

CHAPTER 61

TRANSFUSION THERAPY

Urs Giger, PD, DrMedVet, MS, FVH, DACVIM-SA, DECVIM-CA, DECVCP

KEY POINTS

- *Transfusion therapy* refers to the safe and effective replacement of blood or one of its components, thereby offering support for critically ill anemic or bleeding patients.
- The indications for transfusions need to be clearly determined, and ideally only the deficient blood components are replaced using appropriate dosages.
- Although red blood cells and plasma clotting factors are crucial, the indications and efficacy of transfusing platelets, leukocytes, and other plasma proteins are limited.
- Blood products represent a limited resource; hence they should be given only when indicated, using the minimal dosage required and after carefully considering possible alternatives.
- All canine and feline donor blood must be typed for the dog erythrocyte antigen (DEA) 1 and the feline AB blood groups, respectively, and all donors must have regular health examinations including blood and infectious disease screening.
- All canine and feline recipient blood should be typed for the DEA 1 and AB blood group, respectively. Blood from animals previously transfused (>4 days after first transfusion ever received) should also be crossmatched before receiving another red blood cell transfusion (cats may be crossmatched even prior to the first transfusion because of possible anti-mik antibodies).
- Although acute hemolytic transfusion reactions are feared most, they can be avoided by prior compatibility testing; other transfusion reactions cannot be predicted by compatibility testing.
- The effectiveness and survival of transfused blood cells and plasma proteins should be monitored during and after transfusion using appropriate clinical and laboratory parameters.
- Lyophilized canine platelets and specific plasma components such as albumin and cryoprecipitate have recently become available, although no hemoglobin solutions are currently commercially available for veterinary use.

Critically ill animals or those undergoing surgical procedures often benefit from the administration of blood products. However, blood products are obtained from donor animals and thus represent a limited resource that is not available in all practice settings. Because they are biologic products, they bear the inherent risks of transmitting infectious diseases or causing other adverse reactions. Clinicians in the critical care setting play a key role in providing safe and effective transfusion therapy and therefore should be aware of the principles of transfusion medicine. The interested reader is referred at the end of the chapter to more comprehensive reviews and books on veterinary transfusion medicine.

INDICATIONS FOR TRANSFUSION THERAPY

Blood transfusions are indicated for management of anemia, coagulopathy, and, rarely, for other conditions such as thrombocytopenia, thrombopathia, and hypoproteinemia (Table 61-1). The disorders that lead to these medical problems and their detailed management are described in separate chapters. Fresh whole blood (FWB, kept at room temperature for <8 hours) contains all cellular and plasma components of blood, but specific blood component therapy provides the most effective and safest support and allows for optimal use of every blood donation. The decision to transfuse is based on the overall clinical assessment of a patient's history and clinical signs, routine laboratory test results, underlying cause, and sound clinical judgment. Although the optimal packed cell volume (PCV) is more than 30%, oxygen delivery in a normovolemic, resting animal can be maintained down to a PCV of 10% (although this is completely inadequate under most disease conditions). Thus there is no specific

Table 61-1 Blood Products, Storage Guidelines, and Indications

Blood Product	Storage	Temperature in Celsius	Indications
Fresh whole blood (FWB)	<8 hours	2 to 24	Combined red blood cell and plasma deficiency with need for platelets
FWB	<24 hours	4	Combined red blood cell and plasma deficiency without need for platelets
Stored whole blood (SWB)	28 days	4	Anemia Hypoproteinemia
pRBC	28 days	4	Anemia
Platelet rich plasma (PRP) or platelet concentrates	24 hours*	20-24	Thrombocytopenia with life-threatening bleeding
Fresh frozen plasma (FFP)	1 year	<-20 to -40	Any coagulation factor deficiencies; hypoproteinemia
Stored plasma	1 to 2 years	<-20 to -40	Hypoproteinemia
Cryoprecipitate (cryo)	1 year	<-20 to -40	von Willebrand's disease Hemophilia A (but not B) Hypofibrinogenemia
Cryoprecipitate-poor plasma (cryo-poor)	1 year	<-20 to -40	Hypoproteinemia Some coagulopathies (factors II, VII, IX, XI)

*If constantly mixed gently.

transfusion trigger in any patient (i.e., certain PCV or coagulation times). However, because transfusion carries inherent risks, blood should never be given without a clear indication or before exhausting alternative therapies. Furthermore, blood components represent a scarce resource and should not be used without a proper indication and assessment of the prognosis.

