The A, B, and Cs of Transfusion Medicine

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Introduction

Transfusion medicine, in veterinary medicine, has come a long way from the days of bleeding a donor dog and immediately infusing it into another without any regard for blood type or reactions. With the advent of commercial blood banks and clinical research, the veterinary team can support a critically ill patient with blood products/component therapy in a safe controlled manner. Understanding the need for transfusions, products available, the physiology of transfusions, and how to administer/monitor a transfusion is essential in any veterinary setting. Technicians are paramount to the successful completion of a transfusion, as we are often charged with monitoring the patients receiving the various products available. This presentation will serve as a foundation for the veterinary technician to be able to perform high-quality transfusion medicine.

The need for a transfusion

The need for a blood/blood product transfusion can arise in various situations. With acute hemorrhage, oxygen-carrying red blood cells are lost, as well as essential plasma proteins. Water, proteins contributing to oncotic pressure, and red blood cells which carry oxygen to organs are all not able to provide their normal physiologic functions. Replacing the vascular volume with crystalloid or colloid fluids enhances vascular volume and perfusion to an extent, but does not replace the oxygen-carrying capacity the red blood cells provide. Whole blood transfusions might be used here to replace what was lost. In the case of non-hemorrhagic anemia, a transfusion of packed red blood cells may be required. These patients do not need the plasma component, and having access to blood components might be advantageous to minimize the potential for a reaction. Patients with coagulopathies or other conditions may require a plasma transfusion to replace those and slow hemorrhage caused by the loss of clotting factors. There are also other rare conditions (such as von Willebrand's disease (vWD) that may receive a transfusion as a medical therapy. Finally, transfusions of albumin (human or canine), intravenous immunglobulin (IVIG), or antivenin should be considered "transfusions" and monitored according to the same guidelines as blood products.

Transfusion products

Blood products used in transfusion medicine are numerous. They include: fresh whole blood, stored whole blood, packed red blood cells, fresh frozen plasma, frozen plasma, cryoprecipitate, cryo-poor plasma, platelet-rich plasma, albumin products (human or canine). A product rarely used in veterinary medicine but somewhat in human medicine is packed platelets. Non-blood product transfusions include antivenin, and IVIG. All of the above products can cause some sort of an antigenic reaction in the patient they are administered to.

The whole blood products include fresh whole blood and stored whole blood. Fresh whole blood is harvested from a donor and contains red blood cells, white blood cells, platelets, and plasma. It contains labile (fragile) clotting factors (which only last for a short time in refrigerated products) and platelets (which are also fragile and do not last long). Stored whole blood is typically kept for upwards of 28 days (depending on the anticoagulant used). Stored whole blood contains red blood cells, white blood cells, and plasma proteins (excluding labile clotting factors). It should be noted that cells in stored whole blood (notably RBC's) are not "normal" and do not have the same oxygen-carrying abilities as normal red blood cells. There can also be an accumulation of chemicals in stored whole blood from cell breakdown. The whole blood products are colloid solutions, meaning they will increase blood pressure greatly by the effects of the large plasma proteins. Fluid overload can be a concern with use of these products. Antigenic reactions of all the products will be discussed later.

Packed red blood cells are prepared by taking a whole blood donation, centrifuging the blood and removing the red blood cells after the plasma has been decanted off. The red blood cells are washed and suspended in 0.9% normal saline to rid them of any remaining white blood cells or plasma proteins. The PCV of a packed red blood

cell transfusion is approximately 70-80%. Packed red blood cells are typically not considered colloids; however, they are suspended in a crystalloid solution and can till be implicated in volume overload.

Plasma products include: fresh frozen plasma, frozen plasma, cryoprecipitate, cryo-poor plasma, and platelet rich plasma. Fresh frozen plasma (FFP) is prepared by the removal of the plasma portion of the whole blood donation, and freezing it immediately. Fresh frozen plasma contains labile clotting factors (V, VIII, and vWF) as well as the remainder of the non-labile clotting factors, relatively small amounts of albumin and immunoglobulins, fibrinogen, alpha-macroglobulin, antithrombin III, and other physiologically important proteins. FFP has a freezer life of 4 years. After 4 years it becomes Frozen plasma (FP) and contains all of the above proteins with the exception of the labile clotting factors. Cryoprecipitate is the supernatant from a special centrifugation of plasma (after it has been removed from the red cells). This contains high levels of vWF and is often removed and stored for infusion during a vWF crisis. The remaining plasma, after the cryo has been separated off, is cryo-poor plasma and contains all parts of the fresh frozen plasma, except for vWF. Platelet rich plasma

