GUIDELINES FOR BLOOD COMPONENT TRANSFUSION AT UMC

Date: December 2009

For Consideration by The UMC Transfusion Committee:

General Guidelines:
These Transfusion Blood Component Guidelines are submitted consideration and approval by the newly established University Medical Center (UMC) Transfusion Committee. These guidelines are based on a combination of NIH Consensus Guidelines, literature recommendations and clinical experience. These guidelines serve as a basis for making informed decisions about transfusion therapy. However, such guidelines cannot cover every possible circumstance. Clearly, the thorough evaluation of the physiological and clinical condition of the patient must supersede any transfusion plan based on formula or a single laboratory result. It is hoped that the combination of these guidelines with careful patient assessment will result in appropriate transfusion therapy for every patient. A system of blood utilization review is performed which is based on these guidelines

Blood Component Guidelines:
Transfusion care should be individualized to the needs of each patient.

Packed RBCs should be considered for:

1. Hct < 21 in the absence of cardiovascular disease
2. Among stressed patients for the prevention of ischemia:
    - Age < 40 years, Hct < 24.
    - Age 40-60 years, Hct < 27
    - Age 60-70 years, Hct < 30

Platelets*:*

1. Prophylaxis against spontaneous bleeding for adults with platelet count < 10,000/uL
   (< 50,000/uL in neonates).
2. Bedside invasive procedure and platelet count < 30,000/uL.
3. Bleeding intraoperatively or post-operatively and platelet count < 50,000/uL.
4. Bleeding after cardiopulmonary bypass and platelet count < 100,000/uL.

Do NOT transfuse platelets in the setting of HIT and TTP. Platelets may NOT be useful in ITP, PTP, DIC or uremia.

Fresh Frozen Plasma (FFP):
<u>FFP is indicated:</u>

1. Bleeding among patients with INR > 2 sec (for newborns, INR> 2.5)
   N.B. For bleeding patients on coumadin or with vitamin K deficiency, see below.

2. Preparation for bedside invasive procedure if INR> 2 (for newborns, INR>2.5)

3. As part of the emergency management of coumadin reversal:
   The decision to actively intervene (using Vitamin K or clotting factors) or to simply reduce or discontinue warfarin sodium therapy is based in part on the INR but in large measure on the clinical circumstances. Reversal of the anticoagulant effects of warfarin sodium is not a benign procedure with the risk of thrombosis dependent on patient factors such as the presence of an artificial heart valve, neoplasm, the need for rapid reversal and others. Although clinical judgment should prevail, some general guidelines can be considered:

   a) Management of asymptomatic elevations in the INR

      - If the INR is above the therapeutic range but below 5 and rapid reversal is not indicated, omit the next dose or two of warfarin sodium and resume therapy at a lower maintenance dose when the INR returns to the therapeutic range.

      - If the INR is > 5 and < 9 **or** rapid reversal is required, Vitamin K 0.5-1 mg IV* or Vitamin K 1-2.5 mg subcutaneously or orally may be administered. If there is a high thrombotic risk the option to withhold warfarin for 2 or more doses may be preferred.

      - If the INR is > 9 and < 20, Vitamin K 2.5 mg IV or 5mg subcutaneously may be administered.

      - If the INR is >20, administration of fresh frozen plasma** is indicated along with Vitamin K 2.5 mg IV or 5mg subcutaneously

   b) Management of patients on coumadin who are bleeding. If the INR is elevated and the patient is bleeding, administration of fresh frozen plasma is indicated along with Vitamin K 2.5 mg-5 mg IV.

   Notes on coumadin reversal:
   *Intravenous vitamin K is associated with a small risk of severe allergic reaction. When administered intravenously, the rate should not exceed 1mg/minute. Reversal of anticoagulation by any means (vitamin K or FFP) is associated with a risk of thrombosis depending upon the patient's underlying need for anticoagulation.

**Fresh frozen plasma should be dosed based on patient weight (usual adult dose is 10 mL/kg). If FFP is administered without concomitant vitamin K, the effect of FFP will dissipate in 8-12 hours so the INR must be monitored closely.

4. Among non-bleeding patients with abnormal hemostasis <u>not</u> due to vitamin K deficiency, FFP may be given as prophylaxis to prevent spontaneous bleeding if PT > 30 sec or INR > 6

<u>FFP is Not indicated:</u>

1. For non-bleeding patients with a INR < 1.5 (for newborns, INR< 2)
2. For volume
3. Among non-bleeding patients on coumadin or with vitamin K deficiency, treatment with vitamin K alone is preferred (see above).