Red Blood Cell Transfusions

The most common indication for transfusions in dogs and cats is anemia (see Chapter 108). Transfusions are generally required after major loss of the blood's oxygen-carrying capacity (i.e., loss of hemoglobin) and subsequent tissue/organ ischemia but not as a simple volume expander. Depending on the type, degree, rapidity, and course of the anemia, a transfusion with blood products, such as stored packed red blood cells (pRBCs), FWB, or stored whole blood, may be warranted. Animals with rapidly progressive anemia should be transfused when the PCV is approximately 20% to 25%, but a patient with chronic anemia may not require a transfusion despite having a much lower PCV.

Healthy animals can readily tolerate a loss of up to 20% of blood volume (canine blood donors regularly give 20 ml/kg body weight while cats give 10 ml/kg q6-12wk) without any ill effects. However, animals with acute hemorrhage exceeding 20% of the blood volume may require a blood transfusion in addition to the initial shock fluid replacement therapy (see Chapter 60). It should be noted that animals with peracute blood loss will not show a drop in PCV for several hours after hemorrhage, until intercompartmental fluid shifts occur or fluid therapy is instituted. Hence other parameters are used to decide if transfusion therapy is indicated, such as mucous membrane color, capillary refill time, heart rate, blood pressure, venous oxygen saturation, and possibly blood lactate levels (see Chapter 183 for further details). Arterial blood gas values as well as respiratory rate and effort should be normal in uncomplicated anemia but are useful to evaluate animals with coexisting respiratory disease. In most animals with anemia secondary to acute blood loss, fluid therapy alone will restore vital organ perfusion, although pRBCs should be considered in any animal with evidence of anemia-related tissue hypoxia. A falling PCV is not a contraindication for fluid administration, although excessive blood collection for diagnostic tests may necessitate blood replacement in a sick animal and thus should be

avoided. Animals that require anesthesia and surgery should have a PCV of at least 20% to ensure adequate oxygen-carrying capacity during anesthesia.

In animals with immune-mediated hemolytic anemia (see Chapter 110), red blood cell transfusions have proven lifesaving. There is no evidence that transfused red blood cells “add fuel to the fire” or are destroyed more rapidly than the patient's own erythrocytes. However, mismatched, incompatible transfusions must be avoided and older pRBCs may be less beneficial and safe than fresher pRBCs (<7 days), particularly in dogs with immune-mediated hemolytic anemia. The administration of a bovine hemoglobin solution (Oxyglobin) has also shown beneficial effects but is currently not available in the United States (see Chapter 58 for further details).

Fresh Frozen Plasma

Fresh frozen plasma (FFP) is used most commonly in veterinary practice to treat coagulopathies causing serious bleeding, because this product contains all coagulation factors. FFP is commonly used in animals with hemorrhage secondary to acquired coagulopathies (e.g., liver disease and anticoagulant rodenticide intoxications) or patients with hereditary coagulopathies and subsequent bleeding. Sudden hemorrhage caused by therapeutically used heparin (including accidental use of undiluted heparin flushes) or warfarin to counter thrombosis can also be corrected with FFP, although protamine and vitamin K can also rapidly reverse the heparin- and warfarin-induced effects, respectively. The use of FFP (with or without the administration of heparin) to replace deficient coagulation factors and anti-thrombin in patients with immune-mediated hemolytic anemia or disseminated intravascular coagulation is controversial. There are no studies documenting a definitive beneficial effect in animals or humans, except in a small study using high doses and strict anticoagulant monitoring. Similarly, evidence for the use of FFP in animals with acute pancreatitis (to replace α -macroglobulins and antiproteases) or in parvovirus (to provide antiparvovirus antibodies and additional immunoglobulins and to stop gastrointestinal hemorrhage) is lacking. FFP is also commonly used to correct hypoproteinemias in animals with protein-losing nephropathies and enteropathies, but its effect on oncotic pressure in these animals is minimal at clinically used dosages, especially when compared with synthetic hyperoncotic agents such as the hydroxyethyl starch products. Critically ill

animals with albumin concentrations less than 1.5 g/dl may benefit from plasma therapy because this protein is an important carrier of certain drugs, hormones, metals, chemicals, toxins, and enzymes. A canine albumin product is intermittently commercially available (see Chapter 58 for further details).

