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INTRODUCTION

Since the early 80s the use of blood products in treating critically ill animals and supporting animals undergoing surgical and other procedures has tremendously increased. However, it should be noted that blood products are prepared from donor animals and represent a very limited resource not available in all situations, and as they are biologicals they bear the inherent risks to transmit infectious agents and cause other adverse transfusion reactions. Furthermore, the need for blood typing and crossmatching of patients and donors has now been recognized in order to assure safe and more efficacious transfusions in dogs and cats. Veterinary clinicians play a key role in providing safe and effective transfusion therapy and therefore they need to be aware of the transfusion principles. Here some key points:

- Transfusion therapy refers to the safe and effective replacement of blood or one of its components offering support for many critically ill anemic and bleeding patients.

- The indications for transfusions need to be clearly determined, and ideally only the deficient blood component is replaced at the appropriate dose.

- While red blood cells and plasma clotting factors are crucial, the indications and efficacy of transfusing platelets, leukocyte, as well as other plasma proteins are limited.

- Blood products represent a limited resource; hence they should only be given when indicated, at the minimal dose required and after carefully considering all alternatives.

- All blood donors need to be typed for DEA 1.1 and the feline AB blood groups, resp., and regularly screened for their health including testing for infectious diseases.

- All recipients should be typed for DEA 1.1 and feline AB and any previously transfused (>4 days) animals should also be crossmatched prior to the next red cell transfusion.

- While acute hemolytic transfusion reactions are feared most, they can be avoided by prior compatibility testing; other adverse transfusion reactions may not be predicted.

- The efficacy of survival of transfused blood cells and plasma proteins should be monitored during and post-transfusion with the appropriate clinical and laboratory parameters.

INDICATIONS FOR TRANSFUSION THERAPY

Transfusions are indicated for anemia, coagulopathy, and rarely for other conditions such as thrombocytopenia/-pathia, and hypoproteinemia. However, the decisions to transfuse is based upon the overall clinical assessment of a patient’s history and clinical signs, routine laboratory tests, underlying cause, and hence sound clinical judgment. And because of the inherent risks, transfusions should never be given without a clear indication and exhausting other alternatives.

The most common indication for a transfusion in dogs and cats are anemias and depending on the type, degree and course of the anemia a transfusion with blood products, such as stored packed red cells, fresh or stored whole blood, may be warranted. Animals with rapidly progressive anemia need to be transfused much earlier, when the PCV is still around or above 20%, while patients with chronic anemias may do well at lower hematocrits as long as they are not stressed. It should be noted that animals with peracute blood loss will not show a drop in PCV for hours until fluid shifts have occurred. Hence, other parameters, such as evaluation of mucous membranes and capillary refill time, are needed to assess the hypovolemia and need for blood transfusions. Fluid therapy may be all that is needed to restore vital organ perfusion in acute blood loss anemias, while packed red blood cells (pRBCs) are considered, when there is evidence of tissue hypoxia. In other words the associated lowering of the PCV is no contraindications for fluid therapy to restore normovolemia. Furthermore, if an animal needs to undergo anesthesia and surgery, generally the PCV should be at least 15-20% to assure proper oxygenation during the procedure. Red
cell transfusions have proven life-saving in cases of immune-mediated hemolytic anemia and there is no evidence that transfused red cells would be more rapidly destroyed than the patient’s erythrocyte or that they “add to the fire”, although some clinicians have questioned its value.

Fresh frozen plasma (FFP) is most commonly used to treat coagulopathies causing serious bleeding in veterinary practice as it contains all coagulation factors. Hemorrhage caused by acquired coagulopathies such as liver disease and anticoagulant rodenticide intoxication, just like bleeding due to any of the many hereditary coagulopathies are certainly common indications. Sudden bleeding due to therapeutically used heparin or warfarin to counter thrombosis can also successfully be corrected with FFP. The use of FFP (to replace deficient coagulation factors as well as antithrombin) with or without heparin in the management of disseminated intravascular coagulation remains controversial; there are no studies documenting any definitive beneficial effects. Similarly evidence for FFP to help in acute pancreatitis (to replace alpha-macroglobulins) or in parvovirosis (to provide anti-parvo and other immunoglobulins and stop gastrointestinal hemorrhage) is lacking. FFP is also commonly used to correct hypoproteinemias, but its effect on the oncotic pressure in cases of protein-losing nephropathies and enteropathies is minimal for the FFP doses that are typically administered and practically available. Note lyophilized canine albumin has just become commercially available.