Studies suggest that FFP is widely overused among hospitalized patients. In particular, clinicians should recognize that no study has demonstrated any value to the patient from the transfusion of FFP prior to invasive bedside procedures among patients with mild to moderate prolongation of the PT or aPTT.

Cryoprecipitate:

Indication: Bleeding in the setting of:

1. fibrinogen < 100 mg/dL
2. von Willebrand's Disease

Leukoreduced Blood Components:

The leukocytes present in cellular blood components (red blood cells and platelets) are responsible for three transfusion complications: febrile non-hemolytic reactions, sensitization to HLA antigens, and transmission of intracellular viruses such as CMV.

The UMC Transfusion Committee recommends that the following groups of patients receive leukoreduced Red Cell Blood Cells and Platelets:

1. Patients with documented repeated prior febrile, non-hemolytic transfusion reactions.
2. Patients with hematological malignancy who will require long-term platelet transfusion support
3. Patients with hemoglobinopathies requiring long-term red cell transfusion support.
4. Renal, heart, and lung transplant recipients or candidates.
5. Other patients requiring CMV-reduced risk transfusions. (see section on CMV-reduced risk blood).

Leukoreduction is routinely accomplished by filtration with high performance filters which achieve a two to three logarithm reduction in leukocytes. This filtration step may occur shortly after the blood is collected (pre-storage leukoreduction) or at the bedside. Apheresis platelets are collected by a method which renders them leukoreduced. The residual number of leukocytes in a leukoreduced unit of red blood cells or platelets is approximately 10^6. Leukoreduced cellular components may be requested by writing "Leukoreduce", "Leukopoor", or "WBC filter" on the Blood Requisition Form or by requesting via computerized Physician Order Entry. The units issued will either have been leukoreduced in the lab (and be labeled as such) or issued with the appropriate filter (pink for RBC and white for platelets). Additional filters, such as the routine blood administration set filter or a microaggregate filter, are not necessary if a bedside leukoreduction filter is used. Plasma components and derivatives already lack leukocytes and need no further manipulation.

Irradiation of Blood Components:
Residual donor lymphocytes, present in red blood cells and platelet concentrates, can initiate Graft *vs* Host Disease when transfused into an immunocompromised host. Transfusion-associated Graft *vs* Host Disease (TA-GVHD) has a very high fatality rate because, unlike the GVHD occurring in bone marrow transplantation, host marrow is also a target for the transfused T cells. Gamma irradiation of cellular blood components eliminates the ability of lymphocytes to proliferate thereby preventing them from mounting an effective immunological response to host tissues. Irradiation of blood components has been shown to be effective in preventing TA-GVHD in susceptible hosts. Irradiation does not remove lymphocytes from the blood component, hence alloimmunization and febrile transfusion reactions antigens may still occur. It has no effect on the transmission of infectious diseases. Irradiation results in a small but significant increase in the plasma K^+ concentration of RBCs.

Based on the reported experience and our understanding of the pathophysiology of TA-GVHD, the Transfusion Committee recommends that the following patients be transfused with irradiated cellular blood components:

1. Bone marrow and stem cell transplant recipients - from day 1 of pre-transplant chemotherapy
2. Congenital T cell immunodeficiency syndromes - e.g. SCIDS, Wiskott-Aldrich, DiGeorge
3. Intrauterine transfusion
4. Neonatal exchange transfusion
5. Premature neonates weighing < 1200 g
6. Transfusions from blood relatives
7. Patients with some hematologic malignancies (Hodgkin's, Non-Hodgkin's Lymphoma, acute leukemias) and neuroblastoma
8. Patients receiving fludarabine

In addition, for the pediatric service, patients with the following diagnoses may receive irradiated cellular components:

1. Ewing's(PNET) sarcoma
2. Osteogenic sarcoma
3. Rhabdomyosarcoma
4. Soft tissue sarcoma - combination chemotherapy with alkylating agents
5. euroblastoma- stage 3 and 4.
6. Wilm's tumor- stage 3 and 4
7. Brain tumors- combination chemotherapy including alkylating agents
8. Germ cell tumors-combination chemotherapy including alkylating agents
9. Retinoblastoma- combination chemotherapy including alkylating agents

It is the responsibility of the ordering physician to request irradiated blood components, when they are required. Requests for irradiated blood should be made by writing "irradiate" and the indication for irradiation on the blood requisition. When ordering through the Physician Order Entry software, you may request irradiated blood using the "Restrictions" button.