Other Blood Products

Other blood products are used less commonly in dogs and are generally not available for cats. Cryoprecipitate is rich in fibrinogen, fibronectin, factor VIII, and von Willebrand's factor and is the preferred treatment for bleeding dogs with these plasma protein deficiencies. In addition to frozen or freshly made cryoprecipitate from FFP, a lyophilized canine platelet product is now commercially available. Also cryoprecipitate-poor plasma may be administered to many coagulopathic and hypoproteinemic dogs when synthetic plasma expanders are of limited use or have undesirable side effects (e.g., exaggerate bleeding tendency). Because platelets are relatively short lived (1 week) and cannot readily be stored for any length of time (<8 hours at room temperature with agitation), they are rarely transfused. Life-threatening hemorrhage caused by thrombocytopenia in anemic dogs could be treated with FWB but generally requires only pRBCs to correct the anemia. Rarely, platelet-rich plasma (PRP) and platelet concentrates are required to control life-threatening bleeding (see Chapter 106). Furthermore, in dogs with immune-mediated thrombocytopenia, transfused platelets have a very short half-life (hours) and will not result in any appreciable platelet rise but may transiently stop severe hemorrhage. Cryopreserved platelets are short lived and lose their function and are no longer available, but lyophilized platelets have been intermittently available and may provide adequate hemostasis. Because of the very short half-life of granulocytes (hours), leukocyte transfusions are not generally performed in human or veterinary medicine.¹

BLOOD TYPING

To ensure effective and safe transfusions, blood from both donor and recipient should be typed and, if previously transfused, a crossmatch also performed. Blood types are genetic markers on erythrocyte surfaces that are species-specific and antigenic in individuals that lack the same markers. This antigenicity results in the development of alloantibodies, so that the administration of a small volume (as little as 1 ml) of incompatible blood can result in life-threatening immune reactions. Blood typing is therefore clinically important to ensure blood compatibility and is recommended for any animal in need of a transfusion, any animal becoming a blood donor, and before breeding type B queens to avoid neonatal isoerythrolysis (NI). Unless blood compatibility tests are performed regularly, it is best to send ethylenediaminetetraacetic acid (EDTA) blood to a reputable laboratory for typing and crossmatching.^{2,3}

Canine Blood Types

Dogs have more than a dozen blood group systems known as DEAs. Canine erythrocytes are either positive or negative for a blood type (e.g., DEA 4 positive or negative), and these blood types are thought to be codominantly inherited. In the DEA 1 system, various types (DEA 1.1, 1.2, and 1.3) have been postulated based on serology, but recent studies with monoclonal antibodies have shown that dogs can be either DEA 1 negative or to various degrees DEA 1 positive, similar to the Rh factor in humans.^{3a} Fortunately, there are no clinically important alloantibodies present before sensitization of a dog with a transfusion (pregnancy has never been reported to cause sensitization).^{2,4,5}

The most important canine blood type is DEA 1. DEA 1 elicits a strong alloantibody response after sensitization of a DEA 1-negative

dog by a DEA 1-positive transfusion. This can lead to an acute hemolytic transfusion reaction in a DEA 1-negative dog previously transfused with DEA 1-positive blood. It is currently unknown if weakly DEA 1-positive blood elicits an alloantibody response in a DEA 1-negative dog or if weakly DEA 1-positive patients will react to strongly DEA 1-positive blood after being sensitized. Transfusion reactions against other blood types in previously transfused dogs have been described rarely. They include reactions against the DEA 4, Dal in Dalmatians and likely few other breeds, and another common red blood cell antigen in a Whippet. Additional clinically important blood types may yet be discovered.^{6,7}

