Guidelines for Transfu-sion

2013

Prepared by:

Community Transfusion Committee
Lincoln, Nebraska

CHAIR:	Aina Silenieks, MD
MEMBERS:	L. Bausch, M.D. R. Burton, M.D. S. Dunder, M.D. D. Voigt, M.D. B. J. Wilson, M.D.
COMMUNITY REPRESENTATIVES:	Becky Croner Ellen DiSalvo Christa Engel Phyllis Ericson Kelly Gillaspie Pat Gilles Vic Grdina Jessica Henrichs Kelly Jensen Laurel McReynolds Christina Nickel Angela Novotny Kelley Thiemann Janet Wachter Jodi Wikoff

INTRODUCTION

The Community Transfusion Committee is a multidisciplinary group that meets to monitor blood utilization practices, establish guidelines for transfusion and discuss relevant transfusion related topics. It is comprised of physicians from local hospitals, invited guests, and community representatives from the hospitals' transfusion services, nursing services, perfusion services, health information management, and the Nebraska Community Blood Bank.

These Guidelines for Transfusion are reviewed and revised biannually by the Community Transfusion Committee to ensure that the industry's most current practices are promoted. The Guidelines are the standard by which utilization practices are evaluated. They are also designed to provide helpful information to assist physicians to provide appropriate blood component therapy to patients.

Appendices have been added for informational purposes and are not to be used as guidance for clinical decision making.

ADULT RED CELLS

A. Indications

1. One of the following
    a. Hypovolemia and hypoxia (signs/symptoms: syncope, dyspnea, postural hypotension, tachycardia, angina, or TIA) secondary to surgery, trauma, GI tract bleeding, or intravascular hemolysis, OR
    b. Evidence of acute loss of 15% of total blood volume or >750 mL blood loss, OR
    c. Hemoglobin level of less than 7-8 g/dL or hematocrit less than 21-24%.

    Contraindications: If reason for transfusion is hemoglobin less than 8g/dL and the patient has either: iron deficiency anemia, pernicious anemia, nutritional deficiency, intestinal malabsorption, or autoimmune hemolytic anemia, but does not have symptoms of hypovolemia and hypoxia, the record must be reviewed by the committee.
2. If patient has a chronic disease listed below or is a burn/trauma patient, but hemoglobin greater than 8 g/dL, the record does not require committee review. Chronic diseases include a diagnosis of myocardial disease, cerebral ischemia, history of TIA, previous thrombotic stroke, chronic pulmonary disease, asymptomatic anemia associated with renal disease, patients receiving active chemotherapy, or alcoholic liver disease with anticipated surgery.
3. Blood should be transfused on a unit-by-unit basis, according to patient symptoms. One unit of blood may be sufficient. The outcome or results of the transfusion should be documented in the patient's record. Statements of improved symptoms and/or post-transfusion hemoglobin or hematocrit are examples of documentation.

4. The following information is the latest data from the AABB, relating to red cell transfusion:

Hemoglobin (g/dL)	Recommendation (for hospitalized, hemodynamically stable patients)	Comments
>10	Red cell transfusion not indicated.	There may be exceptional circumstances where red cell transfusion could be considered.
8-10	Red cell transfusion not indicated unless specific circumstances (clinically important signs or symptoms of anemia or ongoing bleeding) are present.	The AABB clinical practice guideline[2] suggests considering transfusion for patients with pre-existing cardiovascular disease who have the following symptoms: chest pain, orthostatic hypotension or tachycardia unresponsive to fluid resuscitation, or congestive heart failure. The AABB cannot recommend for or against a liberal or restrictive transfusion at this hemoglobin level for hospitalized, hemodynamically stable patients with acute coronary syndrome.
7-8	Red cell transfusion should be considered in postoperative surgical patients when the hemoglobin level is <8 g/dL. Red cell transfusion is not indicated in intensive care unit patients until the hemoglobin level is < 7 g/dL.	The AABB recommends adhering to a restrictive transfusion strategy (7-8 g/dL) in hospitalized, stable patients even in the presence of pre-existing cardiovascular disease. Transfusion could be considered but only after evaluating the patient's clinical status. These same recommendations (7-8 g/dL transfusion threshold) are likely to apply to most medical patients with the exception of those with acute coronary syndrome.
<7	Red cell transfusion likely to be indicated.	Inadequate clinical data to assess whether transfusion is necessary in all patients at this hemoglobin level.
<6	Red cell transfusion highly recommended except in exceptional circumstances.	

