These evidence-based recommendations for transfusion are published for general use by the Indianapolis Coalition for Patient Safety Blood Group, an independent panel of interdisciplinary experts including physicians, nurses, medical technologists, and a pharmacist from Coalition member hospitals. These guidelines are based on peer-reviewed material and reviewed periodically for currency, however new or more recent peer-reviewed literature may be taken into consideration when appropriate.

No single measure can replace good clinical judgment as the basis for decision-making regarding the need for transfusions. Chart documentation of indication is <u>required</u> for regulatory compliance. For transfusions ordered outside of these guidelines, additional documentation of clinical reasoning is needed (Napolitano, Kurek, Luchette, Corwin, Barie, Tisherman, ...Yelon, 2009).

Outpatient Statement

Studies supporting transfusion guidelines have been conducted in the inpatient environment. Data to guide evidence-based transfusion in the outpatient setting is lacking. <u>Outpatient Statement</u>

LEUKOREDUCED RED CELLS

RED Cells Clinical Statement

Transfusion of RBCs is indicated when decreased circulatory oxygen-carrying capacity results in inadequate tissue oxygenation. The decision to transfuse should not be made based upon decreased hemoglobin concentration alone, but should be guided by careful consideration of the clinical context including signs/symptoms of inadequate oxygenation, acuity of anemia, comorbidities and the patient's ability to tolerate mild anemia without intervention. Transfusion is not without attendant risk of noninfectious and infectious complications, and a clear assessment of benefit over risk should be present. Clear documentation of indication and rationale for the transfusion beyond simple reporting of the hemoglobin concentration should be included in the patient's chart (AABB, American Red Cross, America's Blood Centers, Armed Services Blood Program, 2011; AABB, 2010). Evidence shows storage length does not affect the efficacy of RBC's; therefore, blood banking practices of using standard-issue blood should be followed (Carson et al 2016).

Autologous Blood Donation

The routine use of pre-surgical autologous blood donation is not advised (AABB et al., 2011; AABB, 2010). <u>Autologous</u>

Directed Donation

The routine use of directed blood donations is not advised (AABB, 2010). Directed Donation

Expected effect of Administration:

Indianapolis Coalition for Patient Safety, Inc.

Guidelines established 2012; version 11.15.16

Blood Group Subcommittee

One unit of packed red cells in an adult will increase hematocrit by approximately 3% and Hemoglobin by 1g/dL in a non-bleeding patient (AABB et al., 2011).

Indications for RBCs – Not Actively Bleeding: Transfuse 1 Unit then re-assess (AABB et al., 2011 & 2012; Napolitano et al., 2009; Nuttall, Brost, Connis, Gessner, Harrison, Miller, ...Spence, 2006; Carson et al., 2012 & 2015).

- Hematocrit less than or equal to 21% or Hemoglobin less than or equal to 7 g/dL
- Hematocrit less than or equal to 24% or Hemoglobin less than or equal to 8 g/dL AND patient with Acute Coronary Syndrome, CHF, or pre-existing ischemic cardiovascular disease.
- Hematocrit less than or equal to 24% or Hemoglobin less than or equal to 8 g/dL AND postoperative patient.
- Hematocrit less than or equal to 24% or Hemoglobin less than or equal to 8 g/dL AND chemotherapy patient OR patient with bone marrow suppression.
- Other: Must specify reason for transfusion clearly. This option will be automatically audited for appropriateness.

Indications for RBCs – Active Bleeding: Transfuse per Assessed Need (Quraishy, Bachowski,

Benjamin, Eastvold, Goldberg, Hopkins, ...Westra, 2012):

- Acute Blood Loss unresponsive to volume resuscitation. Blood loss of >1000cc (~ 20% of estimated blood volume) with hemodynamic instability, inadequate oxygenation, or evidence of organ ischemia (Quraishy et al., 2012).
- Other: Must specify reason for transfusion clearly. This option will be automatically audited for appropriateness.