Simple blood typing cards using anticoagulated blood and a DEA 1 monoclonal antibody are available for DEA 1 typing of dogs (DMS Laboratories, Flemington, NJ), but there is some concern that weak agglutination reactions may be overlooked or autoagglutination may give false positive results (despite the control well). The reliable gel column technique is no longer available for animals, but an immunochromatographic strip-based method for in-clinic use has been documented to be very reliable (Alvedia, Lyon, France).^{3a,8} A cartridge method with automatic reader has also been introduced but is apparently not as accurate and is more time consuming (Abaxis/DMS). Dogs that are DEA 1 negative are considered universal blood donors for a dog that has never been transfused. Canine blood typing sera for DEA 3, 4, and 7 and limited typing services are available (Animal Blood Resources International, Dixon, CA), but other blood group incompatibilities of clinical importance can be identified by cross-matching previously transfused dogs. Typing for the common red cell antigen Dal is currently hampered by the limited availability of antisera. Persistent autoagglutination after saline washing of the recipient's blood negates any typing and crossmatch testing except for the immunochromatographic method. Unless a bitch has been transfused previously with mismatched blood, there is no concern for NI.

Feline Blood Types

The main blood group system recognized in cats is known as the *AB blood group system* and consists of three types: type A, type B, and the extremely rare type AB. Type A is dominant over B.⁹⁻¹¹ Thus cats with type A blood have the genotype *a/a* or *a/b*, and only homozygous *b/b* cats express the type B antigen on their erythrocytes. In the extremely rare AB cat, a third allele recessive to *a* or codominant to *b* (or both) leads to the expression of both A (glycyl) and B (allyl) substances. Cats with type AB blood are not produced by mating of a cat with type A to a cat with type B unless the cat with type A carries a rare AB allele. Cats with type AB blood have been seen in many breeds, including domestic shorthaired cats but particularly in Ragdolls. The frequency of feline A and B blood types varies geographically and among breeds. For instance, all Siamese cats have type A blood, and Turkish Vans and Angoras have equal numbers of type A and B blood. Most domestic shorthaired cats have type A blood, but the proportion of cats with type B blood can be substantially different in certain geographic areas. Thus all donor blood must be typed. Most blood donors have type A blood, but some clinics also keep cats with the rare type B blood as donors.²

Cats have naturally occurring alloantibodies.⁹ All cats with type B have very strong naturally occurring anti-A alloantibodies. Kittens receive anti-A alloantibodies through the colostrum from type B queens, and type B kittens develop high alloantibody titers (>1:32 to 1:2048) after a few weeks of age. Anti-A alloantibodies are responsible for serious transfusion reactions and NI in kittens with type A and AB blood born to type B queens. Cats with type A blood have weak anti-B alloantibodies, and their alloantibody titer is usually very low (1:2). Nevertheless, cats with type A blood can also develop hemolytic transfusion reactions when given B blood (in part due to the anti-A antibody in the type B donor blood), but no type A or AB

queen has had a litter with NI caused by A-B incompatibility. Cats with type AB blood have no alloantibodies, although it is recommended that these cats receive type A pRBCs (mostly devoid of plasma with anti-B antibodies) if type AB blood is not available. Furthermore, additional blood group systems are being identified, such as the Mik RBC antigen in some domestic shorthaired cats. It is thought that Mik-negative cats may have naturally occurring alloantibodies or produce them, leading to blood incompatibility reactions beyond the AB blood group system.¹²

Simple AB blood typing cards are available for use in practice (DMS Laboratories, Flemington, NJ), but there are occasionally concerns that cats with type AB are not being recognized and misclassified as type A or B cats. Since withdrawal of the laboratory gel column AB-typing test, in-clinic immunochromatographic strip typing kits have become available, and one has been found to be very reliable (Alvedia, Lyon, France), although the other (DMS Laboratories, Flemington, NJ) has not yet been formally evaluated and seems to have off-center banding reactions.¹³ Type B and AB should be confirmed by a laboratory and with back-typing; any type B cat older than 3 months has very strong anti-A alloantibodies, while AB cats have no alloantibodies.