This information is derived from a clinical practice guideline* developed by a working group of the AABB Clinical Transfusion Medicine Committee.[2] The group included representatives of the American Society of Anesthesiologists, American College of Cardiology, American Society of Hematology, American Association for the Surgery of Trauma, Society for Critical Care Medicine, and American Academy of Pediatrics. These recommendations apply to hemodynamically stable patients. They do not apply to patients with active bleeding or to preoperative patients when blood loss is anticipated during the surgical procedure.

*Clinical practice guidelines and recommendations are not to be considered standards or absolute requirements. They do not apply to all individual transfusion decisions. Clinical judgment is critical in the decision to transfuse; therefore, red cell transfusion above or below the specified hemoglobin threshold may be dictated by the clinical context.

B. Transfusion reactions will be reviewed and summarized by the Transfusion Service and reported back to the committee. This will also include:

1. Any patient death related to transfusion.
2. Hemolytic or anaphylactic transfusion reactions.
3. Any patient with reported diagnosis of hepatitis or abnormal liver function within 6 months of transfusion.

PEDIATRIC RED CELL TRANSFUSION

I. Newborns

A. Hypovolemia due to surgery, trauma, gastrointestinal hemorrhage, or other blood loss documented by one of the following:

1. With respiratory distress
   a. hematocrit less than 35%
   b. evidence of shock (one of the following):
      1) pallor
      2) poor perfusion
      3) tachycardia
      4) hypotension
   c. greater than 10% of the blood volume has been removed within a 48 hour period (averagenewborn blood volume is ~270 mL)
2. Absence of respiratory distress
   a. hematocrit less than 30% in the first post-natal week, OR
   b. evidence of congestive heart failure, imminent, or present (one of the following):
      1) tachycardia
      2) tachypnea
      3) cardiomegaly

B. Low birth weight (less than 2500 grams) or very low birth weight (less than 1000 grams) with apnea

II. Pediatric patients - four months to two years

A. Symptomatic anemia (one of the following):

1. pallor
2. poor perfusion

3. imminent or current congestive heart failure, from whatever cause if no other medicinal therapy has or is likely to correct it.

B. Chemotherapy when medicinal therapy is unlikely to correct a low hematocrit of less than 30%. OR

C. Prior to surgery and anesthesia, although asymptomatic, with hematocrit of less than 30%. OR

D. Intraoperative estimated loss of blood greater than 10% of the blood volume.

PLATELET TRANSFUSION

The purpose in establishing guidelines for platelet transfusion is to reduce the risk of disease transmission and allosensitization. It is also important to ensure that the use of a product that is in limited supply is clinically indicated.

Assessment of need for platelet transfusion should include evaluation of current or potential risk of bleeding. Pre-transfusion and post-transfusion platelet counts should be used to monitor indications for and response to platelet therapy as well as the need for additional platelet transfusion.

It is difficult to establish a uniform dose of platelets for transfusions. However, the basic adult dose of one unit of pheresed platelets should increase the platelet count approximately 25,000 to 50,000/mm^3 in a stable adult. Decreased platelet increments can be caused by rapid utilization or destruction of platelets and may be an indication of allosensitization and refractory state.