Estimation of blood volume: 70kg male has ~5000mL blood, or ~ 70mL/kg (32mL/lb) (Cameron, Skofronick, & Grant, 1999; Nuttal, et al., 2006; Taggart, & Starr, 1989; World Book Rush Presbyterian St. Luke's Medical Center Medical Encyclopedia, 1997).

PLATELETS

Apheresis Platelets: one apheresis unit is from a single donor and is equivalent to 4-6 concentrates (random donor platelets) (AABB et al., 2011).

Contraindications for Platelets:

- Autoimmune thrombocytopenia (AKA Idiopathic Thrombocytopenic Purpura) (AABB et al., 2011; Quraishy et al., 2012)
- Thrombotic Thrombocytopenic Purpura (Quraishy, 2012)
- Heparin-induced thrombocytopenia (Quraishy, 2012)
- Hemolytic-Uremic Syndrome (Quraishy, 2012)
- In general, patients with thrombotic manifestations should not be transfused with platelets except in the case of life threatening hemorrhage (AABB et al., 2011; Quraishy, 2012).

Expected effect of administration:

Apheresis platelet will increase the platelet count by 20,000-60,000/mL³ (AABB et al., 2011). Measure platelet count 10 to 60 minutes after transfusion to assess targeted platelet count (Quraishy, 2012).

Refractory Platelet Statement

Thrombocytopenic patients who have received multiple platelet transfusions may develop a refractory response where there is failure to achieve or sustain an expected rise in platelet count following platelet administration (AABB et al., 2011; AABB, 2010; Quraishy et al., 2012). <u>Refractory</u>

Indications for Platelets – Not Actively Bleeding (Quraishy, 2012, Kaufman et all, 2015):

- Prophylactic treatment in patients with a platelet count less than 10,000/mm³
- Platelet count less than 20,000/mm³ in patients undergoing MINOR procedure (eg. central venous catheter placement)
- Platelet count less than 50,000/mm³ in patients with MAJOR invasive procedures) MAJOR Cases

Indications for Platelets – Active Bleeding (Quraishy, 2012). Transfuse per assessed need:

- Life threatening hemorrhage
- Platelet count less than 20,000/mm³ and signs of hemorrhagic diathesis (petechiae, mucosal bleeding)
- Platelet count less than or equal to 50,000/ml³ and obvious bleeding
- Platelet count less than 100,000/ml, and
 - o neurosurgical patient or intracranial bleed or invasive neurological procedure
 - intraocular bleed/ophthalmological procedure
 - o diffuse microvascular bleeding following bypass or aortic balloon pump
 - uremic bleeding

Platelet dysfunction (Sarode, 2012):

- Dysfunction is generally only treated when there is active bleeding or high risk for bleeding.
- Types of dysfunction
 - o congenital
 - o acquired
 - o drug-induced
- Treatment of platelet dysfunction or thrombocytopenia varies depending on clinical status.

PLASMA: FRESH FROZEN PLASMA (FFP)

The following types of plasma are interchangeable with FFP (Quraishy, 2012).

- Frozen Plasma 24 (FP24) equivalent to FFP
- Thawed Plasma (TP) frozen plasma that is thawed and stored up to 5 days

Plasma Clinical Statement

Average INR of donor Plasma product may be elevated. Plasma transfusion will not always correct abnormal lab values, or the correction may be transient (Quraishy, 2012). "...only 50% of patients with an INR of 1.7 showed a significant change in INR with FFP transfusion. Therefore, transfusion for patients not meeting current FFP guidelines does not reliably reduce the INR and exposes patients to unnecessary risk." (Holland & Brooks, 2006). For this reason, the Indianapolis Patient Safety Coalition, Inc., Blood Group agrees it is not reasonable to correct coagulopathy in bleeding patients or patients undergoing an invasive procedure if the INR is less than 1.6 (Committee consensus, November 13, 2012). **Coagulopathy can be corrected more effectively with specific therapy** (AABB et al., 2011; Yang et al., 2012):

