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Transfusion Medicine

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GENERAL CONSIDERATIONS

Definition

- I. Transfusion medicine is a multidisciplinary science concerned with the proper use of blood or blood products in the treatment or prevention of disease.
- II. Optimal transfusion therapy requires knowledge of blood types and crossmatching procedures, blood sources and donor selection, blood collection and administration techniques, component therapy, transfusion reactions, and red blood cell (RBC) substitutes.

Canine and Feline Blood Types

- I. Erythrocytes possess characteristic cell-surface glycolipid or glycoprotein antigens.
 - A. A blood group system is a group of antigens produced by allelic genes located at a single locus and inherited independently of any other genes. Blood group systems are species specific.
 - B. Animals commonly make antibodies against foreign blood group antigens. Naturally occurring alloantibodies may be a result of exposure to common environmental antigens that are similar or identical to foreign blood group antigens.
 - C. The importance of any particular blood group system depends on both the frequency with which alloantibodies of the system occur and the characteristics of the alloantibody, such as titer, class, temperature-dependent activity, and ability to activate complement or agglutinate RBCs.
- II. Canine blood groups have the following characteristics:
 - A. Current nomenclature uses the prefix dog erythrocyte antigen (DEA) to describe canine blood types.
 1. Antibodies or typing sera for some of the originally identified canine blood groups are no longer available, and commercial typing sera currently test for six blood types in dogs (DEA 1.1, 1.2, 3, 4, 5, and 7).
 2. Several of these blood types can occur together on the erythrocyte and may vary in frequency with breed, geographic location, and antisera used (Table 71-1) (Bull, 1976; Giger et al., 1995; Hale, 1995).
 - B. DEA 1 is a four-allele system.
 1. Dogs can be DEA 1 negative, DEA 1.1 positive or DEA 1.2 positive.

2. DEA 1.3 also has been described in Australia (Symons and Bell, 1991).
3. Naturally occurring antibody to DEA 1 is not present.
 - a. Transfusion of DEA 1-positive blood into a DEA 1-negative recipient will result in anti-DEA 1 alloantibody synthesis and shortened lifespan of the transfused erythrocytes.
 - b. Subsequent transfusions mismatched at that allele will result in an acute hemolytic transfusion reaction.
- C. DEA 3 and 5 are present in low incidence, and naturally occurring antibody to these antigens can occur (Swisher et al., 1962; Hale, 1995).
- D. DEA 4 is a high-incidence antigen with no naturally occurring antibody. A hemolytic transfusion reaction has been described in a DEA 4-negative dog given repeated transfusions of DEA 4-positive blood (Melzer et al., 2003).
- E. DEA 7 is a soluble nonerythroid antigen that is adsorbed onto the RBC surface (Bull et al., 1975), and dogs that are negative for DEA 7 may have naturally occurring anti-DEA 7 alloantibodies (Bull, 1990; Hale, 1995).

TABLE 71-1

Canine Blood Type Frequencies

DEA	FREQUENCY (%)
1.1	33 to 45
1.2	7 to 20
3	6 to 10
4	87 to 98
5	12 to 23
7	8 to 45

From Bull RW: Canine immunohematology. In *Animal Models of Thrombosis and Hemorrhagic Diseases*. Washington, DC, US Dept. of Health, Education, and Welfare Publication No. 76-982, 1976; Giger U, Gelens CJ, Callan MB et al: An acute hemolytic transfusion reaction caused by dog erythrocyte antigen 1.1 incompatibility in a previously sensitized dog. *J Am Vet Med Assoc* 206:1358, 1995.

DEA, Dog erythrocyte antigen.

