff whenever possible.

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

Introduction: Blood products are ordered using the EPIC system that transmits the order to the blood bank. Ordering a red cell transfusion is a multistep process that first requires one or more blood specimens to be submitted for compatibility testing (see below) then an order to transfuse. First, before type specific rbc can be given, there must be two matching ABO/Rh types on file in the blood bank. Second, the blood ordering panel prompts consideration of whether the patient requires blood with special attributes or restrictions, eg CMV-safe, irradiation, leukocyte-reduced. Third, if a standing blood order is set up for a patient who requires chronic blood transfusion according to a defined protocol (eg each time the Hb decreases to < 8 gm/dl) there is still a requirement for a separate "Transfuse" order, prior to each transfusion and also a new blood sample for compatibility testing every 3 days (see below). Due to the hospital computer, failure to issue a "Transfuse" order will delay the availability of blood and may prevent the posting of the patient's results in EPIC. In the event of computer failure or scheduled maintenance, UCSD maintains a paper system using Blood Bank order form 151-104 that can be used to order blood products and associated testing. Except to order autologous or donor-directed blood from the American Red Cross (ARC; 800 696-1757; Escondido only), or San Diego Blood Bank (619 296-6393; several locations in SD county) all requests for blood products must go though the UCSD Blood Bank.

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. Note that separately drawn second blood specimen for ABO/Rh typing (referred to as ABO/Rh Confirmation or Check Specimen) is required on all patients, before type-specific blood can be administered, 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 and the ABO/Rh Confirmation confirms the blood type, 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 + ABO/Rh Confirmation 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 and ABO/Rh Confirmation, 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 and an ABO/Rh Confirmation 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 ABO/Rh Confirmation (aka ABO/Rh Check Specimen)

Current FDA guidelines and Joint Commission and CAP accreditation standards require a second ABO/Rh type for confirmation to be performed on blood from a separate blood draw before the patient can be issued ABO type specific rbc and before the blood bank can employ a rapid computer-supported blood crossmatch that speeds the delivery of safe blood. If the patient already has one ABO/Rh type on file, a currently drawn blood specimen can serve as the ABO/Rh confirmation. In the absence of two ABO/Rh types, type-specific rbc can be issued only with a signed "Request for Emergency Blood" or type O blood must be used. This policy is designed to reduce the incidence of mistransfusion of ABO-incompatible rbc due to the wrong patient's blood being drawn for T&C, an event that happens with 1/2000 blood specimens and carries a 30% risk of acute hemolytic transfusion reaction. All patients who are new to UCSD or who do not have a historical ABO/Rh test on file will require an ABO/Rh confirmation. The blood bank will help to minimize delays in blood availability by notifying the appropriate location and requesting a 2nd blood specimen to be drawn for ABO/Rh confirmation on all patients for whom a T&S or T&C is ordered and who do not have a historical type. Note that only results of testing at UCSD blood bank are valid for this purpose.

3.d Recrossmatch

A new blood compatibility specimen (recrossmatch) is required every 3 days (expiring at midnight of the 3rd day), since significant new antibodies may arise within 72h if the patient has been transfused within the last 3 months. 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.e Hold Blood Specimen

Obstetrics and Trauma Services only. No type or crossmatch done but this specimen can serve as the ABO/Rh confirmation specimen in the event that blood is needed. Useful when blood use is unlikely, *e.g.*, normal delivery. Specimens are reserved for 3 days.

3.f 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 fully 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 "Request for Emergency Blood" form.

3.g 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, alphmethyldopa. 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 (eg titer > 1/500; 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 *auto*antibody may make it difficult or impossible for the Blood Bank to identify or rule out the coexistence of significant red cell *allo*antibodies 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 the use of "rbc phenotype-matched" blood, IVIG, plasmapheresis, or other pharmacotherapy, eg Rituximab. 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 to platelet transfusion.

3.h Extended Antigen Matching for Sickle Cell Anemia Patients

Patients who have Sickle Cell Disease (SCD) may require repeated or long term transfusion support. Since red cell antibody formation is transfusion dose-dependent, occurs in 30-40% of patients with SCD and may cause repeated delayed hemolytic transfusion reactions, it is UCSD policy to try to prevent red cell antibody formation in SCD 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 (or obtain a molecular testing for genotype). The UCSD Blood Bank will then arrange to obtain optimally matched blood (Rh, K, and Fy(a) depending on patient phenotype). Patients who have made antibodies will be additionally matched for the specific antibody as indicated and complete phenotype. Patients should carry a card indicating their phenotype to facilitate extended antigen matching if they are transfused elsewhere. Note that SCD patients should also receive leukocyte-reduced blood to prevent febrile reactions. Since SCD patients are not at increased risk for either graft vs host disease or CMV, neither irradiation nor CMV-negative blood is required for SCD patients unless there are established indications (see below in this manual). Use of irradiated blood in such patients may be a disservice, since irradiation shortens the viability and lifespan of rbc.