- o Vitamin K
- o 3-factor or 4-factor Prothrombin Complex Concentrate (PCC)
- o Cryoprecipitated Antihemophilic Factor (AHF)
- Specific coagulation concentrates

Expected effect of Plasma Administration:

• A Dose of 10-20 mL/kg is usually adequate to correct a coagulopathy (Quraishy, 2012). <u>Timing of Transfusion for Plasma</u>:

Prophylactic plasma administration for correction of markedly abnormal coagulation parameters requires careful timing of administration due to half-life of coagulation factors (Quraishy, 2012). <u>Timing</u>

Contraindications for Plasma:

- Volume expansion (AABB et al., 2011; AABB, 2010; Quraishy, 2012)
- Nutritional deficiencies (AABB, 2010)
- Consumptive coagulopathy without significant hemorrhage (sepsis, DIC)(AABB, 2010)
- For reversal of Warfarin non-emergently and/or in the absence of bleeding (Vitamin K is preferred)(AABB, 2010; Quraishy, 2012)
- Correction of minor coagulation abnormalities (AABB et al., 2011)
- Replacement of single factor deficiencies when single factor concentrates are available (AABB, 2010)

Indications for Plasma:

- Emergent need for Warfarin reversal (AABB, 2010; Quraishy, 2012).
- As a component for massive transfusion protocol (AABB et al., 2011; AABB, 2010; Quraishy, 2012)
- Patients with selected coagulation deficiencies, for which no specific coagulation concentrates are available (AABB et al., 2011; AABB, 2010; Quraishy, 2012)
- Preoperative or bleeding patients, requiring replacement of multiple coagulation factors (Quraishy, 2012)
- Abnormal coagulation studies and significant hemorrhage (DIC) (AABB, 2010)
- Treatment with plasmapheresis for thrombotic thrombocytopenia purpura or hemolytic uremic syndrome (AABB et al., 2011; Quraishy, 2012)
- Patients with rare specific plasma protein deficiencies and recombinant products not available (C1 inhibitor)(AABB, 2010; Quraishy, 2012)
- Plasma exchange (AABB et al., 2011)

Plasma Cryoprecipitate Reduced

Cryoprecipitate reduced plasma is the remaining supernatant when cryoprecipitate has been removed from plasma (AABB et al., 2011; Raife, Friedman, & Dwyre, 2006). Reduced Cryoprecipitate

CRYOPRECIPITATED ANTIHEMOPHILIC FACTOR (AHF)

Expected effect of administration:

One unit per 10 kg patient weight is usually adequate when cryoprecipitate is required. Cryoprecipitate is usually supplied in 5 or 10 unit pools (AABB et al., 2011; Becker & Shaz, 2011).

Contraindication for Cryoprecipitate:

When virus-inactivated or Factor VIII concentrates or recombinant factor preparations are available for management of von Willebrand disease or hemophilia A. (AABB et al., 2011; Becker & Shaz, 2011).

Indications for Cryoprecipitate:

- Fibrinogen is less than 100 mg/dl (Becker & Shaz, 2011; Quraishy et al., 2012).
- Threshold of 200 mg/dl in massive transfusion (Bollinger, Szlam, Molinaro, Rahe-Meyer, Levy, & Tanaka, 2009; Levy, Szlam, Tanaka, & Sciecienski, 2012; Rossaint, Bouillon, Cerny, Coats, Duranteau, Fernandez-Mondejar, ...Spahn, 2010). <u>Fibrinogen</u>
- Dysfibrinogenemia (including DIC)(AABB et al., 2011; Quraishy, et al., 2012)
- Factor XIII deficiency or Factor VIII deficiency AND concentrates not available (AABB et al., 2011; Quraishy, et al., 2012)
- Type 1 vWD unresponsive to DDAVP or DDAVP contraindicated (AABB et al., 2011; Quraishy, et al., 2012)
- Factor VIII:VWF concentrate not available (AABB et al., 2011; Quraishy, et al., 2012)
- Uremic bleeding unresponsive to DDAVP (AABB et al., 2011; Quraishy, et al., 2012)
- Fibrin glue/sealant (Quraishy, et al., 2012)