- F. Canine blood donors should be DEA 1.1 and 1.2 negative if their blood is to be used with type-unmatched recipients. Dogs that are 1.1 positive can be used with DEA 1.1-positive recipients.
 - G. Dogs that are negative for DEA 1.1, 1.2, 3, 5, and 7 and are positive for DEA 4 are considered to be universal donors.
 - H. Other RBC antigens may be present. The newly described Dal RBC antigen is capable of producing a hemolytic transfusion reaction in sensitized dogs (Blais et al., 2005).
- III. The major blood group system recognized in cats is the AB system; cats can have blood types A, B, or AB.
- A. Types A and B are allelic at the same gene locus, and the A allele (A) is dominant over the B allele (a).
 - B. The rare blood type AB is thought to be the result of a third allele; however, the exact mode of inheritance is unclear (Griot-Wenk et al., 1996).
 - C. The frequencies of feline blood types vary geographically and within breeds.
 1. Type A is most common, with more than 95% of domestic shorthair (DSH) and domestic longhair (DLH) cats being typed as blood type A (Giger et al., 1989).
 2. Type B is seen in a variety of cat breeds (Table 71-2) and is seen with higher frequency in DSH and DLH cats on the west coast of the United States (Giger et al., 1991).
 - D. Cats with type B erythrocytes have strong, naturally occurring anti-A hemagglutinins and hemolysins, consisting primarily of immunoglobulin (Ig) M and a lesser amount of IgG (Bucheler and Giger, 1993). Transfusion of type A blood into a type B recipient will result in an acute hemolytic transfusion reaction following the first transfusion.
 - E. Cats with type A erythrocytes have a low titer of naturally occurring anti-B alloantibodies, consisting

of IgM hemagglutinins and IgG and IgM hemolysins (Wilkerson et al., 1991).

1. A transfusion of type B RBCs into a type A cat may induce only a minor transfusion reaction in the presence of alloantibodies.
 2. However, rapid destruction of the donor RBCs will render the transfusion ineffective.
- F. Type AB cats have neither anti-A nor anti-B alloantibodies.
 - G. Feline blood type A donors are essential, and ideally blood type B cats are also available.
 - H. Neonatal isoerythrolysis (hemolytic disease of the newborn) may be seen in kittens with type A blood born to type B queens (Bucheler and Giger, 1993).
 - I. An additional blood group antigen, the Mik RBC antigen, recently has been described. Cats that lack this antigen can form naturally occurring alloantibodies and may experience a hemolytic transfusion reaction if transfused with the Mik antigen (Weinstein et al., 2005).

TECHNICAL PREPARATIONS

Blood Typing and Crossmatching

- I. Blood typing refers to identifying RBC blood group antigens by reacting RBCs with antibodies or other reagents in an agglutination or hemolytic assay.
- II. Crossmatching refers to detecting the presence of anti-erythrocyte antibodies occurring between the donor and the recipient.
- III. The rationale for blood typing and crossmatching is as follows:
 - A. Avoid an immediate hemolytic transfusion reaction.
 - B. Provide maximum survival of transfused cells by avoiding a delayed hemolytic transfusion reaction.
 - C. Prevent sensitization of the recipient to future incompatible transfusions.
 - D. Avoid sensitization of breeding females and subsequent hemolytic disease of neonates.
- IV. Blood typing is performed in both dogs and cats.
 - A. Dogs
 1. Canine donors are ideally DEA 1.1 and 1.2 negative.
 2. If donors are typed as DEA 1.1 positive, blood is transfused only into recipients typed DEA 1.1 positive.
 3. Antisera for typing is available from Midwest Animal Blood Services (517-851-8244; Stockbridge, Mich.), but the techniques involved require laboratory skills and experience.
 4. Blood typing is also performed by some commercial veterinary laboratories or veterinary blood banks (send 2 to 7 mL of ethylenediamine tetraacetic acid [EDTA] or acid-citrate-dextrose [ACD] anticoagulated blood via overnight mail).
 5. Cards for the typing of DEA 1.1 are available from DMS Laboratories, Inc., 2 Darts Mill Road, Flemington, NJ 08822, (800-567-4367).