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) and if requested, up to 4 units of pre-thawed type AB plasma will be issued provided the patient's physician agrees to sign the appropriate "Request for Emergency Blood" and provides the Blood Bank with a properly labeled EDTA sample of blood from the patient. This sample is essential to determine if significant red cell antibodies are present and for determination of the patient's ABO and Rho(D) type. A second ABO/Rh type (see 3.c.) is still required ASAP so that subsequent RBC units may be type specific. The OB hemorrhage protocol is similar to the above, but 2 units of pre-thawed type AB plasma will be issued. FFP will be thawed if no pre-thawed plasma available. The neonatal emergency blood 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. All requests for emergency blood are reviewed for appropriateness, ie a patient who has symptomatic anemia and who is expected to develop severe or life-threatening complications if the time is taken to complete standard compatibility testing before rbc transfusion.

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 30,000 (Anesth Analg 2010;111:1088), but if the patient has ever been exposed to blood or has been pregnant, 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 performed provided a Request for Emergency Blood form is signed by the physician. Antibody screen, ABORh confirmation and 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, if patient ABO/Rh confirmation has not been performed). Switching to type-specific blood as quickly as possible will preserve resources of scarce type O-pos and rare type O-neg blood for other patients who may need it.

5. MASSIVE TRANSFUSION PROTOCOL

Upon identification of a massive transfusion requirement, the responsible physician, typically the Trauma, Liver Transplant, or OB Service Attending should invoke the "Massive Protocol" or MTP by a telephone communication to the

Blood Bank, including the patient's identification. The blood bank will then mobilize 45 units each of rbc and plasma, and 4-6 units of apheresis platelets ASAP. The initial 4 rbc units may be O Rh negative (see Emergency Transfusions, Section 4 above) along with 4 units of AB plasma. ASAP following this, 6 units of rbc, 6 plasma and 1 apheresis platelet unit will be supplied, followed by batches of 10 rbc, 10 plasma and 1-2 platelets. Type-specific blood will be initiated as soon as possible and depends on the availability of a second blood specimen for ABO/Rh confirmation (see 3.c). If necessary in order to provide sufficient blood without delay, the decision to switch blood types (eg, 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 clinical team should be designated to communicate with the Blood Bank. Following the immediate resuscitation period, standard procedures for blood ordering will be followed, ie rbc, FFP and platelets are supplied as ordered. Note: The MTP should be invoked judiciously. Responding to a massive transfusion may impair service to other patients. The MTP should also be cancelled as quickly as possible if/when it is determined that it is no longer required. 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, eg Trauma, DIC, shock, OB catastrophes, pre-existing coagulopathy. The 10:10:1 ratio of rbc:ffp:platelets that is employed in the UCSD protocol is justified by clinical experience in such patients that demonstrates reduced coagulopathy and morbidity in well selected patients with massive bleeding. However, the absence of the above predisposing factors, eg massive trauma , patients who bleed 1-1.5 blood volumes (in a 70 kg male approximately 10-15 units of PRBC and 3-5L crystalloid) typically 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, especially those whose bleeding has ceased, simply because they have received 10-15 units of PRBC. Rather, patients whose blood loss is >1-1.5 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 in these patients 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. It has been reported that 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. Patients who bleed in excess of two blood volumes (>20 units of PRBC) usually require 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.

6. BLOOD SPECIMEN REQUIREMENTS

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, TJC).

The blood drawing team currently collects blood specimens on a 7/24 basis for inpatients at Hillcrest and from 8AM to 5:30PM M-F at the Ambulatory Care Center. 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 and from 7:30AM to 6PM, M-F at the Moores Cancer Ctr. Lab.

Drawing the blood specimen: Correct patient identification and blood sample labeling at the patient's bedside at the time of blood drawing is **ESSENTIAL.** It is one of the most important ways a physician can ensure blood safety, since fatal transfusion reactions are frequently due to errors in patient identification at the time the blood specimen is drawn (or at 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 patient's armband and requisition and the labels must be 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, the date and time specimen was drawn, and the legible signature of the person who drew the blood.

No specimen will be accepted by the blood bank 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 addition, per FDA guidelines and accreditation requirements, a second ABO/Rh type must be obtained from a separately drawn, 2nd blood specimen, before type-specific blood may be administered (see ABORh Confirmation, 3.c.).

The standard blood specimen for T&S or T&C is a 7-10 mL EDTA (purple top) tube 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 orders that do not require a new specimen (eg additional units of blood within 3 days, platelets, FFP, cryo) may be transmitted to the Blood Bank using the Hospital Computer under the Lab section, and a Blood Products Request will be printed 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^+ 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 before surgery 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. About 3 hours are required to work up the simplest antibodies and to provide compatible blood and it may require much longer. If the patient requires rbc transfusion before the completion of testing and provision of compatible blood, then uncrossmatched type O rbc or the most compatible blood available on short notice may be requested by the physician after signing a ”Request for Emergency Blood” form that acknowledges the existence of a greater risk of hemolytic transfusion reaction under such conditions.

7. ISSUE OF BLOOD COMPONENTS

A physician’s order to transfuse in EPIC (or the backup paper system) is required for the blood bank to prepare blood for administration. To obtain prepared blood units 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 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 patient identification and 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 monitored and the blood stored in them may be damaged and cannot be administrated.

8. ADMINISTRATION OF BLOOD

Before you administer blood: Most fatal transfusion reactions are due to improper patient identification when the blood is administered. 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.