Other blood products are less commonly used in dogs and are not generally available for cats. Cryoprecipitate is rich in fibrinogen, fibronectin, and the von Willebrand factor VIII complex and is the preferred treatment for bleeding dogs with these plasma protein deficiencies. If available, cryo-poor plasma may be administered to hypoproteinemic dogs, where synthetic plasma expanders are insufficiently effective or in case of anticoagulant rodenticide poisoning. Because platelets are relatively short-lived (one week) and cannot readily be stored for any length of time (<24 hours at room temperature), platelet rich plasma and concentrate are rarely transfused. Hemorrhage caused by thrombocytopenias in anemic dogs could be managed with fresh whole blood, but generally only requires the use of pRBCs to correct the anemia. Rarely platelet-rich plasma and platelet concentrates are required to control life-threatening bleeding. Furthermore, in dogs with immune-mediated thrombocytopenia transfused platelets have a very short half-life of hours and albeit they may be helpful to control life-threatening hemorrhage such transfusions will not result in any appreciable platelet rise. Because of the very short normal half-life of granulocytes (hours) leukocyte transfusions are not generally practiced in human and veterinary medicine.

**CANINE AND FELINE BLOOD TYPES**

To assure efficacious and safe transfusions blood donor and recipient should be blood typed and if previously transfused also crossmatched. Blood types are genetic markers on erythrocyte surfaces that are antigenic and species specific. A set of blood types of two or more alleles makes up a blood group system. Because administration of a small (<1ml) of incompatible blood can result in life-threatening reactions, this practice to assess blood type compatibilities is unacceptable. Blood typing is clinically important to assure blood compatibility and therefore is recommended for any animal in need of a transfusion or considered to become a blood donor. Unless blood typing is regularly performed in practice, it is best to send blood for typing to a reference laboratory. There are typing cards (DMS) and cartridges (Alvedia DME) for in-clinic use as well as gel column assays for reference laboratories. Caution should be exercised whenever the patient’s blood is autoagglutinating or has a very low hematocrit (<10%).

In dogs the clinically most important blood type is DEA 1.1: DEA 1.1 (A1) elicits a strong alloantibody response after sensitization of a DEA 1.1 negative dog by a transfusion; thus can be responsible for a transfusion reaction in a DEA 1.1 negative dog previously transfused with DEA 1.1 positive blood. Transfusion reactions against other blood types have rarely been described. They include reactions against the DEA 4, Dal and another common red cell antigen, and other clinically significant blood types may be found in the future. There are no clinically significant alloantibodies present prior to sensitization of a dog with a transfusion (no sensitization by pregnancy). The major feline blood group system thus far generally recognized is known as the feline AB blood group system and contains 3 alleles: type A, type B, and the extremely rare type AB. Most domestic shorthair cats have type A blood, but the proportion of type B cats can be substantial in certain areas. The frequency of A and B blood types also varies greatly between different breeds, but likely not much geographically in purebred cats. Most blood donors have type A blood, but some places also keep cats with the rare type B and type AB as donors. All blood donors must be typed. Naturally-occurring alloantibodies have been well documented in type A and type B cats and require that blood typing be performed prior to both blood transfusion and breeding to assure appropriate blood compatibility. All type B cats have very strong naturally-occurring anti-A alloantibodies. They are responsible for serious transfusion reactions. Furthermore additional blood group systems are being identified such as the Mik red cell antigen in Domestic shorthair cats; Mik-negative cats may produce naturally occurring alloantibodies.
Whereas blood typing tests reveal the blood group antigens on the red blood cell surface, blood crossmatching tests assess the serologic compatibility or incompatibility between donor and recipient. Thus, the crossmatch test checks for the presence or absence of naturally occurring and induced alloantibodies in serum (or plasma) without determining the blood type. These antibodies may be hemolysins and/or hemagglutinins and can be directed against known blood groups or other red cell surface antigens. Beside a standardized tube crossmatching procedure there is a laboratory gel column (DiaMed) as well as tube gel test (DMS) available. The major crossmatch tests for alloantibodies in the recipient's plasma against donor cells, whereas the minor crossmatch test looks for alloantibodies in the donor's plasma against the recipient's red blood cells. A minor crossmatch incompatibility should not occur in dogs if canine donors have not been previously transfused and is of lesser concern because donor's plasma volume is small, particularly in packed red cell products, and will be markedly diluted in the patient. In contrast, the major and minor crossmatch can show incompatibility prior to any transfusion due to the presence of naturally occurring alloantibodies in cats, not only for the AB but also the Mik and possibly other blood group systems. The initial blood crossmatch between two dogs that have never before received a transfusion should be compatible, because dogs do not have naturally occurring alloantibodies. Therefore, one might omit a crossmatch before the first transfusion in clinical practice. Obviously, a blood donor should never have received a blood transfusion to avoid sensitization. In cats mixing a drop of donor/recipient blood with donor/recipient plasma will detect A-B incompatibilities if typing is not available.