TABLE 71-2

Blood Type B Frequencies in Feline Breeds in the United States

TYPE B FREQUENCY (%)	BREEDS
0	Siamese, Burmese, Tonkinese, Russian blue, ocicat, Oriental shorthair
<5	Maine coon, Norwegian forest, DSH, DLH
5 to 25	Abyssinian, Himalayan, Birman, Persian, Somali, sphinx, Scottish fold, Japanese bobtail
25 to 50%	Exotic and British shorthair, Cornish rex, Devon rex

From Giger U, Griot-Wenk M, Bucheler J et al: Geographical variation of the feline blood type frequencies in the United States. *Fel Pract* 19:21, 1991.

DSH, Domestic shorthair cat; DLH, domestic longhair cat.

6. Gel testing for DEA 1.1 (Giger et al., 2005) is available from Diamed North America, Inc. (305-558-0161; Miami, Fla.).
- B. Cats
1. Blood type A and B donors are needed, but the majority of feline recipients are blood type A.
 2. Blood typing can be performed by some commercial veterinary laboratories or veterinary blood banks (send 2 to 3 mL of EDTA or ACD anticoagulated blood via overnight mail).
 3. Cards for the typing of A and B are available from DMS Laboratories, Inc. .
 4. Gel testing for A and B typing (Stieger et al., 2005) is available from Diamed North America, Inc.
- V. Crossmatching is very important.
- A. Crossmatching in dogs is advised, even at first transfusion, to detect the presence of antibodies to blood groups.
- B. Crossmatching is imperative in dogs that have been transfused previously.
- C. Crossmatching in dogs does not indicate that the donor and recipient are the same blood type, and thus does not prevent sensitization.
- D. Crossmatching does not guarantee that a transfusion reaction from white blood cell, protein, or platelet incompatibility will not occur.
- E. Crossmatching is crucial in cats because of the high prevalence of naturally occurring alloantibodies.
- F. Crossmatching is divided into two parts (Box 71-1).
1. In the major crossmatch, the recipient's plasma is mixed with the donor's RBCs.
 2. In the minor crossmatch, the donor's plasma is mixed with the recipient's RBCs.
- G. A major crossmatch kit that uses gel tubes to detect a positive/incompatible response is commercially available (Midwest Animal Blood Services, Inc.).
- H. The major crossmatch is the most important for a safe transfusion.
1. The minor crossmatch is of less clinical significance because donor antibodies administered intravenously are rapidly diluted within the recipient.
 2. Nonetheless, blood resulting in an incompatible minor crossmatch is best avoided for transfusion.

Blood Sources

- I. Commercial sources
- A. Several commercial veterinary blood banks exist in the United States.
 - B. These blood banks can supply canine and/or feline whole blood, plasma, and packed RBCs.
- II. Blood donors
- A. Inpatient donors are those that are kept on the premises, usually for emergency situations.
 - B. Outpatient donors, also known as *volunteer donors*, are generally client-owned animals brought in for emergency or regularly scheduled blood donations.
 - C. Selection and maintenance of canine donors is as follows:

Box 71-1

Crossmatching Procedure

1. Obtain an anticoagulated (EDTA) and nonanticoagulated specimen of blood from animal and donor.
 2. Centrifuge at $1000 \times g$ (2500 to 3500 rpm) for 10 minutes and separate serum from RBCs.
 3. Wash RBCs by adding 2 to 4 drops of EDTA blood to three quarters of a tube (12×75 -mm size) of saline or phosphate-buffered saline, mixing and centrifuging for 1 minute at $1000 \times g$. Decant the saline and repeat three times.
 4. After last wash, decant supernatant and resuspend cells with saline to give a 2% to 4% suspension (0.1 mL of RBCs in 2.4 mL saline gives a 4% suspension).
 5. Make the following mixtures by adding the indicated amount of the well-mixed RBC suspension and serum to 12×75 -mm tubes and mixing gently:
 - a. *Major crossmatch*: 2 drops patient sera, 1 drop donor 2% to 4% RBC suspension
 - b. *Minor crossmatch*: 2 drops donor sera, 1 drop patient 2% to 4% RBC suspension
 - c. *Include controls*: 2 drops patient sera, 1 drop patient 2% to 4% RBC suspension and 2 drops donor sera, 1 drop donor 2% to 4% RBC suspension
 6. Incubate tubes 15 to 30 minutes at 37°C .
 7. Centrifuge for 15 seconds ($1000 \times g$).
 8. Examine tubes for hemolysis and agglutination.
 - a. Rotate gently to observe cells coming off the red cell "button" in the bottom of the tube.
 - b. In a compatible reaction, there is no hemolysis and the cells should float off freely, with no macroscopic or microscopic clumping/hemagglutination (compare to the control tubes).
 9. Rouleaux formation can be falsely interpreted as agglutination. If rouleaux is suspected, a saline replacement technique can be used (replace serum with saline, mix, recentrifuge, and re-evaluate).
1. Use large dogs (>30 kg), 1 to 7 years old, with a packed cell volume (PCV) $>40\%$ and in good physical condition.
 2. Use DEA 1.1- and 1.2-negative donors if possible.
 - a. DEA 1.1 negative status is a must unless recipients are type matched.
 - b. Avoid donors with a history of previous transfusions or pregnancy, as they may have developed antierythrocyte antibodies.
 3. Dogs should have normal von Willebrand factor (vWf) concentrations (if their plasma is to be used to provide this factor) and be negative for *Babesia canis*, *Babesia gibsoni*, *Leishmania donovani*, *Ehrlichia canis*, and *Brucella canis*.
 4. Screening for other infectious organisms may be necessary, depending on the geographic region (Wardrop, 2005).

5. Keep canine donors current on routine immunizations (distemper, adenovirus, parvovirus, coronavirus, rabies, leptospirosis, parainfluenza).
 6. Donor dogs should test negative for *Dirofilaria immitis*, and dogs in endemic areas should be on preventative therapy.
 7. Fecal flotation, hemograms, and chemistry profiles should also be performed to ensure the health of the donor.
 8. Iron supplementation is advisable with frequent donation.
- D. Selection and maintenance of feline donors is as follows:
1. Use feline donors in good physical condition, >3.5 kg, 1 to 7 years old, and having a PCV >35%.
 2. Blood type A donors are essential, and ideally blood type B cats are also available for use.
 3. Cats must be negative for feline leukemia virus (FeLV), feline immunodeficiency virus, and *Mycoplasma* spp.
 4. Screening for *Bartonella* spp. should also be considered (Wardrop, 2005).
 5. Keep feline donors current on routine immunizations (feline parvovirus, viral rhinotracheitis, calicivirus, rabies, FeLV).
 6. Annual fecal flotation, hemograms, and chemistry profiles are performed.
 7. Consider iron supplementation with frequent donation.

Blood Collection and Storage

- I. Canine blood collection
 - A. Jugular venipuncture is performed with the dog sitting, or in lateral or sternal recumbency.
 - B. Blood is collected by gravity or with the aid of a vacuum system into anticoagulant, such as ACD, citrate-phosphate-dextrose (CPD) or derivatives.
 - C. For whole blood, a single ACD, CPD or citrate-phosphate-dextrose-adenine (CPDA-1) plastic bag is used.
 - D. For components, a CPD or CPDA-1 bag is used with sterilely attached satellite bags or an additive solution (e.g., *Adsol*, *Optisol*) system.
 - E. If sedation is required, butorphanol (0.1 mg/kg IV) may be administered 15 minutes before collection (Hohenhaus, 2000).
- II. Feline blood collection
 - A. Blood collection in cats generally requires sedation, and a combination of ketamine (1 to 2 mg/kg), diazepam (0.1 mg/kg) and atropine (0.01 mg/kg) can be administered IV (Griot-Wenk and Giger, 1995).
 - B. Inhalant anesthesia with sevoflurane has also been described (Troyer et al., 2005).
 - C. With the cat in sternal, lateral, or dorsal recumbency, blood is collected from the jugular vein into a syringe containing ACD, CPD, or CPDA-1 solutions (1 mL/9 mL blood), or heparin (5 units/mL blood).