CMV Reduced-Risk Blood Components

Cytomegalovirus (CMV) is a ubiquitous member of the herpes virus family to which approximately 30-60% of adults in developed countries have been exposed as indicated by the presence of antibodies. Three patterns of CMV infection have been described: primary infection, reactivation and re- or co-infection. Only primary infection has been documented to occur following blood transfusion. Primary infection occurs in CMV-seronegative recipients and may be detected by seroconversion (IgM followed by IgG), viral shedding (viruria typically), fever or lymphocytosis. Although CMV infection rarely produces serious disease in immunologically intact hosts, it is associated with systemic infection in immunocompromised patients and may be manifest as pneumonitis, gastritis, retinitis or other infections. CMV infection in immunocompromised patients is also associated with allograft rejection and dysfunction, and superinfection with other organisms. Following recovery, CMV may remain in a latent form in infected cells for years. Neither reactivation infection nor second-strain infection has been documented to occur as a result of blood transfusion.

CMV can infect many tissues including blood mononuclear cells as well as kidney, lung, liver and brain. Therefore, in addition to the usual routes of infection, susceptible patients may also become infected by transplantation or transfusion from an infected donor. The following groups of patients have been shown to be susceptible to transfusion-transmitted CMV primary infection and disease and should receive CMV reduced-risk cellular blood components:

1. Premature, low birth weight (<1200g) neonates
2. CMV-seronegative pregnant women (including intrauterine transfusions)
3. CMV-seronegative recipients of, or candidates for, bone marrow or peripheral blood stem cell transplants

a. If the donor and the recipient are both CMV-seronegative, then the patient should recieve blood which is both leukoreduced and CMV-seronegative, if possible.
4. CMV-seronegative recipients of, or candidates for, heart, lung or kidney transplants.
5. A CMV seronegative liver transplant recipient who receives an allograft from a CMV seronegative donor should receive leukoreduced blood post-operatively.
6. CMV-seronegative, HIV-infected patients.

CMV reduced-risk blood components can be obtained in two ways. Donors can be screened for CMV antibody (IgG) which indicates past exposure. Although approximately 30% blood donors are CMV seropositive, only a small minority of CMV-seropositive donor units are capable of transmitting CMV. A substantial portion of CMV seronegative donors are CMV PCR positive. As an alternative to choosing CMV seronegative blood components, blood mononuclear cells, which may carry CMV in its latent form, can be effectively removed from the blood by filtration with leukocyte filters or by freezing/deglycerolizing the unit. CMV serologic screening and leukocyte removal have been shown to be equally effective in preventing transfusion-transmitted CMV infection. Orders for CMV reduced risk, CMV "safe", or CMV seronegative blood will be filled by providing either CMV seronegative or filtered units at the discretion of the Blood Transfusion Service, depending on the inventory. Only cellular components (red blood cells, platelets and single donor platelets) need to be CMV reduced-risk since intact mononuclear cells are required to transmit CMV.

Patients Refractory to Platelet Transfusion

Poor response to platelet transfusion is observed in 10-20% of patients who require long term transfusion support. The failure to achieve a satisfactory elevation in the platelet count is referred to as refractoriness. An inadequate response may be the result of a number of factors, among them alloimmunization to HLA and platelet-specific antigens. Although platelets themselves are poorly immunogenic, passenger mononuclear cells are capable of eliciting an alloimmune response from the recipient. The frequency of alloimmunization can be effectively reduced by leukoreduction. Patients who are likely to require long-term platelet transfusion support should routinely receive leukoreduced cellular components.

The UMC Transfusion Committee recommends that 10,000 platelets/□L as an appropriate level for prophylactic transfusion for adults; however, this guideline should not be applied blindly. Attempts to achieve this arbitrary level by repeated platelet transfusions to refractory patients who are stable and not bleeding are not warranted.

The following is a suggested strategy to assess and manage the refractory patient. It is important, first of all, to establish that the patient is indeed refractory. A low platelet count the morning after a platelet transfusion does not constitute sufficient evidence of refractoriness. Secondly, non-alloimmune causes should be ruled out or treated. Immunologic compatibility will not protect platelets from consumption or sequestration.

Finally, while these strategies are useful in prophylactic platelet transfusion, they play no role in the treatment of major bleeding.

Strategy for Managing Platelet Refractoriness

1. Obtain a platelet count 10-60 minutes after the platelet transfusion is completed. Usually each unit of platelets increases the count more than 5,000/μL.
2. If the increase is less than 5,000/μL for the transfusion, request ABO-compatible platelets.
3. If the increase is less than 5,000/μL with ABO-compatible platelets on two occasions, call for Transfusion/Coagulation Medicine consult for possible HLA matched platelets.

Reviewed and Accepted by the UMC Transfusion Committee 2009.

Date: _____

Signed: _____

Chair, Transfusion Committee