BLOOD CROSSMATCHING

The blood crossmatch detects the serologic compatibility between the anemic recipient and potential donor and must be performed in cats if blood typing is not available and in dogs or cats that have previously received transfusion therapy.^{1,2,10} This test looks for the presence or absence of alloantibodies in dogs or cats without determining the blood type; it does not replace blood typing. Crossmatching is done with anticoagulated blood from the recipient and the potential donor and requires some technical expertise but may be performed in private practice along with blood typing. Although laboratories use assays in tubes, microgel columns, or microtiter plates, a tube gel method (DMS Laboratories, Flemington, NJ) and strip (Alvedia, Lyon, France) crossmatch method have been recently introduced for clinical practice. The major crossmatch tests for alloantibodies in the recipient's plasma against donor cells. The minor crossmatch tests for alloantibodies in the donor's plasma against recipient's RBCs and is of lesser importance because the donor's plasma is mostly removed in pRBCs and will be diluted in the recipient patient (except if a type B cat is used as donor). It is also of lesser importance if all donors' types are known and if the donors, as generally recommended, have never received transfusions (i.e., have no prior sensitization). Persistent autoagglutination or severe hemoglobinemia (secondary to fragile red blood cells) may preclude testing at least by some methods. Washing the RBCs three times with physiologic saline (1 part blood and 5 to 9 parts saline) may resolve autoagglutination and rouleaux formation.

Because dogs do not have naturally occurring alloantibodies, the initial crossmatch of a dog that has not previously been transfused should be compatible.⁴ However, a compatible crossmatch in a dog does not prevent sensitization against donor cells within 1 to 2 weeks. Thus a dog that was previously given a compatible transfusion from a donor dog may become incompatible with blood from the same donor 1 to 2 weeks later. Because cats have naturally occurring alloantibodies, a blood crossmatch test can detect an A-B mismatch as well as other incompatibilities (e.g., Mik). Mixing a drop of donor blood with recipient plasma (or vice versa) will detect the strong A-B incompatibilities. The practice of administering a small amount of blood (e.g., 1 ml) to the recipient animal to test for compatibility should be abandoned because it may result in fatal transfusion reactions. Transfusion of canine blood to feline patients should be avoided.

BLOOD DONORS AND SOURCES

Many larger veterinary specialty hospitals have few permanent canine and feline blood donors to cover their transfusion requirements or in case FWB or PRP (platelet concentrates) are needed. Several voluntary blood donor programs have emerged with client-owned or staff-owned dogs. More than a dozen commercial canine blood banks have been established in the United States that deliver blood products overnight; however, there may be a blood shortage at any time. Some blood banks are also providing feline products. If blood collection is only occasionally performed, it is advisable to get blood from a commercial resource with expertise in blood banking.

Autologous (self-) transfusion refers to the donation of blood by a patient from 4 weeks to a few days before a surgical procedure with the potential for substantial surgical blood loss. Blood can also be collected immediately before surgery. The patient's blood is diluted with crystalloid (and colloid) solutions, and the previously drawn blood is replaced when excessive bleeding occurs during or after surgery. Autotransfusion is another autologous transfusion technique in which shed blood salvaged intraoperatively or after intracavitary hemorrhage is reinfused intravenously after careful filtering. However, blood from longstanding (>1 hour), contaminated, or malignant hemorrhagic effusions should never be reinfused intravenously.

Blood donors should be young adult, lean, and good-tempered animals; dogs should weigh at least 23 kg to donate 450 ml (smaller dogs could be used if proportionally less blood is collected), and cats should weigh at least 4 kg to donate 40 ml of blood. They must have no history of transfusion and receive necessary vaccinations. In addition, blood donors must be healthy as determined by history, physical examination, and laboratory tests (complete blood cell count, chemistry screen, and fecal parasite examination every 6 to 12 months), as well as free of infectious diseases. Testing depends on species, breed, and geographic area but may include regular microfilaria, *Brucella*, *Babesia*, *Ehrlichia*, *Anaplasma*, *Borrelia*, *Bartonella*, *Mycoplasma*, and *Leishmania* spp testing in dogs and feline leukemia virus, feline immunodeficiency virus, feline infectious peritonitis, *Bartonella* and *Mycoplasma* spp testing in cats. Donors should receive a well-balanced, high-performance diet that may be supplemented twice weekly with oral ferrous sulfate (Feosol, 10 mg/kg q24h) if the donor is bled every 4 to 6 weeks. PCV or hemoglobin concentration should be more than 40% and more than 13 g/dl, respectively, in canine donors and more than 30% and more than 10 g/dl, respectively, in cats.¹⁴