- D. Feline blood cannot be stored in a syringe.
 1. If blood is to be stored, blood obtained via syringe can be sterilely transferred to a small collection bag.
 2. Systems consisting of a syringe attached directly to a blood bag are available from commercial veterinary blood banks.

- III. Frequency and volume of donation for canine and feline donors
 - A. Amount drawn from dogs
 1. A total of 15 mL/kg or 450 mL can be safely taken from a 30-kg dog, with ideal frequency no more than every 6 weeks.
 2. Reduce the frequency of donation if the PCV or total protein fails to return to baseline values.
 - B. Amounts drawn from cats
 1. A total of 10 to 15 mL/kg or 60 mL total can be taken every 6 weeks in cats.
 2. Reduce the frequency of donation if the PCV or total protein fails to return to baseline values.

THERAPEUTIC CONSIDERATIONS

Component Therapy

- I. Whole blood is often centrifuged and processed into blood components, such as packed RBCs, plasma, platelets, and cryoprecipitate, by using multiple, sterilely connected plastic bags.
- II. Advantages to blood component therapy include better conservation of blood resources, longer storage of components, more specific therapy, and fewer complications from circulatory overload because of the minimal volume administered.
- III. Component types and indications are as follows:
 - A. RBCs
 1. Fresh whole blood provides coagulation factors, other proteins (albumin and globulins), RBCs, and platelets.
 - a. It is used where multiple components are needed.
 - b. Stored whole blood does not provide viable platelets or sufficient labile coagulation factors.
 2. Packed RBCs are the best product for most RBC needs and can be supplemented with plasma or platelets if needed.
 3. The shelf life or expiration date of RBCs may vary with the anticoagulant-preservative used.
 4. Whole blood can generally be stored for 3 to 4 weeks at 1° to 6° C, whereas packed RBCs in additive can be stored for 5 weeks (Wardrop, 1995).
 - B. Plasma
 1. Fresh frozen plasma (FFP) is plasma that has been frozen within 6 hours of collection and stored at -18° C or colder.
 - a. It contains labile (V and VIII) and stable (II, VII, IX, and X) coagulation proteins.
 - b. It is used to treat hemophilia A, hemophilia B, von Willebrand disease, warfarin toxicity, or other factor deficiencies.

- c. It can be stored for 1 year from the collection date (Brooks, 2000).
- 2. Cryoprecipitate-poor plasma is plasma with cryoprecipitate removed.
 - a. This plasma contains the more stable clotting factors and can be used in cases of warfarin toxicity or hemophilia B.
 - b. Cryoprecipitate-poor plasma and frozen plasma can be stored for up to 5 years.
- 3. Frozen plasma is plasma that has been frozen >6 hours after blood collection (e.g., removed from expired whole blood units), or FFP that has been stored >1 year.
- 4. Either FFP, cryoprecipitate-poor plasma, or frozen plasma may be used in cases of hypoproteinemia; however, synthetic colloids such as hetastarch are probably more effective in severe hypoproteinemias resulting from renal or intestinal protein loss.
- C. Platelets
 - 1. Platelet-rich plasma or platelet concentrates may be used to stop or prevent hemorrhage in animals with thrombocytopenia or platelet function disorders.
 - 2. Fresh whole blood may be substituted as a source of platelets when components are unavailable.
 - 3. Platelet products must be stored at room temperature (no refrigeration) and their storage time is short—3 to 5 days with continuous agitation.
- D. Cryoprecipitate
 - 1. Prepared from FFP as a concentrated form of factor VIII:C, vWf, and fibrinogen
 - 2. Preferred component for treatment or prevention of hemorrhage resulting from hemophilia A or von Willebrand disease
 - 3. Stored at -18°C or colder for up to 1 year from collection date