A. Indications

1. When platelet count is 5,000/mm^3 or less, platelets should ordinarily be administered, regardless of apparent bleeding.
2. Prophylaxis against bleeding in thrombocytopenic states when platelet counts are between 5,000/mm^3 and 20,000/mm^3 and thrombocytopenia is due to decreased platelet production or when a patient is involved in active chemotherapy.
3. Spontaneous clinical bleeding with platelet counts less than 50,000/mm^3(e.g., oozing at surgical incisions, at venipuncture sites, and from mucosal membranes, widespread petechiae, ecchymoses, conjunctival hemorrhages, epistaxis, easy bruising, melena, menorrhagia, and hematuria.)
4. Prophylaxis against bleeding in premature and extremely ill neonates with active bleeding and platelet counts less than 150,000/mm^3.Prophylaxis for sick infants with platelet count less than 70,000/mm^3 and premature neonates with platelet counts less than 25,000/mm^3.
5. Maintenance of counts above 70,000/mm^3 when there are extensive incisions and large exposed surface areas with evidence of considerable blood loss. Generally, platelet counts of 50,000 to 70,000/mm^3 are adequate both preoperatively and postoperatively for most major surgical procedures. Prophylaxis in patients with platelet counts less than 100,000/mm^3 when patient is to receive neuraxial anesthesia.

6. Prophylaxis after rapid (within 6-12 hours) transfusion of 15-20 units of blood or a single total blood volume replacement for pediatric patients.
7. For bleeding (regardless of platelet count) due to a platelet dysfunction when there is an abnormal platelet function test or documentation of a clinical history or indication of platelet dysfunction (e.g., inherited qualitative disorder; following ingestion of aspirin or platelet inhibitors such as Plavix® or Ticlid®; or chronic uremia.)
8. For bleeding following severe trauma with:
   a. platelet count less than 100,000/mm^3, OR
   b. an abnormal platelet function test or a clinical history or indication of platelet dysfunction, regardless of platelet count, OR
   c. life-threatening hemorrhage requiring massive transfusion
9. For excessive clinical bleeding* after cardiopulmonary bypass (CPB) or aortic balloon pump and either:
   a. platelet count less than 100,000/mm^3, OR
   b. an abnormal platelet function test or clinical history or indication of platelet dysfunction, despite adequate platelet numbers, OR
   c. evidence of emergency situation of uncontrolled bleeding

   *Suggested parameters for excessive bleeding post-CPB (any one of the following):

   1) Bleeding from the chest, with no obvious surgical cause, exceeding 450 mL per hour during the first two post-pump hours.
   2) Bleeding at a rate of 250 mL/hr (3 mL/kg/hr pediatric) for three consecutive hours without sign of reduction.
   3) Oozing from all incisions.
   4) Cardiopulmonary bypass involving the use of global hypothermic circulatory arrest.

B. Contraindications:

1. When bleeding is the result of coagulation factor deficiency, inhibitors, anticoagulants, or von Willebrand's factor deficiency.
2. When platelet function test is normal and platelet range is adequate for hemostasis.
3. For prophylaxis against bleeding when thrombocytopenic state is due to excess platelet destruction or sequestration (e.g., ITP, TTP, immune-mediated drug purpura, DIC, post-transfusion purpura or neonatal isoimmune thrombocytopenic purpura unless accompanied by active bleeding.)
4. For prophylaxis or preoperatively when there is a treatable clinical disease state which causes an extrinsic qualitative platelet defect (e.g., uremia, dysproteinemia.)

5. Routine post CPB platelet transfusion. Prolonged duration of cardiopulmonary bypass per se is not an indication for post CPB platelet transfusion unless the bleeding tendency is appropriately documented by clinical or laboratory parameters.

THAWED FRESH FROZEN PLASMA AND/OR THAWED PLASMA FOR TRANSFUSION

Thawed Plasma is the same as Thawed Fresh Frozen Plasma except that it should not be used to treat coagulation factor deficiencies of factor V and factor VIII.Dose guidelines:10-20 mL per kg. One unit of FFP is ~ 250 mLs.

