Component Therapy and Transfusion Reactions in the ICU

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Transfusion medicine has certainly come a long way, and is continually changing with our growing advancements in veterinary medicine. A crucial understanding of transfusion indications, component therapy, contraindications, blood typing, monitoring and transfusion reactions, can determine the outcome of a successful transfusion. Product handling and administration protocols also play an important role in patient outcome. A thorough comprehension of why, how, and what we should transfuse is pivotal to each ICU case.

Component Therapy

Knowing what disorder we are treating, and the blood product required to treat is the basis of component therapy. Administering only what the patient needs prevents unnecessary transfusion reactions, circulatory overload, and additional blood product waste. Products, dosages, indications, and administration protocols are listed below. It is recommended all blood products be administered through a dedicated, separate IV catheter without additional fluids or medications to prevent complications.

Fresh Whole Blood: Blood collected within 6-8 hours. Contains red cells, white blood cells, plasma proteins, a small amount of platelets, and coagulation factors. Dosage is 10-20ml/kg, but is patient dependant. The “Rule of 1’s” though not proven, may apply. It states that 1ml of transfused blood/1lb of body weight will raise the patients PCV by 1%. Indications include: trauma with massive hemorrhage, hypovolemia, hemoabdomen, rodenticide poisoning, sepsis, hypoxemia due to anemia and coagulopathy or thrombopathia. Administration requires a filter drip set (free drip), or a micro aggregate (ex. Hemonate) filter and syringe pump.

Stored Whole Blood: Blood that has been collected and stored for longer than 8 hours. Contains red blood cells, plasma proteins, and some coagulation factors. Dosage is 10-20ml/kg, but is patient dependant and the “Rule of 1’s” may apply. Indications include: trauma with massive hemorrhage, hypovolemia, hemoabdomen, and hypoxemia due to anemia. Administration is the same as fresh whole blood.

Packed Red Blood Cells: Blood collected and separated (removing plasma from whole blood). Contains red blood cells, a small amount of platelets, white blood cells, and a minimal amount of plasma. Dosage is patient dependant, approximately 6-10 ml/kg over 2-4 hours. Indications include: trauma with hemorrhage (including surgical), hemoabdomen, sepsis, hypoxemia due to anemia, Immune Mediated Hemolytic Anemia (IMHA), and Immune Mediated Thrombocytopenia (ITP). Keep in mind the “10/30” rule is not proven in indicating transfusion. This rule states that a hemoglobin of 10gm/dl, and a PCV of 30% are markers for transfusion requirement. However, many patients do not show clinical signs of transfusion requirement until their PCV is below 20%. Transfusion indications should not be based on patient numbers, and are always patient dependant! Administration requires a filter drip set (free drip), or a micro aggregate (ex. Hemonate) filter and syringe pump.

Fresh Frozen Plasma: Blood that has been separated within 6 hours of collection (removing blood cells from plasma). Contains plasma, albumin, globulins, coagulation factors (V, VIII, IX, vWF), and
electrolytes. Dosage is patient dependant, approximately 6-10 mls/kg over 2-4 hours. Indications include: coagulation disorders (congenital vs. acquired), Hemophilia A & B, von Willebrands disease, Disseminated Intravascular Coagulation (DIC), sepsis, envenomation, liver disease, and pancreatitis. Administration requires a filter drip set (free drip), or a micro aggregate (ex. Hemonate) filter and syringe pump. Filter drip sets are available that are compatible with IV pumps, allowing more precise administration.

Frozen Plasma: Blood that has been separated after 6 hours of collection (removing blood cells from plasma), FFP that was thawed and re-frozen, or Fresh Frozen Plasma that is greater than 1 year old. Contains a decreased amount of coagulation factors with varying stability, plasma, and albumin. Dosage is patient dependant, approximately 6-10 mls/kg. Indications include: some clotting factor deficiencies, and colloid necessity. Administration requires a filter drip set (free drip), or a micro aggregate (ex. Hemonate) filter and syringe pump. Filter drip sets are available that are compatible with IV pumps, allowing more precise administration.

Cryoprecipitate: Portion of plasma that precipitates after fresh frozen plasma has been slowly thawed. Contains heavily concentrated von Willebrand’s factor and factor VIII, fibrinogen/fibronectin. Dosage is patient dependant, approximately 1 unit/10kg over 2 hours. Indications include: complications due to von Willebrands disease, or hemophilia A. Administration requirements include a micro aggregate filter (ex. Hemonate) and syringe pump.