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; the only exception being for neonates, whose rbc are filtered as above by the blood bank, immediately prior to issue. Microembolic filters (20-40 micron pore size) have only limited applications (eg re-administration of shed blood or in arterial circuits) and will not remove leukocytes effectively. Since 2001, nearly all rbc and platelets supplied to UCSD have been leukocyte reduced using a filtration method by the American Red Cross. However, directed donor blood is leukocyte reduced only on special order by the physician, who should order them as leukocyte-reduced from the blood supplier to comply with UCSD policy. In the unlikely event that pre-storage leukocyte reduced blood is unavailable blood may be administered through leukocyte-reduction filters at the bedside.

After baseline vital signs are taken and patient identification is complete, RBC units should be started slowly at first, ie < 50 mL in the 1st 15 minutes, and the patient should be carefully monitored during this time (ie every 5 min) since the rare life-threatening immediate reactions are dose-dependent. 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/dL, or the hematocrit about 3%. Only isotonic saline, or intravenous solutions that are known not to damage the blood or react with the anticoagulant solution 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. Blood administration sets should be changed every 4 hours, when additional units are administered, except in the OR

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

9. POSITIVE ANTIBODY SCREEN OR INCOMPATIBLE CROSSMATCH

Approximately 1 in 20 patients who require blood at UCSD have an unexpected anti-rbc antibody that can cause a hemolytic transfusion reaction. In most cases the antibody can be identified and 2-4 units of compatible blood can be provided within 4 hours, but in about 20% of cases, this process may require a day or more, and in unusual cases, even longer. If the blood bank cannot provide compatible rbc within the requested turn-around time, the blood bank protocol is to immediately inform the ordering physician regarding the problem, to indicate emergency transfusion alternatives, and to suggest immediate consultation with the blood bank physician, who will also be informed. Alternatives to waiting for full completion of compatibility testing may include; a) Emergency Uncrossmatched RBC (10-15 min) which may carry a significantly increased risk of a hemolytic transfusion reaction, or b) crossmatch-compatible rbc (if possible) or least incompatible rbc (30-60 min) which may be somewhat safer than uncrossmatched rbc but may still result in an acute or delayed hemolytic reaction. Transfusion of rbc before completion of full compatibility testing requires the completion of the "Request for Emergency Blood" form that indicates the physician's understanding of the increased risk of a hemolytic reaction. Discussion with the blood bank physician is highly recommended before proceeding with rbc transfusion in this situation. The increased risk that is associated with transfusion of blood that is compatible in the crossmatch when the patient has an unidentified antibody is due to the fact that the crossmatch procedure, alone may not be sufficiently sensitive to detect some weak antibodies. Thus, an apparently compatible unit may result in hemolysis or significantly shortened red cell survival following transfusion.

In all the above cases and in some emergencies in which no compatible blood can be found (*e.g.* autoimmune hemolytic anemia), but the Blood Bank workup shows that there is no clincally significant rbc alloantibody, an "in-vivo crossmatch" may be performed by administering a small volume (50-100 mL) of blood 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. As of June, 2011 there is no compassionate-use protocol for an artificial

oxygen carrier (previously the stroma-free Hb preparation, Polyheme[tm] was available, but the company closed in May 2009 following FDA disapproval of the drug due to safety considerations).

10. RED BLOOD CELLS

10.a Packed Red Blood Cells (RBC) *

(AS1,3, or 5; 250-350 mL; Hct-57-62%; Shelf Life = 42 days)
(CPDA1; 250-275 mL; Hct-70-80%; Shelf Life = 35 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^+, K^+, 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 Additive Solution blood preservative solutions, eg AS1, -3, or -5 which contain only 10-15 mL of donor plasma may have advantages over Citrate-Phosphate-Dextrose-Adenine (CPDA1) RBC, which contain about 70 mL of donor plasma, 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 for adults is preserved in one of the AS solutions and newborns receive rbc in CPDA1 preservative.

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

10.b Leukocyte-reduced RBC (LRC)

(same as RBC but < 5 x 10^6 WBC)

Whole Blood, Red Cells, and Platelets also contain large numbers of leukocytes (eg 2 to 5 x 10^9 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 10^6 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 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 or if your patient has an unusual antibody), you should specify in the blood order "Leukocyte-reduced" RBC. Blood may also be leukocyte-reduced at the bedside by transfusion using a "3rd generation" leukocyte-reduction filter which, if used properly will usually be adequate for prevention of recurrent febrile reactions, and CMV transmission. 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 (HLA Class I) antibodies supports the diagnosis of FNHTR due to anti-leukocyte antibodies and may be a useful test on selected patients with recurrent FNHTR. The UCSD HLA lab can perform a test for anti-HLA antibodies. Leukocyte-reduced blood is also indicated in some patients who are destined to have long-term blood requirements (eg leukemia, malignancy, refractory anemia, eg SCD, thalassemia), 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. Leukocyte-reduced rbc and platelets is also indicated in patients who have recently had a TRALI reaction, to prevent the infusion of additional leukocytes. 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. The blood bank physician may authorize the extended storage of rare-phenotype thawed rbc units (eg up to 72-96 hr) if they cannot be transfused within 24 hr. 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 or PTP. Washed RBC are **not** considered leukocyte-reduced by today's standards (see leukocyte-reduced RBC) and will **not** reliably prevent CMV transmission or immunization to leukocyte antigens. Washed RBC are not stocked at UCSD, but must be ordered from the American Red Cross or San Diego Blood Bank. 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. The blood bank physician may authorize the extended storage of washed rbc units (eg up to 72-96 hr) if they cannot be transfused within 24 hr. 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 UCSD's blood suppliers. Packed red blood cells combined with balanced salt solutions are as effective as whole blood for non-massive 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)