**BLOOD DONORS SOURCES AND COLLECTION**

Many larger veterinary hospitals have permanent canine and/or feline blood donors to cover their transfusion requirements or in case fresh whole blood or platelet-rich plasma (concentrate) is needed. Several larger voluntary blood donor programs have emerged with client or staff owned dogs. More than a dozen commercial canine blood banks have been established in the United States and deliver overnight blood products, however, there is generally a shortage. Some are also providing feline products. Autologous (self) transfusion refers to the donation of blood by a patient four weeks to a few days prior to surgery when major surgical blood loss is anticipated. Blood can also be collected immediately prior to surgery. The patient will be hemodiluted with crystalloid and colloid solution and receives the blood when excessive bleeding occurs or after surgery. Autotransfusion is another autologous transfusion technique in which shed blood salvaged intra-operatively or following trauma can be reinfused after careful filtering. However, do not reinfuse blood from long-standing (<4 hours), contaminated, or malignant hemorrhagic effusions.

Blood donors should be young adult, lean, and good tempered animals, and weigh at least 23 kg for dogs (to donate 450ml) and 4 kg for cats (40ml); have no history of prior transfusion; have been regularly vaccinated and are healthy as determined by history, physical examination, and laboratory tests (complete blood cell count, chemistry screen, and fecal parasite examination every 6-12 months) as well as free of infectious diseases (testing depends on species/breed and geographic area but may include serology, antigen assays and PCR assays). Donors should receive a well-balanced, high performance diet, and may be supplemented twice weekly with ferrous sulfate (Feosal, 10 mg/kg), if bled every 4 weeks. Packed cell volume (PCV) or hemoglobin (Hb) should be >40% and >13 g/dl in canine donors and >30% and >10 g/dl in cats.

Canine donors are generally not sedated while cats are regularly sedated with a combination of ketamine (10 mg), diazepam (0.5 mg), and atropine (0.04 mg) by intravenous injection. Some sedatives, such as acepromazine, interfere with platelet function and induce hypotension, hence they should not be used. Blood is collected aseptically by gravity or blood bank vacuum pump from the jugular vein over a 5 to 10 minute period. Plastic bags containing citrate-phosphate-dextrose-adenine (CPD-A1) with or without satellite bags for blood component separation are optimal. These commercial blood bags represent a closed collection system in which the blood does not come into contact with the environment at any time during collection or separation into blood components, thus minimizing the risk of bacterial contamination and allowing storage of the blood products. A large plastic syringe containing 1 ml CPD-A1 or 3.8% citrate per 9 ml blood and connected to a 19 gauge butterfly needle is commonly used for cats. This represents an open collection system in which connections allow exposure of blood to the environment; because of the potential risk for bacterial contamination, blood collected via an open system should not be stored for more than 48 hours. Vacuum glass bottles containing acid-citrate-dextrose (ACD) allow rapid collection, but are not recommended because blood components are readily damaged and cannot be separated and stored for long. The maximal blood volume to be donated is 20 ml blood/kg or one regular blood bag unit of 450 ± 45 ml per ≥ 25 kg dog and 10 ml blood/kg or 50 ml blood (one typical feline unit) per ≥ 5 kg cat.

Blood components are prepared from a single donation of blood by simple physical separation methods such as centrifugation generally within 8 hours from collection; thereby, fresh whole blood can be separated into packed red cells, platelet-rich plasma or concentrate, fresh frozen plasma, and cryoprecipitate and cryo-poor plasma. Blood...
component preparation is best accomplished by using plastic blood bags with satellite transfer containers in order to assure sterility. Fluctuations in storage temperature significantly alter the length of storage; thus, temperature controlled and alarmed blood bank refrigerators and freezers are ideal, but others are acceptable as long as the temperature is monitored and the refrigerator/freezer are not too frequently opened. Blood components that have been warmed to room or body temperature should not be recooled and cannot be stored again. Similarly, partially used or opened blood bags should be used within 24 hours because of the risk of contamination.

**ADMINISTRATION OF BLOOD PRODUCTS**

For routine transfusion in the treatment of anemia, it is not necessary to warm blood after removal from the refrigerator. Warming may in fact accelerate the deterioration of stored red blood cells and permit rapid growth of contaminating microorganisms. However, there are specific clinical situations such as transfusion of neonates or resuscitation of trauma patients necessitating rapid, massive transfusions, in which warming of blood is indicated to prevent complications associated with hypothermia (e.g., cardiac arrhythmias and coagulopathies). A temperature-controlled waterbath (37°C) is ideal to warm blood products. A warm water bowl in which the water is periodically changed may be used to warm blood products. Care should be taken to maintain absolute sterility and to not overheat the blood products. Blood components that have been prewarmed cannot be refrozen/refrigerated.