Hemostatic factor content of factor V and VIII in a typical fresh frozen plasma unit are shown in the following table:

Factor	Level when freshly thawed	Level at 24 hours	Level at 5 days
V	80 IU/mL	75 IU/mL	66 IU/mL
VIII	92 IU/mL	51 IU/mL	41 IU/mL

A. Indications - one of the following:

1. Replacement of isolated factor deficiencies when specific component therapy is not available
   a. Factors II, V, VII, X, and XI
2. Replacement for multiple factor deficiencies
   a. Liver disease
      1) when an invasive procedure is to be performed and
         a) INR > 1.4, OR
         b) PT > 15 seconds, OR
         c) PTT > 50 seconds
   b. Warfarin effect prior to surgery or with active bleeding
      1) INR > 1.5, OR
      2) PT > 16 seconds, OR
      3) PTT > 60 seconds
   c. Consumptive coagulopathy (DIC)
      1) PT > 16 seconds; PTT > 60 seconds OR
      2) D-Dimers increased
3. Thrombotic Thrombocytopenic Purpura
4. Infants with secondary immunodeficiency associated with severe protein-losing enteropathy

5. Difficulty heparinizing a patient withAntithrombin III Deficiency
6. Plasma exchange
7. Low birth weight infants(less than 2500 grams) with DIC with laboratory confirmation
8. C1 Esterase Deficiency

B. Contraindications:

1. Volume expansion or colloid replacement
2. Protein source
3. von Willebrand's disease and factor VIII deficiency
4. Prophylaxis in multiply transfused patients who do not have a documented coagulation defect

CRYOPRECIPITATE TRANSFUSION

Principle: Cryoprecipitate is a cold-insoluble protein that is harvested when fresh frozen plasma is thawed at 1-6°C. Each unit comes from a single donor. Therefore, the risk of transfusion transmitted disease such as hepatitis increases concomitantly with each unit administered in the pool. Cryoprecipitate is an excellent source of Factor VIII:C (the Factor VIII procoagulant portion), Factor VIII:vWF (von Willebrand's factor), fibrinogen, and Factor XIII.

Composition:

1. Factor VIII:C - 80-120 units/cryo unit
2. Factor VIII:vWF -40-70% of vWF/single FFP unit
3. Fibrinogen – averages ~ 250 mg/cryo unit
4. Factor XIII - 20-30% of F XIII/one FFP

A. Indications - one of the following:

1. Hemophilia A (Factor VIII: C deficiency)

   If available, commercial Factor VIII concentrates are recommended. However, if not available, cryoprecipitate may be used for the following:

   a. Prophylaxis prior to surgery/dental extraction

      1) DDAVP (desmopressin) is preferred in mild form (6-30% VIII:C levels)

   b. Traumatic hemorrhage

      1) If mild and when following minor trauma

         a) DDAVP initially

   c. CNS hemorrhage

2. von Willebrand's disease (Factor VIII:vWF deficiency)

   a. Congenital

1) Prophylaxis prior to surgery/dental extraction
    a) DDAVP is recommended in Type I
2) Spontaneous hemorrhage
    a) DDAVP recommended initially only for Type I but contraindicated for Type IIb

b. Acquired
1) Collagen Vascular Disease
    a) SLE
    b) Scleroderma
2) Lymphoproliferative disorders
    a) non-Hodgkin's lymphoma/CLL
3) Other neoplasms

3. Dysfunctional platelets - DDAVP recommended initially
    a. Congenital
        1) platelet storage pool disease
    b. Acquired
        1) Uremia
4. Plasma Fibrinogen level below 100 mg/dL or dysfunctional fibrinogen
    a. Dosage calculation
        1) Adults: Normal dose for a 70 kg adult is 10 units which is expected to raise the fibrinogen level by 50-100 mg/dL.
        2) Pediatrics: One unit/5 kg body weight
5. Factor XIII deficiency
6. Fibrin glue as “tissue sealant”
7. For removal of kidney stones located in the renal pelvis and calyces
8. For topical tissue adhesive

B. Contraindications:
1. Coagulation deficiencies secondary to factors not present in cryoprecipitate
2. Quantitative platelet defects

LEUKOREDUCED RED CELLS AND PLATELETS

All red cell and platelet products, with the exception of autologous products, must be leukoreduced. The preferred method is prestorage leukoreduction, providing leukoreduction under controlled conditions. Prestorage filtration of red cells reduces the leukocyte count to less than 5×10^6 white cells per unit, retains 85% of the original red cells, and reduces certain cytokines

released from leukocytes during storage. If the product is prestorage leukoreduced, a leukocyte reduction filter is not required for transfusion and will not be issued by the Transfusion Service.