Each UCSD Medical Center Blood Bank attempts to maintain a stock of apheresis platelets in anticipation of use, but cannot always guarantee having platelets available. Apheresis platelets are collected from an individual donor during a 2-3 hour apheresis procedure and contain about 3×10^{11} platelets (equivalent of 6-8 units of platelet concentrate; a therapeutic dose for an adult). Since 11/1/98 UCSD has employed only pre-storage leukocyte-reduced apheresis platelets ($< 5 \times 10^6$ WBC/unit) from the Red Cross. 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). . 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 (> 1 °C or 1.7 °F temperature increase) within 4 h after platelet transfusion. For reference only, platelet concentrate (PC) derived from single units of whole blood contain about 5.5×10^{10} platelets in 50 ml plasma. PC are NOT used at UCSD and should not be confused with apheresis platelets, which are equivalent to 6 units of PC. Apheresis platelets, which are used at UCSD, are preferable to platelet concentrate since their use results in diminished donor exposures and therefore a lower risk of most transfusion side effects.

11.b 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 to prevent alloimmunization to HLA antigens, to prevent CMV infection, and sometimes TRALI or to prevent febrile reactions in patients who are alloimmunized (these indications are the same as for leukocyte-reduced rbc). Note that patients who have repeated febrile reactions after platelet or rbc transfusion are almost always alloimmunized to HLA antigens and are refractory to random donor platelet transfusion (see below).

11.c Indications for Platelets:

Platelets are indicated for bleeding in thrombocytopenic patients (usually <50,000/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 and generally not effective in patients who have immune thrombocytopenia (ITP) or Thrombotic Thrombocytopenic Purpura (TTP), or "hypersplenic" thrombocytopenia, except if serious or life threatening bleeding exists (then use larger doses). Platelets are not usually effective in uncontrolled DIC. .

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 or higher in patients with fever or evidence of minor bleeding. 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 and especially in aplastic anemia, the development of platelet refractoriness due to alloimmunization (**see Transfusion Risks**).

11.d Platelet Matching:

ABO matching of platelets is desirable, but not required in adult patients. Platelets do not contain Rh antigens and the few remaining rbc in apheresis platelets (< 0.003 mL) are deemed insufficient to cause immunization to Rh (D antigen); consequently platelets from Rh-positive and Rh-negative donors are used interchangeably in males and females > 50 y/o. Platelets from Rh-neg donors are preferably employed for Rh-neg females < 50 y/o but if necessary to employ platelets from Rh-pos donors in these patients, the physician is notified of the option to administer Rh immune globulin (RhIg) to prevent sensitization to Rh. RhIg is available in a 300 micrograms (mcg) dose for IM use only (RhoGAM) from the blood bank or preferably the IV preparation, WinRho available from the Pharmacy (120 mcg per dose). One dose of either of these products should be sufficient to prevent Rh sensitization from > 25 units of Rh positive apheresis platelets

administered over at least one month's time. 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. 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 deemed safe, ie non-reactive for anti-A or –B at a 1/100 dilution will be selected for transfusion. See also, Platelet Refractoriness, below.

11.e Platelet Administration:

Platelets must be administered through a filter set, usually the standard 170 micron screen filter; the only exception being for neonates, whose platelets are filtered as above by the blood bank, immediately prior to issue. 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.f 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 $1.8m^2$ body surface area (or $30{,}000/mm^3/m^2$). 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.g Platelet Refractoriness:

This refers to failure of platelet transfusion to satisfactorily increase the post transfusion platelet count, typically drawn 10 min to 1 hour after platelet infusion. 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:

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

BSA = body surface area in m^2. For apheresis platelets, assume 3.5×10^{11} platelets/transfusion. A CCI of $< 7.5 \times 10^9$/L from a blood sample drawn 10-60 minutes post transfusion, or a CCI $< 4.5 \times 10^9$/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 by immune and/or non-immune mechanisms. The latter include fever, infection, disseminated intravascular coagulation, active bleeding, splenomegaly, and veno-occlusive disease of the liver, TTP, and patients who are status post recent high dose chemotherapy, or have severe multiorgan disease (eg many ICU patients), a very low starting platelet count frequently have suboptimal responses to platelets. Immune refractoriness includes patients who have platelet antibodies to HLA or platelet specific antigens (eg due to alloimmunization or ITP), Drug-Induced Thrombocytopenia (DIT), Heparin Induced Thrombocytopenia (HIT), and about 5% of patients are refractory to ABO incompatible platelets.

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.h Management of Platelet Refractoriness: 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). About 1/3 patients who are refractory to platelets have immune causes and the remaining 2/3 have non-immune causes, and many refractory patients have both problems; consequently when refractoriness is identified, the patient should be carefully evaluated for both immune and non-immune mechanisms, as outlined above. Management of non-immune refractoriness requires control of the underlying problem and/or more frequent or higher doses of platelets. The following algorithm is used at UCSD to diagnose and manage immune platelet refractoriness, after it has been established that the patient has had at least 2 poor responses to platelet transfusion (ie, < 30,000 platelet increment) based on a platelet count drawn between 10 – 60 min post-infusion.