Blood bags are connected to blood infusion sets that have an in-line microfilter. A long (85 cm) blood infusion set with a dripping chamber and a short infusion set for small dogs and cats to connect with syringes are available. Use a latex-free infusion set for platelet administration to avoid aggregation. Microfilters with 170 μm pores are commonly used to remove clots and larger red cell and platelet aggregates. Finer filters with 40 μm pores will remove most platelets and microaggregates and clog after 50 ml. Leukocyte reduction filters (expensive) may be used to decrease febrile adverse reactions to WBC components. Sterility has to be maintained when connecting blood component bag to infusion set and tubing to catheter.

Blood components are best administered intravenously. Ideally, an indwelling catheter (16-22 gauge depending on size of animal) is placed into the jugular vein, but the cephalic or saphenous vein on extremities or intraosseous catheters may also be used. Avoid concurrent feeding and administration of drugs or fluids other than physiologic saline through the same catheter in order to prevent lysis of erythrocytes and blood coagulation.

Rate of transfusion depends on the hydration status, degree of anemia, and general health condition of an animal. Initial rate is slow, starting with 1-3 ml over the first 5 minutes to observe for any transfusion reactions, even with blood typed and/or crossmatched transfusions. In animals with cardiac failure, do not exceed 4 ml/kg/hr. Transfusion of a single bag should be completed within 4 hours to prevent functional loss or bacterial growth. Volume of blood component to be administered depends on the type of deficiency and size of the animal. In anemia: Volume (ml) of whole blood = 2 x PCV rise desired (%) x body weight (kg) or in other words, administration of 2 ml whole blood/kg body weight raises the PCV by 1%. If packed red cells are used without prior resuspension in a red cell preservative, half the volume has to be administered, since packed red cells have a PCV of 70-80%. In the absence of bleeding and hemolysis, at least 70% of transfused erythrocytes survive 24 hours (required blood bank standard) and transfused erythrocytes may be thereafter expected to have a normal life-span (approximately 70 days in cats, 110 days in dogs). Monitor response to transfusion by obtaining PCV/TP readings prior to, immediately, and 6 and 24 hours post-transfusion, and consider continued blood loss and/or hemolysis.

In thrombocytopenia or thrombopathia, one unit of PC, PRP or FWB will increase the platelet count by 10,000/μL in a recipient weighing 30 kg. In animals with serious or life-threatening bleeding, the platelet count should be increased to >40,000/μL. Platelet counts are monitored prior, 1 hour and 24 hours after the platelet transfusion.

In coagulopathies and von Willebrand’s disease, FFP at 6-10 ml/kg is an initial dose to stop bleeding or avoid excessive bleeding during surgery. In some cases, larger volumes may be needed to control bleeding. Depending on the coagulopathy, repeated administration of FFP may be necessary. Because of the short half-life of factor VII and VIII and von Willebrand factor, deficient animals need to be treated twice to four times daily. Other coagulopathies may be treated daily. Cryoprecipitate at a dose of 1 CRYO unit/10 kg or 1-2 ml/kg body weight twice daily is ideal to treat hemophilia A and von Willebrand’s disease. Plasma support should be provided for an additional 1-3 days after the bleeding has been controlled to allow for healing and prevent rebleeding.

**ADVERSE TRANSFUSION REACTIONS**

While transfusion of blood and its components is usually a safe and temporarily effective form of therapy, there is always a risk for potential hazards. Adverse reactions usually occur during or shortly after the transfusion and can be due to any component of whole blood. Most transfusion reactions can be avoided by carefully selecting only healthy donors, using appropriate collection, storage, and administration techniques, performing blood typing and crossmatching, and administering only needed blood components. The most common clinical sign of a
transfusion reaction is fever, followed by vomiting and hemolysis. Hemolytic transfusion reactions can be fatal and are, therefore, most important, while fever and vomiting are usually self-limiting. Adverse effects of transfusions can be divided into non-immunologic (pyrogen-mediated fever, transmission of infectious agents, vomiting, mechanical hemolysis, congestive heart failure, hypothermia, citrate toxicity, pulmonary complications) and immunologic reactions (acute and delayed hemolytic transfusion reactions, urticaria to anaphylaxis, graft versus host disease). Note that some clinical signs may be caused by both mechanisms. In surveys of blood product usage, transfusion reactions were observed in 2-13% of recipients, but none of them were definitely associated with blood group mismatches and hence could have been caused by other blood components or blood collection, processing and storage as well as host factors.