Administration

- I. General guidelines
 - A. Use blood or component administration sets with filters (150 to 170 μm) to administer all blood or blood products.
 - B. Only normal saline (0.9%) may be mixed with blood components.
 - C. Monitor temperature, pulse and heart rate, and respiratory rate and sounds before, during, and after transfusion.
 - D. Volume overload can occur if too much of a blood product is given or if the product is given too quickly, especially if the animal has cardiac or renal disease.
 - E. Complete the transfusion within 4 hours.
 - F. Use the intravenous route; the osseous intramedullary route may be used if necessary.
- II. Rate and volume
 - A. The desirable rate of infusion varies with the patient's blood volume, hemodynamic condition, and cardiac, renal and hepatic status of the animal.
 - 1. Give slowly (<5 mL/kg/hr IV) for the first 15 minutes, then increase rate.

- 2. Give more rapidly in hypovolemic animals.
- 3. Give more slowly in animals with cardiac, hepatic, or renal failure (approximately 1 mL/kg/hr IV).
- B. Volume of whole blood or packed RBC to administer is calculated as follows:
 - 1. Determine the PCV of the animal.
 - 2. Volume (mL) of donor blood in anticoagulant to administer is calculated as follows:

$$\frac{\text{Animal weight (kg)} \times \text{blood volume}}{\text{desired PCV} - \text{present PCV}} \times \frac{\text{PCV of donor blood in anticoagulant}}{\text{PCV of donor blood in anticoagulant}}$$

NOTE: The blood volume in the dog is approximately 90 mL/kg; the volume in the cat is approximately 70 mL/kg.

- 3. Transfusion of 20 mL/kg of whole blood or 10 to 15 mL/kg of packed RBC raises the PCV of the recipient by 10%.
- C. FFP, frozen plasma or cryoprecipitate-poor plasma are given as follows:
 - 1. To thaw, place in a waterproof plastic bag and thaw at 37°C .
 - 2. Thawing at room temperature or in a refrigerator is avoided because cryoprecipitate will form.
 - 3. Administer immediately on thawing, or store between 1° and 6°C .
 - 4. Administer FFP within 24 hours of thawing if used as a source of labile coagulation factors.
 - 5. Give at the rate of 5 to 10 mL/kg/hr IV.
 - 6. Use 10 to 20 mL/kg of plasma to treat coagulation deficiencies or hypoalbuminemia (NOTE: Synthetic colloids may be preferred for increasing oncotic pressure in hypoalbuminemic cases).
- D. Administer platelet-rich plasma or platelet concentrate as follows:
 - 1. Give at 5 to 10 mL/kg/hr IV.
 - 2. Dosage is 1 unit (from 450 mL of blood)/10 kg to increase the platelet count by 20,000 to 40,000/ μL .
 - 3. Frozen canine platelets are available commercially.
 - a. One unit of frozen platelets/10 kg increases the platelet count by approximately 20,000 platelets/ μL .
 - b. The product expires 6 months from the time of collection.
- E. Cryoprecipitate requires special handling.
 - 1. Thaw in a waterproof plastic bag at 37°C ; do not thaw in a refrigerator or at room temperature.
 - 2. A bag of cryoprecipitate prepared from 200 mL of plasma contains approximately 100 to 150 units of vWf and factor VIII:C.
 - 3. The product is administered at a dosage of 10 to 20 U/kg IV.