Miscellaneous transfusion products include: human albumin, canine albumin, IVIG and antivenin. Human/canine albumin is typically used to treat severe hypoalbuminemia. IVIG is an anti-inflammatory infusion used in severe hematologic/dermatologic autoimmune disease states (IMHA, ITP, etc). Finally, antivenin is an immunoglobulin infusion that has been sensitized to snake venom and is used to treat snake envenomations.

Blood types

Although not all transfusions involve blood, giving blood products requires knowledge of the physiology of blood types in the canine and feline patient. Canine patients have a receptor and allele system, where their red blood cells express receptors for various different receptors corresponding to a corollary blood type. Canines may have upwards of 18 different blood types; the most notable being DEA (dog erythrocyte antigen) 1, (with 1.1, 1.2 and 1.3 subgroups), DEA 2, DEA 3, DEA 4, DEA 5, DEA 6, etc. There is another antigen that may be of importance called the dal antigen present in dalmation dogs. Canines are either positive or negative for the various receptors and can have multiple receptors present on their red blood cells. The most antigenic receptors are the DEA 1.X antigens which is why commercial kits test for the DEA 1.1 antigen. Dogs do NOT have naturally occuring alloantibodies, meaning they are not sensitized to different blood types initially. However, after they receive a transfusion they now create circulating antibodies against the blood type infused. Most dogs (99%) are positive for the DEA 4 allele, so a DEA 4+ dog can be considered a universal donor if they are negative at all other allele sites. Ideally, dogs should be typed and cross-matched prior to infusion of DEA 4+ (only) blood products.
Feline patients have a slightly different system: the AB system. Cats either have an A protein, B protein, or A AND B protein present on their red blood cell. Cats DO possess naturally occuring alloantibodies and can react to any blood type but their own on the first transfusion. A type cats have weak anti-B antibodies and will typically have a delayed hemolytic reaction where some, but not all, of the infused red blood cells (if Type B blood was infused to a Type A cat) will become destroyed and unusable. In contrast, type B cats have very strong anti-A antibodies and can die if transfused with type A blood. As of 2006, 90% or greater of all domestic shorthair cats in the US and in most european countries are type A. Type B occurs in a decent percentage of Abyssinian, Birman, British Shorthair, Cornish Rex, Devon Rex, Exotic shorthair, Himalayan, Persian, Scottish fold, Somali, Sphinx, and Turkish Angora/Van cats. All cats should be typed if a transfusion might be in their future, given type-specific blood products, and cross-matched prior to infusion as well. There is a small percentage of cats that are type AB. They contain both the A and B-type sugar on their red blood cells and have no natural alloantibodies.

Recommendations for transfusing AB cats is to use Type A blood.

There are various kits available to type patients in the hospital. The canine versions typically screen for DEA 1.1 to see whether the patient is 1.1 positive or negative. Many canine patients are DEA 1.1 negative and should only be transfused with DEA 1.1 negative blood. DEA 1.1 positive patients can receive DEA 1.1 positive or negative blood. The biggest concern is transfusing DEA 1.1 positive blood to a DEA 1.1 negative patient. Feline blood typing kits identify Type A and Type B blood types, and potentially Type AB cats.

Blood typing is very important to prevent serious life-threatening mis-matched blood types. Crossmatching can identify blood type incompatiibilities and other potential antigen-antibody reactions by causing agglutination. Crossmatching can be done with a manual method or a gel tube method (using a commercial kit).

Administering/Monitoring Transfusions

Regardless of the product being administered, transfusions are not entirely safe. There are several categories of transfusion reactions, each of which with their own pathogenesis and clinical signs. There are several different classes of reactions. The acute immunologic reactions include: acute hemolytic reactions (typically mis-matched blood types), allergic reactions (antigen-antibody reactions to foreign proteins), febrile non-hemolytic transfusion reactions, and transfusion-related acute lung injury (TRALI). The acute reactions occur immediately and tend to be life-threatening. Delayed immunologic reactions include: delayed hemolytic transfusion reactions (possibly from mis-matched blood types), and post-transfusion purpura. Acute non-immunologic reactions include: volume overload (TACO), citrate toxicity, hypothermia, and bacterial contamination (sepsis). And finally, the delayed non-immunologic reactions include infectious disease transmission.