1. Order HLA-matched platelets in EPIC.
2. If the patient's HLA type is available, fax it to the blood bank
3. Send 2 red top (no gel) tubes to blood bank on Misc. form for "Platelet Refractory work-up" which will be performed by the Am. Red Cross (ARC) platelet immunology lab.
4. If NO HLA type is available on the patient, also send 3 yellow top (ACD) tubes to blood bank.
5. Notify the blood bank to call the blood bank physician who will assess the responses to platelets, the relevance of non-immune vs immune mechanisms, current medications, and will also determine if the poor responses are only to ABO incompatible platelets, in which ABO compatible units will be supplied.
6. While waiting for matched platelets, transfuse random donor units for serious bleeding & consider the use of EACA, and/or IVIG if ITP is a consideration and/or rHu VIIa.
7. The blood bank will obtain 3 units of best-matched apheresis platelets ASAP as follows:
    a. If the HLA type is available, it is faxed to ARC and 3 "best-matched" plts are secured ASAP
    b. If no HLA type available ARC will simultaneously: a) use the patient's serum to perform crossmatching (XM) and supply 3 platelet XM-compatible plt units asap, and b) perform a screening test for HLA Class I and for platelet-specific antibodies asap and c) determine the patient's HLA type at a "serological" level. If the screening tests are positive, the specificity of the HLA or platelet specific antibodies will be determined, and "antigen-negative" donors will be sought.
    c. Based on this information, the blood bank MD will order the best available antigen negative and/or HLA matched platelets and/or XM-negative platelets ASAP. Even, if all tests are negative, the blood bank will supply 3 units of best HLA matched platelets available as a therapeutic trial. Finally, if family members are readily available and are acceptable donors, one in four may be HLA matched with the patient. This process requires close coordination with the UCSD Blood Bank Resident.
    d. HLA-matched or crossmatched platelets should be irradiated to prevent transfusion associated GVHD.
    e. It is ESSENTIAL for the clinical team to perform 10-60 min post-infusion counts for each platelet unit administered, in order to assess the response.
    f. If good responses to matched platelets, the blood bank will continue what works (HLA-matched, antigen-neg, and/or XM-neg).
    g. If poor responses to matched platelets and no antibodies are detected, the refractoriness is most likely due to non-immune factors or possibly ITP. The blood bank will supply random units as, needed and recommends reassessment for HLA & platelet-specific antibody testing in 14 days if still indicated. For serious bleeding, see item 6, above. 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/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 after treatment with dexamethasone, 0.1-0.15 mg/kg PO, 8-12 h before apheresis to increase the WBC. Since the patient frequently is also thrombocytopenic, platelets are also collected (leukoplateletpheresis). HLA matched donors are preferable, but not essential 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 are preferable for susceptible (CMV seronegative) individuals. Donors may be treated with G-CSF, 5-10 mcg/kg SC 8-12 h before apheresis as well as dexamethasone . 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 x 10^9/10 Kg) in 50 - 300 mL. Granulocytes should be irradiated to prevent GVHD. Granulocytes contain red cells and must be ABO compatible with the recipient, therefore a T & S must also be current, to test for alloantibodies to rbc. Granulocytes are stored at room temperature without agitation for up to 24 hours. NOTE: Granulocytes have a very limited shelf life and must be administered as soon as possible after they are obtained but within 24 h of collection. 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□) slowly, ie over 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. One unit of granulocytes should be given daily for at least 4 days or until either 72 h after a clinical response is noted, or the granulocyte count increases spontaneously above 1000/microL. For practical purposes, granulocytes are ordered for at least 7 days at a time, extending through the following Monday. 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 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), 5 day Thawed Plasma (5DP)

(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 and 5 day Thawed Plasma (5DP) are 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/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. 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. Thawed plasma contains normal coagulation factor levels after 5 days except for Factors VIII (75 – 86 % of normal) and V (84 – 91%) of normal and is used interchangeably with FFP/FP in all patients except neonates and as noted above. Hillcrest maintains a constant supply of 4 U thawed AB plasma for Trauma and 6 U type A plasma for other urgent requirements in type A or O patients (> 90% of all persons are A or O) Thornton currently maintains 2 U thawed AB plasma for urgent use.

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 for FFP/FP/5DP:

FFP, FP, and 5DP 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 severe trauma, DIC, or pre-existing coagulopathy. Generally, plasma is 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/5DP 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/5DP 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/5DP are NOT indicated for blood volume expansion or protein supplement. FFP/FP/5DP 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/5DP provides the equivalent of all coagulation factors and plasma proteins found in the plasma of a single unit of freshly drawn blood (except FP/5DP have 10-25% lower factor V and VIII), and more fibrinogen than in a single unit of cryoprecipitate. It takes 25 minutes to thaw each unit FFP and a few minutes extra to issue, but 5DP is available within minutes, if in stock. FFP/FP/5DP should be ABO compatible with recipient and are transfused via standard (170□) blood filters. One unit of FFP/FP/5DP would be expected to raise the level of a given coagulation factor by 7-10% (except as above), 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/5DP 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 within 30 min, since it can be used 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 like FP, should not be used, alone for replacement for Factor V or VIII. This product may not always be available, but if so, it can be issued within 5 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/5DP in patients who have failed FFP/FP/5DP 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 ^{TM}) 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 level < 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 (RiaSTAP) is FDA approved only for treatment of congenital fibrinogen deficiency.