A. Benefits of leukoreduction of cellular products

1. Prevention/reduction of febrile transfusion reactions for patients with a history of nonhemolytic febrile transfusion reactions, especially when two or more reactions have been reported.
2. Prevention/reduction of HLA alloimmunization. This may be important to prevent/lessen future platelet refractoriness in chemotherapy patients and to improve graft survival in certain kinds of transplants.
3. Prevention/reduction of transfusion transmitted CMV infection and other leukotropic viruses (EBV, HTLV).
4. Prevention/reduction of immune modulation. Immune modulation may cause increased susceptibility to viral or bacterial infection and diminished immune surveillance against tumors.

OTHER SPECIAL NEEDS (IRRADIATION, CMV NEGATIVE OR SAFE, AND/OR HEMOGLOBIN S NEGATIVE)

OTHER SPECIAL NEEDS CHART	For Cellular Products (Red Cells, Platelets and Granulocytes)			For Red Cells Only
Indication	**Irradiation**	**CMV Neg***	**CMV Safe**	**Hb S Neg**
Transplants				
Bone marrow transplant or stem cell (peripheral blood progenitor cell) transplant	Yes	Yes		
AUTOLOGOUS bone marrow transplant	Yes			
Lung and/or liver transplant patients (both before and after transplantation)	Yes	Yes		
Heart, kidney, pancreas, and/or other solid organ not named transplant patients		Yes		
Neonates				
All Neonates and fetuses	Yes**	Yes**		
Neonates requiring exchange transfusion	Yes	Yes		Yes

OTHER SPECIAL NEEDS CHART	For Cellular Products (Red Cells, Platelets and Granulocytes)			For Red Cells Only
Indication	**Irradiation**	**CMV Neg***	**CMV Safe**	**Hb S Neg**
Other				
Patients known to have a diagnosis or past history of Hodgkin's disease	Yes			
Patients treated with fludarabine (current or past)	Yes			
Patients with primary immune deficiency syndromes, particularly SCIDS	Yes			
Patients being maintained for organ retrieval			Yes	
Pregnant women prior to delivery or termination of pregnancy			Yes	
Sickle Cell Patients				Yes
Patients receiving white cell products	Yes			
Recipients of directed units from blood relatives	Yes			
Recipients of HLA-selected platelets or platelets known to be HLA homozygous	Yes			

*If CMV Negative products cannot be obtained in the required time frame, CMV Safe products may be used with physician permission.

**For emergent transfusion of babies not known to be at high risk of GVHD, medical approval has been obtained to suspend Irradiation and CMV Negative requirements. Babies at high risk of GVHD include those who have had intrauterine transfusion and/or have a birth weight of less than 1200 grams.

Irradiation of Red Cells, Platelets, and Granulocytes: Irradiation is indicated for patients at risk of Transfusion Associated Graft vs Host Disease (TA-GVHD). Irradiated blood products receive a minimum of 25 GY of gamma radiation. This effectively renders the lymphocytes incapable of proliferating. The effect on red cells results in a slight increase in plasma hemoglobin and potassium and the product outdate is reduced from 42 to 28 days. The effect on other cells is variable and probably not significant.

In addition to the absolute indications listed in the chart, irradiation may also be indicated for patients with Secondary Immunodeficiencies, including lymphoreticular disease, malignancy, other solid organ transplants, heavy chemo- or radiotherapy.