Reaction category	Type of reaction	Cause	Clinical signs	Treatment
Acute immunologic	Acute hemolytic	Blood type mismatch	Collapse, vomiting, hemolysis	Stop transfusion, administer fluids, steroids
	Allergic	Antigen binding in donor blood.	Typically dermatologic: urticaria, pruritis, edema	Slow/stop transfusion, diphenhydramine
	Febrile non-hemolytic	Leukocyte antigens on donor leukocytes and platelets. WBC's release inflammatory mediators during storage	Elevation of body temperature by 1 C above baseline after starting transfusion	Slow or stop transfusion, diphenhydramine or NSAID.
	TRALI	Donor leukocytes in the product react with recipient leukocytes inciting an immune response	Pulmonary edema with normal cardiac function	Fluids, Oxygen, potentially mechanical ventilation
Delayed Immunologic	Delayed hemolytic	Antibody response to donor antigens. Cells are prematurely removed from circulation	Drop in PCV, Rise in bilirubin	No treatment typically
	Post transfusion purpura	Platelet fragments get targeted and initiate immune response destroying host platelets	Spontaneous bleeding (gums, teeth, nose)	Immunosuppressive therapy
Acute non-	Transfusion-	Volume overload	Coughing, edema,	Administer the

immunologic	Associated Circulatory Overload (TACO)	from administration of high molecular weight fluids or over-zealous administration	pulmonary edema, chemosis, nasal discharge	transfusion at a slower rate, administer diuretics
	Citrate Toxicity	Anticoagulant in blood products, can bind calcium if given in large quantities	Tetany, cardiac arrhythmias	Slow/stop transfusion, administration of parenteral calcium. ADMINISTER IN ANOTHER LINE
	Hypothermia	Giving cold blood products	Hypotension, cardiac arrhythmias	Provide warming measures (towels, forced air warming, IV fluids warming, ets). Warm blood product
	Bacterial contamination	Administering contaminated or expired blood products	Hypotension, collapse, SIRS, Septic syndromes	Fluids, antibiotics, stop/slow transfusion, supportive care
Delayed non-immunologic	Infectious disease transmission	Non-screened blood products transmit a blood-borne disease	Clinical signs of disease	Treatment of the respective disease.

Monitoring the infusion of a transfusion is incredibly important and veterinary technicians should be diligent about doing so. The transfusion is typically administered slowly (1/4 of the normal rate) and the rate is slowly increased if the patient can tolerate the transfusion. Most transfusions of blood products NEED to be given over 4 hours to reduce the chance of bacterial contamination. All blood product transfusions (plasma and red blood cell products) must be given through filters to prevent foreign material (notably clots) from entering the patient. Special filters are made to screen for bacteria and WBC's. Filters contained within pre-made intravenous sets can typically handle an entire transfusion load. In-line filers (often used for smaller doses of transfusion that are administered on a syringe pump) must be used according to the manufacturer directions. There is a brand of filter that can only handle 25-30 cc of packed red blood cells; after which it cannot be considered effective. Blood transfusions are often administered on an IV pump, but red blood cell viability is determined, in part, by the mechanism of administration. If IV pumps that are NOT rated for blood are used RBC's can be lysed before administration, or may have their cell walls weakened and they will not survive in circulation long. Thus, recommendations include to free-drip the transfusion (or hand push it) if you are not using a blood-rated pump. Contrary to popular belief, the HESKA IV pumps are not actually rated for blood products, although their technology is typically the style used for blood transfusions.

Although administration of blood products is somewhat commonplace, diligent monitoring and knowledge of the biology of blood types is essential to perform high-quality transfusion medicine. The veterinary technician needs to stay updated on new and emerging trends in transfusion medicine and should be proactive about monitoring patients who are receiving a transfusion. Transfusions can be life-saving, but can also do more harm than good if not administered properly.