Some private clinics and universities have their own canine and feline donor programs to source blood products for transfusion.
Hematology

Blood Transfusions in Anemic Dogs and Cats

Anemia is a condition of decreased oxygen carriage capacity that may be caused by an absolute decrease in red blood cell (RBC) numbers, hemoglobin concentrations, or packed cell volume (PCV). Normal reference values may vary based on species, breed, sex, reproductive status, age, and geographic location. Sources of error in laboratory findings that can lead to incorrect diagnosis of anemia may include inadequate mixing of sample, hemolysis due to inappropriate sample handling, and improper ratio of blood volume to ethylenediaminetetraacetic acid (EDTA) concentration.

Mechanisms of true anemia include:
- Destruction of RBCs, such as in immune-mediated hemolytic anemia, bloodborne parasite infection, neoplasia, and toxicoses.
- Increased loss of blood from hemorrhage, such as in trauma, neoplasia, bleeding disorders, and internal/external parasitism.
- Decrease in RBC production, such as in iron deficiency, drug toxicosis, neoplasia, and renal failure.

Anemia can be categorized as regenerative or nonregenerative. In regenerative anemia, there is evidence of active erythropoiesis such as increased numbers of reticulocytes, nucleated RBCs, and polychromasia. Regenerative responses indicate that anemia is due to loss or destruction of RBCs. Nonregenerative anemia is the result of inadequate erythropoiesis. Although decreased bone marrow

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HemoSolutions, LLC
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production is the most common cause of nonregenerative anemia, blood loss and RBC destruction cannot be ruled out. Since bone marrow takes 3 to 5 days to respond to anemia, acute hemorrhage or hemolysis may appear nonregenerative. Clinical signs of anemia are listed in BOX 1.

ROLE OF BLOOD TRANSFUSION IN MANAGEMENT OF ANEMIA

RBC-containing transfusion products are used to replace or restore oxygen-carrying capacity in patients with anemia when fluids alone are not sufficient to correct tissue hypoxia.

A specific PCV at which RBC transfusion is necessary has not been identified. The entire clinical picture of the patient must be considered. Ideally, the approach to treatment should be individualized for each patient and be guided by its clinical signs and hematologic values. The goal of an RBC transfusion is to restore oxygen delivery to the tissues, and normalizing the PCV is typically not necessary to achieve this goal; therefore, the transfusion plan should be tailored to the patient’s needs and not to a specific PCV. The following clinical signs may indicate the need for an RBC transfusion.

- Tachycardia
- Tachypnea
- Prolonged capillary refill time
- Hypotension
- Mucous membrane color
- Acute blood loss >30% of body weight
- PCV <20% with other clinical signs consistent with hypoxia
- Hypoproteinemia
- Unresponsive to crystalloid or colloid therapy

BLOOD PRODUCT SELECTION

Component therapy is the separation of whole blood into individual fractions containing the transfusable components, including red cells, platelets, plasma, proteins, and cryoprecipitate. The use of component therapy is considered the most effective method of balancing clinical needs, risks of reaction, and restrictions of blood product availability. Appropriate blood products to treat anemia include fresh whole blood, stored whole blood, and packed RBCs (PBRCs).

Whole Blood

Fresh whole blood contains all blood components, including RBCs, white blood cells, platelets, coagulation factors, albumin, globulins, and electrolytes. It is not processed and can be administered immediately or within 4 to 6 hours of collection at room temperature for optimal platelet activity. Transfusion of fresh whole blood is rarely indicated, as it increases the risk for transfusion reaction and is an inefficient use of limited resources.

Stored whole blood can be maintained in the refrigerator for 35 days at 1 °C to 6 °C. Platelets in stored whole blood are not viable after 24 hours. Administration of stored whole blood is only indicated for RBC replacement and volume expansion.

Packed Red Blood Cells

Unites of PRBCs contain RBCs, white blood cells, nonviable platelets, and a small amount of plasma. PRBCs can be stored for 35 to 42 days at 1 °C to 6 °C. During storage, PRBC units should be gently rocked daily to allow the cells access to nutrients, and they should be placed with space between them to allow appropriate oxygen exchange for RBC viability. PRBCs are used to improve oxygen-carrying capacity. When volume expansion is also necessary, the use of crystalloid fluids along with PRBCs produces results comparable to that of whole blood while decreasing the risk for transfusion reactions.