Frozen Platelet Concentrate: A concentrated platelet product, made from the cryopreserving and freezing of fresh platelet concentrate. Contains platelets, has been leukoreduced, and preserved in DMSO (dimethyl sulfoxide). A dose of approximately 1 unit/10kg over 1-2 hours may increase the platelet count 20,000/µL 1-2 hours post transfusion. Though efficacy data on this product has not been published, potential indications include: Thrombocytopenia/pathia, DIC, sepsis, and ITP. Administration requirements include a filter drip set, allowing the product to free drip. Gentle handling of the product is a must! Because this product contains DMSO, it must be transfused slowly to avoid bradycardia.

Human Albumin: Derived from human blood, it contains human serum albumin (HSA). Dosage is dependent on patient, not to exceed 1ml/min over 4 hours and not to exceed 2g/kg/day. Indications include hypoalbuminemia, sepsis, Systemic Inflammatory Response Syndrome (SIRS), and burn patients. Administration requirements include dilution of HSA into normal saline to maintain a 10% solution. Some protocols call for no dilution. Use of a regular fluid administration set is required. It is recommended to wear gloves when handling, as this is derived from human blood. Severe transfusion reactions with this product have been published and caution should be taken when transfusing this product.

Lyophilized Canine Albumin: Derived from canine blood using a heat shock process, it contains pure canine albumin. Dosage is patient dependant, however a formula courtesy of Animal Blood Resources Intl. has been provided (BodyWeight (kg) x 90 ml/kg x (2gm/dl - Patient albumin) x 0.2 dL/gm). No maximum dose has been identified. Indications include: hypoalbuminemia, sepsis, SIRS and burn patients. Administration requires a filter drip set (free drip), or a micro aggregate (ex. Hemonate) filter and syringe pump. This product is currently not available due to the high incidence of transfusion reaction.

Typing and Crossmatching

Typing should be done on every patient prior to transfusion, especially in felines. This greatly reduces the risk of transfusion reaction. Most canines can typically tolerate their first transfusion of Universal type blood, as they have not yet built up antibodies. Felines however, have naturally occurring antibodies which require typing prior to transfusion. In house typing of the recipient allows the option of
type specific transfusion, i.e. D.E.A. (Dog Erythrocyte Antigen) 1.1 positive or negative and type A, B, or AB in cats. In house recipient blood typing takes only a few minutes. Alvedia typing cartridge, RapidVet typing cards, and RapidVet-H IC are available for canine and feline typing while in hospital. Though blood typing can be difficult with agglutinating patients, causing false type results, the Alvedia typing cartridge allows typing in spite of agglutination for accurate type specific transfusion. It is possible to transfuse a canine with a D.E.A. of 1.1 positive with a D.E.A. 1.1 negative unit. However, it is contraindicated to transfuse a D.E.A. 1.1 negative dog with a D.E.A. 1.1 positive unit. This could lead to severe transfusion reaction. With cats, blood transfusions must be type specific i.e. a type A cat, must receive type A blood and a type B cat must receive type B blood. It is acceptable practice, though not ideal, to transfuse a type AB cat with type A blood when AB blood is not available. It is important to also note that in regards to ferrets, they appear to have no identifiable blood type, and thus do not require typing or crossmatching.

Crossmatching should be performed in every patient who has had previous transfusions, or if it has been longer than 4 days since the animals first transfusion, as the animal has had time to build up antibodies which could lead to transfusion reaction. It has been recommended to crossmatch cats with every transfusion, as cats with potential lymphoproliferative disorders (ex. Felv/FIV) are difficult to type and may yield a false blood type when tested in house. Major crossmatching is the most common method performed, and uses recipient serum or plasma against donor red blood cells. Minor crossmatching is less commonly performed and uses recipient red blood cells and donor plasma. Crossmatching takes approximately 40 minutes, and can be performed in house using a testing kit (ex. RapidVet) for both canine and feline. Results will yield a positive or negative crossmatch via evidence of agglutination/hemolysis. A negative crossmatch likely means a safe transfusion between donor and recipient.

**Transfusion monitoring**

Any patient receiving a transfusion requires close monitoring. Monitoring parameters include temperature, heart rate and pulse quality, respiration rate and quality, mucous membrane (MM) color and capillary refill time (CRT), blood pressure, drip rate, IV catheter patency, and patient attitude. Typically, a dedicated technician and detailed monitoring sheet are recommended. Monitoring forms can also be used at a later date to determine patient compatibility with donor, transfusion rate, and blood product used. It is not recommended to feed a patient during a transfusion, as vomiting can occur with transfusion reactions. Though not proven, it may be beneficial to administer diphenhydramine to a patient prior to transfusion if they have had a history of immunologic allergic-type reactions with previous transfusions. Diphenhydramine is not indicated in febrile non-hemolytic transfusion reactions.