CMV Negative or Safe Red Cells, Platelets and Granulocytes: When CMV transmission by transfusion is a concern, some specialties will only accept CMV negative products while others will accept "CMV Safe".

CMV Safe is defined as either CMV negative or prepared by a method known to reduce the leukocyte number in the final component to less than 5×10^6. Prestorage leukoreduction is known to reduce the leukocyte number in the final component to less than 5×10^6 and is therefore

CMV Safe. Bedside leukoreduction does not always reduce the leukocyte count sufficiently and therefore is only to be used if prestorage leukoreduced products or CMV seronegative products cannot be obtained and the ordering physician agrees.

REFERENCES

1. Becker, Joanne & Beth Shaz. *Guidelines for Patient Blood Management and Blood Utilization.* Bethesda, MD: AABB Press, 2011.
2. Carson, Jeffrey L., MD, Brenda J. Grossman, MD, MPH, Steven Kleinman, MD, et al for the AABB clinical Transfusion Medicine Committee. "Red Blood Cell Transfusion: A Clinical Practice Guideline from the AABB." *Annals of Internal Medicine* 157 (2012): 49-58.
3. Duguid, J, D.F. O'Shaughnessey, C. Atterbury, et al. "Guidelines for the Use of Fresh-Frozen Plasma, Cryoprecipitate and Cryosupernatant." *British Journal for Haematology,* 126.1 (2004): 11-28.
4. Kuehn, Bridget M. "Guideline Tightens Transfusion Criteria." *Journal of the American Medical Association* 307.17 (2012): 1788-789.
5. Weinstein, Sharon M. *Plumer's Principles & Practice of Intravenous Therapy.* Philadelphia, PA.: Lippincott Williams & Wilkins, 2007.
6. AABB, the American Red Cross, America's Blood Centers, and the Armed Services Blood Program. *Circular of information for the use of human blood and blood components.* Bethesda, MD: AABB, current edition.
7. Blood Transfusion Therapy: A Physician's Handbook, AABB, current edition.
8. Standards for Blood Banks and Transfusion Services, AABB, current edition.
9. Technical Manual, AABB, current edition.
10. "UW Medical Center Anticoagulation Services." *UW Medicine Pharmacy Services: UW Medical Center Anticoagulation Clinic*. N.p., n.d. Web. 9 Jan. 2013. <http://www.uwmcacc.org/index.html>.

APPENDICES

A. Blood Component Transfusions in Nonemergency Settings
B. AnticoagulantMedications
C. Antiplatelet Medications
D. Glossary of Abbreviations

APPENDIX A **Blood Component Transfusions in Nonemergency Settings**

Component	Suggested Adult Flow Rate First 15 minutes	Suggested Adult Flow Rate After 15 minutes	Pediatric Dosage/ Rates	Special Considerations	ABO Compatibility	Filter
Red Blood Cells (RBCs)	1-2 mL/ min (60-120 mL/hr)	As rapidly as tolerated; approx 4 mL /min or 240 mL/hr	10 mL/kg, not to exceed 15 mL/kg at 2-5 mL/kg/hr	Infusion should not exceed 4 hours For patients at risk of fluid overload, adjust flow rate to 1 mL/kg/hr	Whole blood: ABO identical RBCs: ABO compatible with recipient's plasma Crossmatch required	In-line (170-260 micron) Leukocyte reduction if indicated
Platelets	2-5 mL/ min(120 - 300 mL/ hr) during the first 5 min	300 mL/hr or as tolerated (after the first 5 min)	50-70 mL/ 7-10 kg of body weight Run over 30 minutes to a max of 4 hr	Generally given over 1 hr	Crossmatch not required ABO/Rh compatibility preferable but not required May be HLA matched	In-line (170-260 micron) Leukocyte reduction if indicated
Plasma	2-5 mL/min (120-300 mL/hr) during the first 5 min	As rapidly as tolerated (after the first 5 min); approx 300 mL/hr	Clotting deficiency: 10-15 mL/ kg at 1-2 mL/min	Thaw time may be needed before issue	Crossmatch not required ABO compatiblity with recipient red cells	In-line (170-260 micron)
Granulocytes	1-2 mL/min (60-120 mL/hr)	120-150 mL/hr or as tolerated		Over approx 2 hrs Infuse ASAP after collection/ release of product Irradiate	Crossmatch required ABO compatibility required May be HLA matched	In-line (170-260 micron) No LR filter or depth-type microaggregate filters
Cryoprecipitated AHF	As rapidly as tolerated		1 unit/5 kg, not faster than 1 mL/kg/min	Infuse ASAP after thawing; pooling is preferred	Crossmatch and ABO compatibility not required	In-line (170-260 micron)