Appendix

Autologous Blood Donation: Presurgical

The advent of better infectious disease testing technologically, particularly nucleic acid testing (NAT) has greatly mitigated the risk of viral transmission by allogeneic blood components. Therefore, the putative benefit of preoperative autologous blood donation (PAD) in reducing risk of transmission of infectious disease is offset by the increased occurrence of preoperative anemia and the overall higher transfusion rates for these patients. In addition, PAD does not eliminate the potential need for allogeneic blood transfusion, and does not eliminate risks. Risks associated with PAD include (a) the risks associated with donation, (b) bacterial contamination, (c) transfusion of the wrong unit, and (d) fluid overload. Even Transfusion-Related Acute Lung Injury (TRALI) has been known to occur with PAD blood transfusions (Becker & Shaz, 2011). Hypothetical benefits, such as reduction of immunomodulatory effects of transfusion have not been well supported. Autologous units must be discarded if not transfused, and cannot be crossed over to the donor blood supply. Since PAD can defeat one of the main goals of blood conservation – the optimization of the patient's hemoglobin level prior to surgery – consideration of other blood conservation methodologies is preferred. PAD should be reserved for carefully selected patients with rare blood types or unusual antibodies that make it difficult to find appropriate amounts of adequately crossmatched blood (AABB, et al., 2010). Return to Autologous

Cryoprecipitate Reduced Plasma

Cryoprecipitate reduced plasma is the remaining supernatant when cryoprecipitate has been removed from plasma. It is therefore depleted of Factor VIII, XIII, von Willebrand factor (vWF), fibrinogen, cryoglobulin and fibronectin; but contains the remaining coagulation factors found in plasma. It has sometimes been used as a replacement fluid in plasma exchange for the treatment of refractory TTP, where it was thought to be beneficial due to depletion of high molecular weight vWF. However, this benefit is equivocal, and FFP, FP24, or TP are all suitable for plasma exchange in TTP (AABB et al., 2011; Raife et al., 2006). <u>Return to Reduced Cryoprecipitate</u>

Directed Blood Donation

Although many patients may request directed donations based on the belief that the risk of infectious disease transmission is lower, evidence has shown that directed donors are no safer than volunteer blood donors. According to the FDA, the blood supply is safer today than at any time in history due to several factors including advances in donor screening and improved testing for infectious diseases. And, directed donors may succumb to social pressure associated with directed donation that may compromise the reliability of the donor's answers to health-history questions (AABB, 2010)

Directed donations are most appropriate in the setting of a patient with a rare blood type or unusual antibodies such that appropriate compatible blood components are difficult to obtain. This includes transfusion of washed maternal platelets to the fetus or neonate in the setting of neonatal alloimmune thrombocytopenia (NATP) (Technical Manual 17th Edition, 2011).

Special considerations related to directed donation include:

- All directed donations from the patient's blood relatives must be irradiated due to the higher risk of Transfusion-associated graft-versus-host disease (TA-GVHD) (AABB, 2010).
- Directed donations from family members who are prospective bone marrow donors should be avoided.