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 Desmopressin (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 Cryo 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 labeling 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-only preparation (eg, RhoGam ™) primarily used for prophylaxis against sensitization to the Rho(D) antigen in D-negative pregnant women, and as an IV/IM preparation (eg WinRho ™, or Rhophylactic ™). WinRho is primarily used IV in therapy of Autoimmune Thrombocytopenic Purpura (ITP) but may also be used IV or IM for suppression of immunization to Rho(D) in D-negative 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 is no longer routinely recommended after transfusion of apheresis platelets from Rho(D) positive blood donors to Rho(D) negative patients, since modern apheresis platelets contain so few rbc.
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. The IV preparations have advantages in this setting by eliminating the need for multiple IM injections. 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. Studies suggest that WinRho has as rapid an onset of action in ITP therapy as IVIg and it is far less costly than IVIg. However, due to uncommon severe hemolytic events, manufacturer's instructions and warnings should be consulted before using WinRho for ITP, especially in persons with a Hb < 10 gm/dL. WinRho 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 of one full dose 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 optional to prevent sensitization to anti-D in Rh-negative females of childbearing potential who are recipients of Rh-positive apheresis platelets; since recent data suggests that the immunization rate is undetectable or very low. 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 Rh-positive blood, eg after emergency transfusion with 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, per manufacturer's guidelines, 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 recommended or necessary unless there is a compelling reason, eg an 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. Autologous donations can be scheduled with the American Red Cross (Escondido only; call 800 696-1757) or in various locations in San Diego County by the San Diego blood bank (619 296-6393). This requires a physician's verification of patient health status, eligibility, and an order requesting that blood be drawn for autologous transfusion. 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 and/or San Diego Blood Bank 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. Donations may be scheduled through the American Red Cross (Escondido only; 800 696-1757) or in various locations in San Diego County by the San Diego blood bank (619 296-6393).

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 EPIC or manual Blood Bank forms, and indicating that it is for therapeutic apheresis.

20. TRANSFUSION REACTIONS & HAZARDS

All suspected transfusion reactions should be reported to the blood bank, including acute and delayed reactions and suspected cases of infectious disease transmission. 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 blood specimen. The only exception is that very mild 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 Bank (Hillcrest 3-5640/1; Thornton x7-6161/2) 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 a specific 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 352,000	HBV (HBsAg) tested since 1971, HBcAb in 1989: NAT(PCR) since 2010
HCV	1 in 1.3 – 1.9 million	HCV since 5/90; improved assays 3/92, 5/96, 1/01 NAT (PCR) since 5/02
HDV	rare	HDV occurs only in HBV carriers.
HGV, et al	1 in 100	HGV (GBVc) et al 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) ~1/100 (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 250,000 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 (Hematology (ASH) 2003;575)
Malaria, Chaga's, Dengue, Babesia and other viral & 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 (Borrelia)	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^{th} 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	< 1 in 40,000	Donor NAT (PCR) testing since 2003

Window period to seroconversion or positive test after infection.

Virus	Days (EIA)	Days (NAT)
HIV	22	11
HTLV	36 – 72	n/a
HCV	70	10
HBV	38 – 59	24

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; 5-30% 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 antigens	1 in 8 transfusions (non-leukocyte reduced)	Refractory state to platelet transfusion; usually due to anti-HLA antibodies. Decreased to 1 in 25 by leukocyte-reduced rbc & platelets NEJM (1997;337:1861)
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 50 - 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 1,000 - 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.
Post Transfusion Purpura	1 in 50,000 – 100,000	Allo/auto-antibody to Plt-specific Ag, esp HPA-1A

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 (mislabeled or mixed-up crossmatch specimens, blood unit given to the wrong patient, etc.).

1. **MONITOR** all patients frequently after the start of transfusion (ie, 15 min). 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, flank, 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 & deaths are rare with < 50 mL. 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. Administer 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, but the latter has some support from animal studies. * (Sodium bicarbonate IV, 130 meq/L (150 mL [3 amps] of 8.4% NaHCO3 in 1 L 5% dextrose) in a line separate from line for NaCL infusion. Initial rate, 200 mL/hr; adjust to urine pH >6.5; with q 2h monitoring of serum bicarb, art pH, Ca++. Discontinue if urine pH < 6.5 in 4 hr, or if bicarb > 30, art pH > 7.5, or hypocalcemia.)

9. Recall that hemolysis accompanying transfusion may be due not only to blood incompatibility, but also to hemolytic immune drug reaction (eg administration of 2nd generation cephalosporins), administration of hemolyzed blood (excessive heating, cooling, incompatible IV solutions), mechanical trauma of blood, (eg bypass machine), infected blood, and/or infections, eg malaria, clostridia.