A typical transfusion monitoring protocol includes a baseline set of vitals including blood work, while taking into account any abnormalities such as hypothermia/hyperthermia, tachycardia, tachypnea, and mm color. These abnormalities should be expected in critical patients requiring transfusion, and may resume to normal parameters during and after transfusion. Once a baseline set of vitals is achieved and transfusion is initiated, a full set of vitals (as indicated above) should be taken routinely, and protocols differ from hospital to hospital. Initial protocol should be baseline vitals, a set of vitals every 15 minutes for a half hour, then every 30 minutes for 1 hour, then hourly during the remainder of the transfusion. It is important to keep in mind that patients can have delayed transfusion reactions. Some reactions can be delayed days.

**Transfusion Reactions**

There are different types of transfusion reactions. A complete understanding of the types of transfusion reactions and their cause can aid in the reduction of reaction progression and patient risk.
There are four types of transfusion reactions: acute immunologic (non-hemolytic and hemolytic), acute non-immunologic, delayed immunologic, and delayed non-immunologic.

A. Acute Immunologic Reactions: This type of transfusion reaction is due to the antibodies in the recipients' blood reacting to foreign antigens in the transfused blood. These reactions can be acute or delayed by days.

Febrile non-hemolytic transfusion reactions are the most common. This reaction typically occurs because of antibodies reacting to donor IgA or donor white blood cells, platelets, and plasma proteins. Symptoms of this reaction often entail vomiting, facial swelling, pruritis, and fever. Treatment for this reaction may include slowing down the transfusion rate, and supportive care. If the temperature continues to climb, transfusion should be stopped.

Acute immunologic type 1 hypersensitivity/anaphylaxis reactions are rare. This type of transfusion reaction typically occurs due to mast cell release. Pruritis, urticarial (hives), edema, elevated temperature, and anaphylaxis with shock type symptoms can occur. Treatment plan includes immediate cessation of transfusion, anti-histamines, IV fluids, and shock treatment plan if indicated (i.e. oxygen, vaspressors, epinephrine, glucocorticoids, etc…).

Acute hemolytic transfusion reactions are extremely rare and very serious. Antibody sensitivity to antigens being transfused can cause this reaction. Hemolysis occurs because the immune system recognizes the antigens being transfused, as foreign. Symptoms noted during this reaction include hemoglobinuria, hemoglobinemia, tremors/seizures, vomiting, weakness, pyrexia, tachypnea, and tachycardia/bradycardia, and death. This reaction is most severe in cases of a type B cat receiving type A blood, because of their naturally occurring antibodies. This reaction can also be seen in cases where a D.E.A. 1.1 negative dog is transfused with D.E.A. 1.1 positive blood. Treatment involves discontinuing the transfusion, supportive care with IV fluids, shock treatment plan if indicated, urine output monitoring, hemoglobin and bilirubin monitoring. (Delayed hemolysis can also occur. Patients should be closely monitored after transfusion.)

B. Acute Non-immunologic Reactions: This reaction type can occur for a variety of reasons aside from blood type mismatch. Tainted blood products, patient illness, and technician error can all induce a non-immunologic transfusion reaction. Some examples include thromboembolic complications, bacterial contamination, circulatory overload, citrate toxicity, and elevations in the patients’ ammonia levels.

Transfusion associated circulatory overload: (TACO) This non-immunologic transfusion reaction can occur in patients with compromised cardiovascular systems. This can also occur in patients who are transfused too rapidly, due to technician error, causing circulatory overload as well. The colloid components of some blood products and the risk for rapid infusion of large volumes of blood products can lead to vascular overload with cardiogenic pulmonary edema. Signs of reaction include dyspnea, coughing, hypertension, tachycardia, vomiting, elevations in central venous pressures and systemic blood pressures, and cyanosis. Treatment for transfusion related circulatory overload is supportive care, discontinuation of transfusion, oxygen therapy, and diuretics if indicated. The use of component therapy vs. whole blood transfusion can reduce the risk of TACO.

Transmission of infectious disease or bacterial contamination: Inappropriate donor screening for infectious disease can lead to transmission of disease to the recipient, and delayed symptoms. Poor handling of blood products during donation and transfusion can also lead to bacterial contamination, thus compromising the recipient. It is important to have strict aseptic technique during donation, blood product
separation and transfusion. Signs of reaction can include GI signs, fever, dyspnea, hypoglycemia, hypotension, and tachycardia. Typically signs occur relatively early during the transfusion. Treatment involves immediate cessation of the transfusion, with blood cultures of the recipient and the blood product. Antibiotics and supportive care should be initiated.