Transfusion Reactions

- I. Immediate, immune-mediated reactions
 - A. Hemolytic transfusion reaction
 - 1. Caused by antibodies in recipient plasma that destroy donor RBCs

2. Can occur as early as 5 minutes after initiating transfusion
 3. Clinical signs: fever, tachycardia or bradycardia, hypotension, dyspnea, cyanosis, emesis, defecation, collapse, opisthotonus, cardiac arrest, hemoglobinemia, or hemoglobinuria (Giger and Akol, 1990; Giger et al., 1995)
 4. Treatment
 - a. Stop the transfusion and treat for shock, with maintenance of cardiac, respiratory, and renal function.
 - b. Avoid this reaction through appropriate typing and crossmatching before transfusion.
- B. Nonhemolytic febrile reaction
1. Characterized by temperature rise of 1° C (2° F) occurring within 1 to 2 hours of transfusion without hemolysis or another explanation.
 2. The reaction arises from recipient antibodies directed against donor leukocyte antigens.
 3. Rule out early hemolytic or septic reaction.
 4. Stop transfusion; use antipyretics if necessary.
- C. Urticarial reaction
1. Recipient antibodies directed against donor plasma proteins
 2. A relatively common but mild complication of transfusions
 3. Treatment: stop or slow transfusion, diphenhydramine 2 mg/kg IM
- II. Immediate, nonimmune-mediated reactions
- A. Sepsis
1. Usually not a problem if care has been taken to properly prepare donor phlebotomy site, a closed system is used, and the blood product is appropriately stored
 2. Reactions generally from endotoxins
 3. Signs of endotoxic shock: fever, hypotension, disseminated intravascular coagulation, renal failure
 4. Treatment: for shock, antibiotics
 5. Culturing of blood bag indicated
- B. Circulatory overload
1. Seen more commonly with compromised cardiac, pulmonary or renal function, especially in cats and miniature or toy breeds of dogs
 2. Signs: coughing, cyanosis, and dyspnea (pulmonary edema)
 3. Treatment: stop transfusion, institute diuretics and cardiorespiratory support
- C. Citrate toxicity
1. Hypocalcemia from rapid infusion of citrated products (whole blood, plasma)
 2. Signs: vomiting, tremors, tetany
 3. Treatment: stop transfusion, resume at slower rate, and administer calcium gluconate if reaction severe
- D. Hemolysis
1. From improper blood handling (e.g., freezing or overheating of blood or mixing with nonisotonic solutions)

2. Causes hemoglobinemia/hemoglobinuria and must be differentiated from an immune-mediated hemolytic transfusion reaction

III. Delayed reactions

- A. Immune-mediated: delayed hemolytic transfusion reaction
1. Within 3 days (anamnesic response) or several weeks (primary response) after transfusion
 2. Not detected by crossmatching
 - a. An unexplained decline in PCV and positive direct antiglobulin test
 - b. Possibly asymptomatic or presence of fever and icterus
 - c. Treatment: not generally required
- B. Nonimmune-mediated
1. Reactions arise from infectious diseases.
 2. All donors must be carefully selected and screened to avoid transmittance of disease.

Red Blood Cell Substitute

- I. A hemoglobin-based oxygen-carrying solution (Oxyglobin, Biopure Corp., Cambridge, Mass.) has been approved by the Food and Drug Administration (FDA) for use in dogs with anemia (Rentko and Sharpe, 2000).
- II. Oxyglobin is purified bovine hemoglobin in a modified lactated Ringer's solution.
 - A. It is isosmotic, with a pH of 7.8, and half-life of 18 to 43 hours, depending on dosage.
 - B. The product comes in 125 mL bags and can be stored for 3 years at room temperature.
- III. The recommended dosage in dogs is 10 to 30 mL/kg IV at a maximal rate of 10 mL/kg/hr.
- IV. A standard IV infusion set can be used, and crossmatching is not required.
- V. Overdose or rapid administration can cause circulatory overload.
 - A. Monitor using hemoglobin, not PCV.
 - B. It is contraindicated in dogs with advanced cardiac disease or with acute renal failure, because of the potential for circulatory overload.
- VI. Side effects include skin and mucous membrane discoloration, vomiting and diarrhea, alterations in serum chemistries from discoloration of serum, and transient hemoglobinuria.

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