10. Delayed hemolytic reactions are due to the rapid emergence of a new antibody post-transfusion and may occur from 1 to 14 days after transfusion. They are usually manifest by fever, icterus, a rapidly falling hematocrit and symptoms of anemia. 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 and bacterial contamination must be excluded. The lab workup accomplishes these goals. If serious reactions can be excluded and the patient's underlying condition can be ruled out as causing the reaction, the fever is mostly likely due to the patient's underlying condition. FNHTR due to leukocyte antibodies are very uncommon if leukocyte-reduced units of rbc and platelets are employed. If non-leukocyte-reduced units are used, FNHTRs due to leukocyte antibodies are usually recurrent and are characterized by 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, which are generated 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 or non-existent. Rarely, 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 mostly 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 H1 antihistamine receptor blocker within one hour of giving the blood, (e.g., 25-50 mg diphenhydramine, [benadryl] PO or IM or if drowsiness is to be avoided, 10 mg cetirizine [ZyrTEC] PO). Some patients respond more favorably to H2 blockers (Famotidine [Pepcid] 40 mg PO or 20 mg IV) or a combination of H1 and H2 blockers. 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 severely IgA deficient persons (less than 0.05 mg/dL; 1/600 incidence), who develop antibodies to foreign IgA. However, the majority of severe allergic reactions occur in persons who are not IgA deficient, 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 (25-50 mg diphenhydramine, 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 consider use of 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 available only upon a pre-order from the San Diego Blood Bank and they outdate in 4 hr after washing. Premedication with steroids and antihistamines is effective in preventing most allergic reactions associated with platelets. IgA deficient FFP may be obtained from the blood supplier (ARC), but requires prior notification.

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

TRALI is the most common cause of transfusion-related fatality and is characterized by acute, non-cardiogenic pulmonary edema and respiratory failure, occurring in proximity with transfusion of FFP or apheresis platelets (< 6 h) in 1 in 5,000 to 10,000 transfusions, 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 and less commonly from previously transfused males or females. About 85% of TRALI is due to antibodies to Class I or II HLA antigens and 15% due to anti-neutrophil antibodies. There is also sufficient plasma in PRBC and cryo to cause this reaction albeit far less commonly than Apheresis Platelets and 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 distress or failure due to non-cardiogenic pulmonary edema, and associated with a "white out" on chest film usually within 0.5 - 4 hr after blood transfusion. The differential diagnosis includes fluid overload (TACO), sepsis, and an allergic reaction. Diagnostic criteria for TRALI and Possible TRALI have been published (Transfusion 2004;44:1774):

TRALI:

1. Acute Lung Injury (ALI; ASA criteria)
    a. Acute onset; < 6 hours from transfusion
    b. Hypoxemia - PaO2/FiO2 < 300 or SpO2 < 90% on room air or other clinical evidence of hypoxemia (oximetry < 90% sat [UCSD criteria])
    c. Bilateral infiltrates on frontal chest radiograph
    d. No clinical evidence of left atrial hypertension (ie, circulatory overload)
2. No preexisting ALI before transfusion
3. 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). TRALI, but not TACO is frequently accompanied by fever and acute transient neutropenia. 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 and also the patient (post + pre-transfusion) for anti-HLA Class I and Class II antibody 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 donor testing should be done, since 15% of cases are due to anti-PMN antibodies (eg HNA-3) and some may be due to monocyte antibodies. Additional testing may include determination of the donor antibody specificity and the patient's HLA type, to determine if they match. 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 is unclear and diuretics have been reported to worsen TRALI due to hypotension. All rbc and platelet transfusions should be leukocyte-reduced. 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. TRALI mitigation strategies include restriction of plasma and platelet donations to untransfused males, which appear to have steadily reduced the incidence of this reaction since 2006.

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

TA-GVHD is a rare but nearly always fatal complication of transfusion of cellular blood components, occurring primarily in immunocompromized hosts. TA-GVHD 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 TA-GVHD 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, patients ever previously treated with Fludarabine (and possibly other purine analogs, eg cladribine or 2-CDA and deoxycoformicin) or alemtuzumab (anti-CD52), recipients of HLA matched blood products and directed donor blood from blood relatives, due to the possibility of HLA similarity; less commonly, non-Hodgkin's lymphoma, acute

leukemia and rarely selected other oncology patients given high dose chemotherapy (neuroblastoma, rhabdomyosarcoma). UCSD policy is to irradiate all directed donor blood, except if a blood relationship between a directed donor and the patient has clearly been excluded. The degree of risk for TA-GVHD in term newborns, and except as above, non-transplanted 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. TA-GVHD is prevented by blood irradiation, but TA-GVHD 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 blood irradiation is ordered, if indicated.** Note that blood irradiation is not indicated universally since it may be counter-productive in some patients who are transfusion dependent, eg sickle cell disease, thalassemia, because irradiation shortens the lifespan of rbc which may increase transfusion requirements and may thus increase iron deposition.

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 (eg, SARS, West Nile Virus, and most recently Dengue and Babesia). Autologous blood transfusions should be considered in well-selected patients as an alternative to homologous transfusions to reduce these risks, but will not prevent clerical errors, bacterial sepsis, and 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, 2011. Other old and 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. Despite the recent addition of nucleic acid testing (NAT), HBV (donors tested by HBsAg, HBcAb, and NAT) is still 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 since 1985 and by nucleic acid testing since5/02). 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 only by cellular blood components, especially those containing large numbers of leukocytes, 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)