BLOOD COLLECTION

Canine donors generally are not sedated, but cats regularly require sedation. Some sedatives, such as acepromazine, interfere with platelet function and induce hypotension and therefore should not be used. Blood is collected aseptically by gravity flow or blood bank vacuum pump from the jugular vein over a 5- to 10-minute period. Plastic blood bags (e.g., ABRI, Dixon, CA) 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 for rapid storage of the blood products. Large plastic syringes containing 1 ml CPD-A1 or 3.8% citrate per 9 ml blood and connected via three-way stopcock to a 19-gauge butterfly needle (and blood bag) are used commonly for blood collection in cats or toy breed dogs (ABRI, Dixon, CA). This represents an open collection system in

which connections allow exposure of blood to the environment and potential contamination.¹⁵ Because of the risk of bacterial contamination, blood collected via an open system should not be stored for more than 48 hours. A closed collection system for cats using small collection bags has been introduced but requires a tube welder to add the anticoagulant and connect to a pediatric apheresis catheter. Vacuum glass bottles containing acid-citrate-dextrose allow rapid collection but are not recommended because blood components are readily damaged and cannot be separated and stored for long periods. The maximal donated blood volume is 20 ml blood/kg or one regular blood bag unit of 450 ± 50 ml per 25-kg or larger dog and 10 ml blood/kg or 40 ml blood (one typical feline unit) per 4-kg or larger cat. Fluid replacement is generally not needed but can be considered in cats. Feeding donors should be limited to small amounts immediately post blood collection.

Blood components are prepared from a single donation of blood by simple physical separation methods, such as centrifugation, within 8 hours of blood collection; thereby, FWB can be separated into pRBCs, PRP or platelet concentrates, FFP, cryoprecipitate, and cryopoor plasma according to the *Technical Manual of the American Association of Blood Banking*, but this does require some expertise and equipment such as a large-volume cooled centrifuge. Blood component preparation is best accomplished by using plastic blood bags with satellite transfer containers to ensure sterility. Fluctuations in storage temperature significantly alter the length of storage; thus FWB and pRBCs should be kept at $4 \pm 2^\circ\text{C}$ ($39 \pm 3^\circ\text{F}$) and all plasma products at less than -20°C (-4°F) using blood bank refrigerators and freezers with alarms, if possible. Alternative refrigerator-freezer devices may be used as long as the temperature is monitored and the unit is not opened frequently. The bottom and top shelf in regular refrigerators may not hold the required temperature and may lead to freeze-induced hemolysis or bacterial growth, respectively. Storage of canine pRBCs will result in a gradual reduction of erythrocytic 2,3-diphosphoglyceride and accumulation of potentially large amounts of ammonia, but these metabolites are rapidly regenerated or eliminated, respectively, and do not typically affect pRBC efficacy or safety. Fresher pRBC units may be safer and have longer survival in vivo than older units, but using only FWB or fresh pRBCs is logistically impractical. Caution must be exercised, however, in animals that have severe liver insufficiency; these patients may also develop hypocalcemia when given large volumes of anticoagulated plasma products. Blood components that have been warmed to room or body temperature should not be re-cooled or stored again because of safety concerns (it affects product quality). Similarly, partially used or opened blood bags should be used within 24 hours because of the risk of contamination and product damage. Stored blood products should be rotated regularly and inspected; discolored units should be discarded.