 $P_{age}6$

- Women of child-bearing age should not receive directed donations from their sexual partner or his blood relatives, as this increases the risk of immunization against paternal antigens which may result in hemolytic disease of the fetus and newborn (HDFN) or NATP in future pregnancies.
- Transfusion of maternally-derived components to children should occur with caution, since there is a risk of TRALI due to HLA antibodies formed against the child during pregnancy. <u>Return to Directed Donor</u>

Fibrinogen in Massive Transfusion

"The revised European trauma guidelines published in 2010 recommend a trigger fibrinogen concentration of 1.5 to 2.0 g/L, which was increased from below 1.0 g/L in earlier guidelines. This change is in agreement with other in vitro evidence that concentrations larger than 2.0 g/L are required to produce effective clot formation." (Levy, et al., 2012). <u>Return to Fibrinogen</u>

MAJOR case examples

In the absence of coagulopathy or thrombocytopathy, major invasive procedures including paracentesis/thoracentesis, respiratory tract/gastrointestinal [GI] biopsies, closed liver biopsy, lumbar puncture, sinus aspiration, and dental extraction, require functional platelet counts of at least 40,000-50,000/uL (Quraishy, 2012). <u>Return to MAJOR</u>

Outpatient Statement

Outpatients who present for transfusion generally have a transfusion dependent condition related to bone marrow failure to produce red cells. It is unknown whether different transfusion criteria should be applied to outpatients as compared to their hospitalized counterparts since no research has been done on the topic. What is known, it is standard practice to take a more liberal approach to transfusion in these patients. This approach includes transfusing at Hgb values around 8gm/dL to preserve quality of life by reducing fatigue. In addition, two units are frequently given to prevent an excessive number of recurring visits to the outpatient clinic and reduce the number of times IV lines need to be accessed. It is recognized that more research is needed. Until this is accomplished, this practical approach to outpatient treatment with red cells is accepted practice (Indianapolis Coalition for Patient Safety Inc. Blood Group, committee consensus, June 19, 2012). <u>Return to Outpatient</u>

Platelet: Refractory Statement

A refractory response that renders the platelet transfusion ineffective may be related to platelet destruction or sequestration. Causes may be immune (HLA or anti-platelet (HPA) antibodies), or nonimmune (splenomegaly, sepsis, DIC, intravascular devices, fever). A platelet count obtained 10 to 60 minutes post-infusion that demonstrates poor recovery is suggestive of an immune refractory state secondary to serologic incompatibility. Nonimmune mechanisms typically demonstrate adequate recovery within 1 hour of infusion, but longer term (i.e. 24-hour) survival is reduced.

Serologic tests can confirm the presence of alloimmunization. Laboratory tests (HLA typing and antibody identification, platelet antibody identification, or a platelet crossmatch) are useful for selection of platelets with acceptable survival in these patients. The Corrected Count Increment may also be useful in determining response to transfusion (AABB et al., 2011; AABB, 2010; Quraishy, 2012).

Corrected Count Increment

The corrected count increment (CCI) is a calculated measure of patient response to platelet transfusion, adjusting for the number of platelets infused and the size of the recipient, and based upon body surface area (BSA).

CCI = (post-transfusion platelet count - pre-transfusion platelet count (/µL)) X BSA (m²)# of platelets transfused*

*For apheresis platelets, a minimum estimate of 3.0 x 10¹¹ platelets may be used. In the clinically stable patient, the CCI is typically >7500 at 10 minutes to 1-hour postinfusion, and remains above 4500 at 24 hours. A CCI of less than 5000 at 10 minutes to 1 hour after transfusion, along with supportive serologic test results is indicative of an immune refractory state (AABB et al., 2011). <u>Return to Refractory</u>

Plasma: Timing of Transfusion

Plasma provides transient correction of coagulopathy related to the short half-lives of the coagulation factors. Therefore, if plasma is to be administered prophylactically for correction of markedly abnormal coagulation parameters, the timing of administration requires careful consideration. For maximum benefit, plasma is best administered immediately prior to a planned procedure. At worst, transfusion should occur within a few hours before procedural start time (Quraishy, 2012).

Transfusion of a surgical patient with plasma the night before a procedure is ineffective. The failure of such patients to bleed abnormally during surgery supports the lack of correlation between mild-to-moderate coagulation abnormalities and clinical bleeding, and underscores the argument that many prophylactic plasma transfusions are unnecessary (Quraishy, 2012). <u>Return_to_Plasma_Timing</u>

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