APPENDIX B	**Overview of Anticoagulant Medications**				
Anticoagulant Medication	**Mechanism**	**Usual Elimination Half Life**	**Routine Monitoring**	**Effect on Other Lab Tests**	**Reversal**
Coumadin® (warfarin)	Inhibits vit K dependent coag factors II, VII, IX & X and anticoagulant proteins C & S	One Week	INR/PT	PT/INR ↑, aPTT SL ↑ or no change, Mixing Studies show correction with PNP	Vitamin K, FFP, Factor VII, PCC
Heparin	Binds to antithrombin to activate it which then inactivates thrombin (Factor II) & Xa. Inhibits coag cascade at multiple sites (basically all factors except III)	30-90 Minutes (dose dependent)	Heparin Level, Anti Xa (unfractionated or UFH), PTT	PT/INR no change or SL ↑, aPTT ↑, Mixing Studies: looks like inhibitor	Protamine
Low Molecular Weight Heparin, Lovenox® (enoxaparin), Innohep® (tinzaparin), Fragmin® (dalteparin)	Inhibits Factor X and Factor II	Enoxaparin 3-5 hours	Heparin Level, Anti-Xa LMWH, (Lovenox)	PT/INR no change, aPTT no change or SL ↑, Mixing Studies: Looks like inhibitor Xa activity	Protamine partially reverses the anticoagulant effect (60%); FFP*, PCC*
Pradaxa® (dabigatran)	Inhibits IIA, Direct thrombin inhibitor, prevents activation of Factors V, VIII, XI & XIII	12-17 hours, with renal impairment 15-34 hours	No FDA approved test available	thrombin time ↑ (indicates residual drug effect), PT/INR ↑, aPTT ↑, Mixing Studies: Looks like inhibitor	No reversal agent or antidote; Factor VIIa*, PCC*, FFP* may be helpful
Argatroban®	Direct thrombin inhibitor	39-51 minutes	PTT	aPTT ↑ PT/INR ↑, Mixing Studies: Looks like inhibitor	No reversal agent or antidote

*This modality may have been used by others, but experience is limited and without consensus.

The information in this Appendix is intended for educational purposes only, and should not be used to direct specific patient therapy. Current literature and prescribing information should be consulted for the purpose of clinical decision-making.

APPENDIX B (continued)		**Overview of Anticoagulant Medications**			
Anticoagulant Medication	**Mechanism**	**Usual Elimination Half Life**	**Routine Monitoring**	**Effect on Other Lab Tests**	**Reversal**
Refludan® (lepirudin)	Direct thrombin inhibitor	1.3 hours	PTT	aPTT ↑, PT/INR ↑, Mixing Studies: Looks like inhibitor	No reversal agent or antidote
Angiomax® (bivalirudin)	Direct thrombin inhibitor	25 minutes	ACT	PT/INR ↑, aPTT ↑, Mixing Studies: Looks like inhibitor	No reversal agent or antidote
Arixtra® (fondaparinux)	Factor Xa inhibitor	17-21 hours	Anti-factor Xa, if needed (referred test)	PT/INR minimal change, aPTT minimal change, mixing studies: Looks like inhibitor	No reversal agent or antidote; PCC* or FFP* may be helpful
Xarelto® (rivaroxaban)	Direct Factor Xa inhibitor without need of a co-factor for activity	5-9 hours in healthy individuals; 11-19 hours in elderly	No FDA approved test available	PT/INR minimal change, aPTT minimal change, Mixing studies: Looks like inhibitor	No reversal agent or antidote; PCC* or FFP* may be helpful
Eliquis® (apixaban)	Direct Factor Xa inhibitor without need of a co-factor for activity	Oral - 12 hours due to prolonged absorption. IV - 6 hours	No FDA approved test available	Prolongs PT, INR, aPTT, but changes are small and variable, and not helpful to monitor anticoagulant effect. Mixing studies: Looks like inhibitor	No reversal agent or antidote; PCC* or FFP* may be helpful