ADMINISTRATION OF BLOOD PRODUCTS

For routine transfusion therapy in anemic patients, it is not necessary to warm blood after removal from the refrigerator. Warming may accelerate the deterioration of RBCs and permit rapid growth of contaminating microorganisms. However, there are specific clinical situations (such as transfusion of neonates or resuscitation of trauma patients) that necessitate the administration of rapid, massive transfusions such that warming of the blood products is indicated to prevent complications associated with hypothermia (e.g., cardiac arrhythmias). A temperature-controlled waterbath or bowl ($\leq 39^\circ\text{C}$ [$<102^\circ\text{F}$]) is used to warm the blood products; a microwave should never be used because of the risk of regional overheating. Care should be taken to maintain absolute sterility and not to overheat any part of the blood products.

Blood bags are connected to infusion sets that have an in-line microfilter. Long (85 cm) blood infusion sets with a drip chamber for medium to large dogs and short infusion sets that can be attached to a syringe for small dogs and cats are available. A latex-free infusion set should be used for platelet administration to prevent aggregation. Microfilters with $170\text{-}\mu\text{m}$ pores are used commonly to remove clots and larger red blood cell and platelet aggregates. Finer filters with $40\text{-}\mu\text{m}$ pores will remove most platelets and microaggregates, but these commonly clog or become dysfunctional after filtering 50 to 100 ml of blood. Leukocyte reduction filters may be used at the time of blood collection to decrease febrile adverse reactions to white blood cell components, but they are expensive. Sterility must be maintained when connecting the blood component bag to the infusion set and the tubing to the catheter.

Blood components are best administered intravenously, although an intramedullary (intraosseous) catheter may be used when venous access cannot be obtained (see Chapter 194). Intraperitoneal administration is not generally recommended because absorption time is delayed and RBCs get damaged in the peritoneal cavity. Concurrent administration of drugs or fluids other than physiologic saline should be avoided to prevent lysis of erythrocytes or coagulation. Thus fluids containing calcium or glucose or those that are hypotonic or hypertonic should not be administered through the same intravenous line during the transfusion. Similarly no food should be given during a transfusion. Dripping blood via gravitational flow is preferred; most infusion pumps are not safe for the administration of RBC and platelet transfusions.

The rate of transfusion depends on the cardiovascular status, hydration status, degree of anemia, comorbidities and general condition of the recipient. The initial rate should be slow, starting with 1 to 3 ml over the first 5 minutes to observe for any transfusion reactions, even with blood-typed or crossmatched transfusions. In animals with cardiac disease, the transfusion should be given more slowly (i.e., 4 ml/kg/hr), and close monitoring is of utmost importance. Transfusion of a single bag should be completed within 4 hours to prevent functional loss or bacterial growth. The volume of the blood component needed depends on the type of deficiency and size of the animal. For treatment of anemia:

$$\text{Volume (ml) of whole blood} = 2 \times \text{PCV rise desired (\%)} \times \text{body weight (kg)}$$

In other words, administration of 2 ml whole blood/kg body weight raises the PCV by 1%. If pRBCs are used without prior resuspension in a RBC preservative, $\frac{1}{2}$ to $\frac{3}{4}$ the volume should be administered, because non-resuspended pRBCs have a PCV of 70% to 80%.

In the absence of bleeding and hemolysis, at least 70% to 80% of transfused erythrocytes survive 24 hours (required blood bank standard) and transfused erythrocytes may thereafter be expected to have a near normal life span (up to 70 days in cats, 110 days in dogs). The response to the transfusion is monitored by obtaining a PCV and total protein reading before, during, and 6 and 24 hours after transfusion, and the clinician must consider continued blood loss and hemolysis when interpreting values.

In animals with thrombocytopenia or thrombopathia, one unit of platelet concentrate (~ 50 ml), PRP (~ 200 ml), or FWB (~ 450 ml) will increase the platelet count by approximately $10,000/\mu\text{l}$ in a recipient weighing 30 kg. In animals with serious or life-threatening bleeding, the platelet count should be increased to greater than $20,000$ to $50,000/\mu\text{l}$. Platelet counts should be monitored before and 1 hour and 24 hours after platelet transfusion.

In bleeding animals with coagulopathies or von Willebrand's disease, FFP is initially administered at a dosage of approximately 10 ml/kg to stop bleeding or prevent excessive bleeding during surgery. In some cases, larger volumes may be needed to control

bleeding and, depending on the etiology of the coagulopathy, repeated administration of FFP may be required. Because of the short half-life of factors VII, VIII, and von Willebrand's factor, deficient animals may need treatment 2 to 4 times daily. Animals with other, less severe coagulopathies may be treated daily. Plasma support should be provided for an additional 1 to 3 days after the bleeding has been controlled to prevent rebleeding.