Hyperammonemia: This reaction can occur in patients with liver dysfunction, when older blood products are transfused which contain large amounts of ammonia. Ammonia levels rise in the unit during blood product storage. It may be recommended to use a newer unit of blood to transfuse patients with compromised liver function. Neurologic signs are to be expected with elevated levels of ammonia. Such signs include depressed mentation, ataxia, head pressing, seizures, and circling. Immediately stop the transfusion if signs occur and treat supportively to decrease ammonia levels. Oral lactulose, lactulose enemas, monitoring of mentation, serum ammonia levels, and decreased dietary protein intake may be considered during treatment.

Citrate toxicity: This occurs when large volumes of citrated blood products are administered to patients with liver dysfunction, causing hypocalcemia. Citrate is used in stored blood products as an anticoagulant which chelates calcium. Tremors, seizures, facial twitching, decreased cardiac output, and arrhythmias will be seen with this form of reaction. Treatment includes discontinuing the transfusion, calcium supplementation, supportive care, and calcium monitoring.

Transfusion related acute lung injury: (TRALI) Though more prevalent in human medicine, this complication can be seen in veterinary transfusion medicine as well. Signs are respiratory in nature, including; dyspnea, pulmonary infiltrates, hypoxemia, and fever. Though the exact pathophysiology of TRALI is unknown, it is thought to involve recipient leukocyte antigens which react to donor leukocyte antibodies, as well as cytokine involvement allowing fluid to enter the alveoli creating lung injury. Signs can be delayed up to 6 hours after transfusion and are respiratory in nature. Treatment includes oxygen supplementation and ventilation. Leukoreduction may be beneficial in prevention.

Transfusion related immunomodulation: (TRIM) Thought to occur as a result of immunosuppression post transfusion. Can allow increased chance of organ survival post transplant, but also increase risk of infection. It is thought that leukoreduction may be beneficial in reduction of immunosuppression and thus infection.

C. Delayed Immunologic Transfusion Reaction: These reactions can occur 4-21 days post transfusion and can result from development of antibodies that shorten the transfused RBC lifespan.

D. Delayed Non-immunologic Transfusion Reaction: This results from the contamination of transfused blood. For example, retro-viruses such as Felv/FIV. These reactions can be prevented through complete donor screening.

New findings to consider in transfusion medicine include the emergence of leukoreduced blood products. It is thought that the use of leukoreduction filters can decrease risk, and possibly eliminate transfusion reaction by removing leukocytes which have inflammatory effects and can sensitize the immune system. Leukoreduction has proved to be beneficial in humans by reducing frequency and severity of febrile non-hemolytic transfusion reaction. The use of leukoreduction filters may also increase red cell survival. There are few studies in veterinary medicine to warrant mandatory animal blood banking protocol changes; however leukoreduction in veterinary medicine is emerging in a positive light.

The DAL antigen is newer and requires attention when transfusing Dalmations in particular. This antigen exists commonly in most dogs, but is not found in some Dalmations. Thus transfusing a dog that
does not have the antigen, with the DAL antigen can lead to severe transfusion reaction. It is strongly recommended to cross match any Dalmation before transfusion. More recently, this antigen is found to be lacking in Dobermans as well. Cross matching Dobermans prior to transfusion is also suggested.

MiK is an antigen that has been recently identified in cats. MiK is found to be present in most cats; however some have naturally occurring antibodies against this antigen. If a cat has naturally occurring antibodies to MiK, and is transfused with this antigen, Hemolytic Transfusion Reaction will occur. The importance of cross matching each cat prior to transfusion must be stressed.

Xenotransfusion is the transfusion of blood from one species to another. This has been studied in the past with k-9 to feline transfusions. However these studies are dated and patients had severe and often fatal transfusion reactions. This practice is not currently recommended, and requires further study.

Cryopreservation (freezing) of red blood cells is currently performed in human medicine, in cases of mass casualty, by some of our armed forces. Through a process of glycerolization and deglycerolization of red blood cells, the product can be considered to have a stable shelf life of 10 years. This process does require special equipment and tools. However, by removing the plasma and washing the white blood cells, there is a significant decrease in transfusion reactions. Some articles show evidence of virtually no transfusion reactions with this product. There are no current studies using this cryopreservation process in veterinary medicine.

The importance of knowing patient requirements, component therapy, potential complications and monitoring protocols is absolutely necessary when transfusion medicine is indicated. Safe transfusions allow better patient outcome and blood product preservation. While transfusion medicine is growing, and the emergence of safer products are made available, transfusion outcome still rests on the knowledge and nursing skill of the veterinary team.