*This modality may have been used by others, but experience is limited and without consensus.

The information in this Appendix is intended for educational purposes only, and should not be used to direct specific patient therapy. Current literature and prescribing information should be consulted for the purpose of clinical decision-making.

Appendix C	**Overview of Antiplatelet Medications**				
Antiplatelet Medications	**Mechanism**	**Usual Elimination Half Life**	**Routine Monitoring**	**Effect on Other Lab Tests**	**Reversal**
Aspirin	Inhibits cyclooxygenase	5-10 days	Platelet Function Assay (PFA)		No specific reversal agent or antidote; platelet transfusion
Aggrenox® (aspirin and dipyridamole)	Prevents CMAP degradation, irreversible platelet inhibitor	14 hours		Variable effect on PFA	No specific reversal agent or antidote; platelet transfusion
Effient® (prasugrel)	Inhibits platelet aggregation	7 hours	Verify Now/ P2Y12	Variable effect on PFA	No specific reversal agent or antidote; platelet transfusion
Plavix® (clopidogrel)	Inhibits platelet aggregation	6-8 hours	Verify Now/ P2Y12	Variable effect on PFA	No specific reversal agent or antidote; platelet transfusion
Ticlid® (ticlopidine)	Inhibits platelet aggregation	7-13 hours single dose, 4-5 days if repeat dosing		Variable effect on PFA	No specific reversal agent or antidote; platelet transfusion
Brilinta® (ticagrelor)	Inhibits platelet aggregation	7 hours		Variable effect on PFA	No specific reversal agent or antidote; platelet transfusion
Pletal® (cilostazol)	Inhibits platelet aggregation	11-13 hours		Variable effect on PFA; may see some degree of platelet inhibition in Verify Now /P2Y12	No specific reversal agent or antidote; platelet transfusion
Persantine® (dipyridamole)	Inhibits thrombus formation	10-12 hours		Variable effect on PFA	Aminophylline, Desmopressin

The information in this Appendix is intended for educational purposes only, and should not be used to direct specific patient therapy. Current literature and prescribing information should be consulted for the purpose of clinical decision-making.

Appendix D

Glossary of Abbreviations	
AABB	formerly American Association of Blood Banks
ACT	Activated clotting time
ASAP	As soon as possible
CLL	Chronic lymphocytic leukemia
CMV	Cytomegalovirus
CNS	Central nervous system
CPB	Cardiopulmonary bypass
DDAVP	Desmopressin
DIC	Disseminated intravascular coagulation
EBV	Epstein Barr virus
FFP	Fresh frozen plasma
GI	Gastrointestinal
GVHD	Graft versus host disease
HLA	Human leukocyte antigen
HTLV	human T-cell lymphotropic virus
INR	International Normalized Ratio
ITP	Idiopathic thrombocytopenic purpura
LMWH	Low molecular weight heparin
PCC	Prothrombin complex concentrate
PT	Prothrombin Time
PTT	Partial thromboplastin time
RBC	Red blood cell
SCIDS	Severe combined immunodeficiency syndrome
SLE	Systemic lupus erythematosus
TA-GVHD	Transfusion associated - graft versus host disease
TIA	Transient Ischemic Attack
TTP	Thrombotic thrombocytopenic purpura