PLASMA: Most Trauma Center Blood Banks keep Thawed Plasma ready, so that in emergency situations, with Physician signature, **uncrossmatched group AB Rh positive Plasma** can be released immediately. In urgent situations, **ABO/Rh group specific uncrossmatched** Plasma can be released in about 30 minutes.

Plasma products include Fresh Frozen Plasma, Plasma Frozen within 24 Hours, and Thawed Plasma. Blood Banks will usually attempt to give precedence to filling orders with Fresh Frozen Plasma, but will substitute among the other Plasma products listed above, depending on Blood Bank inventory and anticipated hospital needs.

In most hospitals, Plasma orders for adults will be filled with at least 50% Fresh Frozen Plasma; but orders for children (under 15) will receive entirely Fresh Frozen Plasma, without substitution. Blood Banks consider the above listed Plasma products to be therapeutically equivalent for treatment of multifactor coagulopathies, including warfarin (coumadin) effect.

A Blood Bank Pathologist must be on-call at all times, and can be reached through the Blood Bank.

PLASMA **definitions**: Fresh Frozen Plasma (FFP) consists of citrated plasma frozen within 8 hours of collection, and Plasma Frozen within 24 Hours is frozen within 24 hours. By definition, FFP must contain one unit of all coagulation factor activities per mL. FFP and Plasma Frozen within 24 Hours are therapeutically equivalent except for negligible losses of Factor V, VII, and VIII activities in the latter. After thawing, Plasma stored at 1 to at 6^{o} C for more than 24 hours is re-labeled Thawed Plasma, and may be stored as such for up to 5 days. Thawed Plasma has additional loss of Factor VIII activity, but may be safely used for treatment of multifactor coagulopathies, including warfarin (coumadin) effect.

One Unit of Plasma has a fluid volume of 200 to 350 mL, and can take up to 30 minutes to be thawed out prior to being available for issue from the Blood Bank. Plasma must be ABO-compatible with the recipient's RBC's. The rare patient who is IgA deficient should be given plasma from IgA deficient donors. Plasma is considered to be an acellular blood product, so requests for Special Attributes do not apply. Please note that NO unused Plasma products can be returned to inventory if they have been out of the Blood Bank for more than thirty (30) minutes.

PLASMA **dosages and indications**: The usual dosage of Plasma for adults is 10 to 20 mL/Kg, and is often given 2 Units (400 to 700 mL) at a time, usually over 2 hours via a standard 180 to 260 micron filter. The usual dosage for neonates and children is 10 to 15 mL/Kg. For maximal effect, Plasma given to

treat coagulopathy prior to a surgical or invasive procedure should be administered immediately prior to the surgery because the therapeutic effect of Plasma is most limited by the half-life of Factor VII, which is approximately 4 hours. The volume delivered must include consideration of the cardiopulmonary and renal status of the patient. Plasma infusion must be completed in less than 4 hours. Drugs or medicines must NOT be infused via the same intravenous line during the transfusion. Many hospitals have Massive Transfusion Protocols for severely injured patients (massive transfusion due to blood loss greater than 10 units of RBC's/24 hours), and these protocols often recommend greater reliance on plasma than on crystalloid during resuscitation, with ratios of RBCs to Plasma of 1:2, or even 1:1 during emergency resuscitation (Transfusion, 2011; 51: 1925-1932).

The most common indication for Plasma is for correction of multifactor coagulopathies with active bleeding or prior to an invasive procedure. The INR will be abnormally prolonged, and is often due to liver disease, Warfarin (Coumadin) effect, or Vitamin K deficiency. If available, it is preferable to treat bleeding due to Warfarin effect with a combination of Prothrombin Complex Concentrate and Plasma; however, one must be careful because there are two products named Prothrombin Complex Concentrate: "four factor" and "three factor" PCC. Only four factor PCC contains sufficient Factor VII as well as Factors II, IX, and X. Because it is a concentrate, the usual dosage of PCC to achieve 50 to 100% levels of prothrombin complex factors is 1 to 2 mL/Kg.