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. 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. UCSD Medical Center Hospitals employ **only** leukocyte-reduced blood, in order to minimize the risk of transfusion-associated CMV infection in all patients. In addition both leukocyte-reduced and CMV-seronegative donors are routinely employed, if available for neonates and CMV-seronegative bone marrow transplant recipients with CMV-seronegative donors, in order to prevent confusion regarding lab tests caused by passive administration of anti-CMV IgG and because CMV infection may be especially catastrophic in these patients. CMV seronegative donors are also preferred for CMV-seronegative recipients of granulocyte transfusion. Neither saline-washing nor irradiation will prevent CMV. Acellular blood components (FFP, cryo) do not transmit CMV. Contact the Blood Bank Resident (3-5640/1) 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 recipients from CMV-seronegative donors (includes autologous bone marrow)
CMV-seronegative patients with congenital or acquired immune deficiency syndromes, including HIV infection
CMV-seronegative recipients of granulocyte transfusion
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 (1/250,000), is more common with platelets (currently 1 in 75,000 transfusions) because they are stored at room temperature. For this reason, all platelets are currently cultured by the blood supplier to eliminate contaminated units, prior to shipment. 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 Physician, after notifying the responsible clinician, 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 had 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 for WNV was implemented on blood donors in July, 2003, following which the incidence of transfusion transmitted WNV decreased to < 1/44,0000 transfusions. 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.

20.c.8 Emerging infectious diseases

A host of other viruses and microbial agents are known or suspected to be transmitted by blood transfusion, eg HHV-8, XMRV, but their overall clinical significance is unclear. The AABB Transfusion Transmitted Disease Committee maintains an up to date website of the known and some emerging infectious risks of blood at the following URL (accessed 6/16/11). http://www.aabb.org/resources/bct/eid/Pages/default.aspx

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-I/II	yes	yes	no	No	no	no
Hepatitis	yes	yes	yes	No	no	no
CMV	yes [1]	yes [1]	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 (some)	no	no
WNV	yes	yes	yes	No	no	no

[1] 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. 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+ 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, CPDA-1, HbS 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 from directed donors are that donor's RBC are compatible with maternal or infant's plasma and donor's plasma is compatible with infant's RBC and CMV-seronegative. Maternal plasma is ideal for

crossmatching, and must be drawn 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, HbS negative type O Rh-neg CPDA-1 RBC (and/or that 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-Pl^{A1} (HPA-1a) antibodies to a Pl^{A1} positive fetus (pathophysiology similar to hemolytic disease of the newborn), platelets from a HPA-1a-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 is cumbersome and seldom employed, but can 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 for susceptible patients). All directed donor units and HLA matched platelets are irradiated. The request for blood or blood products should indicate the need to "Irradiate." Thornton Hospital obtains irradiated blood from the Red Cross and nearly all of it is irradiated, however orders for irradiation should still be made for patients in whom this is indicated, since special units, ie antigen-negative, etc may not be routinely irradiated by 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 (both La Jolla, at MCC, and at Hillcrest) 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. IMPORT OF BLOOD

Patients sometimes inquire whether autologous units drawn at locations outside the San Diego area can be used at UCSD. Autologous or directed donor units should be drawn locally at the American Red Cross or the San Diego Blood Bank. If the patient needs to make an autologous blood donation outside of the San Diego area, but within California, arrangements can be made through the American Red Cross. Units drawn outside of California can only be transported into the state if the collection facility possesses an FDA license to collect the specific blood product the patient needs to donate. Many blood centers do not have an FDA license to collect autologous blood. Therefore, if a patient is considering autologous donation outside of California, they need to contact the American Red Cross locally to determine if the blood can be shipped, before making a donation. Because of strict FDA requirements regarding the shipment of blood components, UCSD will not accept any blood components hand carried or shipped by patients.

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 Escondido (800-696-1757) or the San Diego Blood Bank (619-296-6393) which has multiple locations throughout the county. ARC holds blood drive on UCSD hospitals and campuses 2-3 times a year.

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.

27. CHARGES FOR BLOOD TESTS AND COMPONENTS

The following charges are representative of average charges and are presented for information only. Actual charges may differ based upon provider.

Test	Representative Charge*
ABO/Rh type	$ 79
Red Cell Antibody Screen	59
Type and (antibody) Screen (T&S)	138
Crossmatch, electronic, per unit	38
Crossmatch, antiglobulin, per unit	77
Antibody Identification	130
Coombs test, direct	34
Blood Irradiation	75
RhIg, 300 mcg vial	88
Neonatal aliquot preparation (+ blood + irradiation cost)	168
Autologous blood fee per unit ** (+ blood cost)	129
Directed donor fee per unit ** (+ blood cost)	129

* Charges vary by provider and 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.

Item	Recent Cost of Blood Components & Services
Red Blood Cells Leukocyte-reduced (LR) (pre-storage)	$ 238
Neonatal aliquot	93
Autologous Blood fee / unit *	125 (+ 238 / unit)
Directed Donor Blood fee / unit*	125 (+ 238 / unit)
Saline-washed red cells	450
Frozen, thawed red blood cells	655
Leukocyte-reduced (LR) apheresis platelets (pre-storage)	469
HLA type (serological level)	331
HLA antibody identification	281
HLA-matched LR apheresis platelets	380 (+ 469 / unit)
HLA antigen neg LR platelets set-up fee	127 (+ 469 / unit)
Crossmatched LR platelets set-up fee	253 (+ 469 / unit)
Fresh Frozen Plasma / Frozen Plasma	36
Cryoprecipitate (one unit)	36
Cryosupernate (TTP only)	36
CMV negative blood (additional charge/unit)	40
Apheresis granulocytes	2100