Cryoprecipitate at a dosage of 1 cryo unit (~50 ml)/10 kg or 1 to 2 ml/kg body weight twice daily is ideal to treat a bleeding animal with hemophilia A or von Willebrand's disease.

In contrast, cryo-poor plasma (6 to 10 ml/kg) is ideal for the treatment of bleeding induced by anticoagulant rodenticide poisoning because it contains the vitamin K–dependent coagulation factors.

ADVERSE TRANSFUSION REACTIONS

Although transfusion of blood and its components is usually a safe and temporarily effective form of therapy, there is always some risk involved. Adverse reactions usually occur during or shortly after the transfusion and can be caused by any component of the infused blood product. 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 necessary blood components (see Chapter 62). The most common clinical sign of a transfusion reaction is fever, followed by vomiting and hemolysis; any reaction should lead to immediate cessation of the transfusion. Hemolytic transfusion reactions can be fatal and are therefore most concerning, whereas fever and vomiting are usually self-limiting. Adverse effects of transfusions can be divided into nonimmunologic reactions (transmission of infectious agents, vomiting, mechanical hemolysis, congestive heart failure, hypothermia, citrate toxicity, and pulmonary complications) and immunologic reactions (febrile non-hemolytic transfusion reactions, acute and delayed hemolytic transfusion reactions, manifestations ranging from urticaria to anaphylaxis, and graft-versus-host disease). Note that some clinical signs may be caused by both mechanisms.

Treatment of a suspected transfusion reaction initially involves stopping the transfusion, at least temporarily. Diphenhydramine, glucocorticoids, epinephrine, and isotonic crystalloid fluid administration are most commonly used to treat these reactions. Further details on these and other treatments can be found in Chapter 62.

ALTERNATIVES

Because blood is a scarce resource and may cause serious transfusion reactions, alternatives should be considered. In many animals, treatment of the underlying disease and other supportive measures are all that is needed. Crystalloid or synthetic colloidal fluids are appropriate when hypovolemia and low oncotic pressure are the main concerns. There are currently no alternative oxygen-carrier products, such as free hemoglobin, available for veterinary use. Placing a critically ill animal in an oxygen cage with an inspired oxygen concentration greater than 21% adds little to the oxygen content in a severely anemic patient (because of a lack of hemoglobin); it will increase the oxygen content only slightly, but it does allow the animal to rest away from the hustle of a busy treatment room. Furthermore, anemic animals with concomitant pulmonary disease (as often occurs with immune-mediated hemolytic anemia caused by pulmonary thromboemboli or pneumonia) will benefit from oxygen supplementation. Although human recombinant erythropoietin has a role in the treat-

ment of anemia caused by chronic renal failure and a few other types of anemia, its effect is delayed. Therefore it is not effective for short-term treatment of anemia in the critical care patient (and does carry the risk of causing crossreacting antierythropoietin antibodies).

Although various recombinant human products are available as alternatives for supplementation of plasma proteins in human medicine, these treatment options have not been evaluated completely in small animals and may not be safe or cost effective. Human albumin concentrates have been used in dogs and cats with severe hypoalbuminemia, but serious concerns have arisen regarding its safety and effectiveness (lack of impact on survival in humans). Recombinant coagulation factors have drastically reduced the use of FFP in human patients. For instance, recombinant human FVIIa has been evaluated in dogs with factor VII deficiency (showing efficacy with minor bleeding) and other hemostatic diatheses. Similarly, there is no commercial product of a canine or feline immunoglobulin concentrate, and thus human intravenous immunoglobulin has been used successfully in the acute treatment of dermal and systemic toxic drug reactions, as well as the treatment of severe immune-mediated diseases. Again, these are human products that bear the risk of potentially fatal reactions, especially with repeated use. In conclusion, a good understanding of transfusion medicine and its benefits and risks is crucial for today's criticalist.

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