Plasma is also indicated for treatment of bleeding due to dilutional coagulopathy or for disseminated intravascular coagulation (DIC) due to consumptive coagulopathy. If there is active bleeding, INR greater than 1.5 is a threshhold for transfusion. Prior to an invasive procedure, such as placement of a central line or fine needle liver biopsy, the generally accepted transfusion threshholds are INR greater than 2.0 and platelet count less than 30,000 ("Use of Blood Components prior to Invasive Bedside Procedures" in Mintz, PD (ed.) Transfusion Therapy: Clinical Principles and Practice, 3rd edition, AABB Press, 2011).

Rare patients with isolated coagulation factor deficiency for which no specific replacement is available (e.g. factors V and XI) may require Plasma during clinical urgency. In all types of coagulation factor deficiency, when the specific factor is not available, Plasma is an acceptable alternative until the factor concentrate can be obtained. Rare patients with plasma protein deficiency for which specific concentrate is not available [i.e. deficiency of protein C or protein S, or C-1 esterase inhibitor (angioneurotic edema)] may require Plasma during clinical urgency. Because warfarin-induced (coumadin-induced) skin necrosis is due to Protein C or S deficiency, Plasma may be given to stop progression.

Plasma by transfusion or plasma exchange is the treatment of choice for thrombotic thrombocytopenic purpura (TTP) because it contains the enzyme ADAMTS13. Cryoprecipitate-reduced plasma is reserved for treatment of refractory TTP due to its reduced concentration of vWF. Plasma is also indicated as a secondary line of treatment of hemolytic uremic syndrome (HUS) when it is refractory to IVIG. Heparin resistance is caused by the rare condition of

antithrombin III deficiency, and is managed by Plasma transfusion when urgent heparinizaiton is necessary. (Recombinant antithrombin III is clinically available, but is in limited supply.)

PLASMA **product contraindications and hazards**: Plasma must NOT be given for reversal of Heparin because Antithrombin III can potentiate Heparin anticoagulation. Mild to moderate elevations of INR without ongoing bleeding should be corrected with Vitamin K injection. Isolated coagulation factor deficiencies should be corrected by administration of the specific factor concentrate. It remains uncertain whether dialysis, Plasma, or plasma exchange can significantly reverse direct thrombin inhibitors (i.e. argatroban, dabigatran, lepirudin, bivalirudin) or direct Factor Xa inhibitors (i.e. xabans) in patients with life threatening hemorrhage; and in such cases, reversal is usually first attempted with activated Factor VII (rVIIa) prior to consideration of Plasma.

Intravascular volume expansion should be done with solutions of crystalloids, albumin, and/or plasma protein fraction, e.g. Plasminate. Plasma products are not concentrates, so administration must include consideration of the patient's cardiopulmonary and renal status, in order to avoid transfusion-associated circulatory overload (TACO).

Transfusion-related acute lung injury (TRALI) is the most common serious complication of Plasma infusion, and is due to donor anti-neutrophil or anti-HLA antibodies causing pulmonary microvascular injury. TRALI presents as acute respiratory insufficiency, with bilateral diffuse infiltrates on chest X-ray, during or shortly after transfusion. Aggressive respiratory support is indicated, similar to treatment of acute respiratory distress syndrome (ARDS). TRALI will usually resolve within 48 to 96 hours (see **Transfusion Reactions**).

Hypersensitivty reactions may accompany or follow Plasma infusion, but serious allergic reactions, such as anaphylaxis, are rare. Anaphylaxis may occur with the rare IgA deficient patient who has anti-IgA alloantibodies, but can also be caused by preformed antibodies to other proteins deficient in the recipient.

Donor selection and product testing have made Plasma products extremely safe, but the very rare risk of transmission of infectious agents of disease must always be considered when ordering Plasma products for transfusion.