Although plasma products are not directly indicated for the treatment of anemia, products such as fresh frozen plasma, frozen plasma, cryoprecipitate, and platelet products may be necessary to control specific coagulopathies and decrease blood loss.
SOURCES OF BLOOD PRODUCTS
Several commercial blood banks can provide blood products. A list is available on the Association of Veterinary Hematology and Transfusion Medicine website (avhtm.org). Except for the California Department of Food and Agriculture, no organizations govern or regulate animal donor programs. Many blood banks voluntarily follow the 2016 American College of Veterinary Internal Medicine (ACVIM) consensus statement.¹

Some private veterinary clinics and universities have their own canine and feline donor programs that use employee-, student-, and/or volunteer-owned donors. Screening protocols should be evaluated before using their products. Clinics are encouraged to critically evaluate the operating procedures of their preferred blood source to ensure safe and efficacious transfusions.

BLOOD TYPING AND CROSSMATCHING
Over the past several years, veterinary transfusion medicine has made continuous strides to ensure the safety and efficacy of transfusions. Typing and crossmatching between donors and recipients not only significantly reduces the risk of transfusion reactions but also allows for more efficient use of colony donors and available resources. Use of incompatible products is detrimental to the intended recipient and the purpose of the transfusion and reduces the life span of the transfused product.

Dog Erythrocyte Antigens
Blood types in dogs are determined by the different proteins and complex carbohydrates located on RBC membranes, known as dog erythrocyte antigens (DEAs). Canine blood types include DEA 1, 3, 4, 5, and 7. One dog may possess multiple DEAs. DEA 1 is highly antigenic and is known to cause the more recognizable transfusion reactions. To further complicate compatibility discussions, the Dal, Kai 1, and Kai 2 antigens have also been identified. The absence of the Dal antigen is rare but is most common in Dalmatians, Doberman pinschers, and Shih Tzus.²³ The clinical relevance of Kai 1 and Kai 2 is uncertain at this time. In addition, 8 other antigens with variable clinical relevance have been described in dogs over the past 50 years.

Although the percentages vary geographically, approximately 63% to 67% of the canine population is positive for DEA 1. Recently, testing for DEA 4 and 5 has also become available. Ideally, DEA 1–positive blood products should be administered to DEA 1–positive recipients, allowing DEA 1–negative blood to be administered to DEA 1–negative recipients when necessary.

Feline Erythrocyte Antigens
There are 3 blood types in the feline population: A, B, and AB. Type A is the most common, type B occurs in 5% to 10% of cats, and AB is exceedingly rare in all breeds. The Mik antigen has also surfaced. Its relevance is not entirely understood at this time. The Mik antigen is present in most cats. Cats that are Mik negative are at risk for transfusion reactions. There is no “universal” blood type in cats. Cats have naturally occurring alloantibodies to the other blood groups even without prior transfusions.

Two typing systems for identifying feline erythrocyte antigens (FEAs) are commercially available.

Blood Typing Tests
Both tests described in BOX 2 have advantages and disadvantages. Veterinary nurses must acquaint themselves with the products and form their own preference.

Major and Minor Crossmatching
Blood typing identifies certain known antigens in the patient and donor but does not identify antibodies in the patient or donor. The crossmatch procedure...
Blood Typing Tests: Step by Step

RapidVet-H Blood Typing Cards
Complete within 2 minutes in any clinical setting. The results of these tests are difficult to read when the patient has a low packed cell volume (PCV) and there are not enough cells to agglutinate. They may be subjective if performed by someone not comfortable with reading agglutination results. These tests have a shelf life of 24 months.

Canine
- Designed to identify a single dog erythrocyte antigen (DEA) (1, 4, or 5, **FIGURE A**).
- The test is set up with 3 wells: negative control, positive control, and patient. The provided buffer solution is added to each well. A positive control and a negative control are placed in their respective wells, and the recipient blood is placed into the patient well.
- Any agglutination in the patient well, no matter how subtle, means that patient is positive for the tested antigen.
- Always use the agglutination card that comes in the test. If agglutination is present, cell washing is necessary to continue. Continuing without cell washing will give a false-positive result.

Feline
- Designed to identify type A, B, or AB feline erythrocyte antigens (FEAs) (**FIGURES B, C, AND D**).
- One drop of buffer and one drop of patient blood are placed into each well.
- An additional drop of buffer is placed only into the type A well and observed for agglutination. This is an especially important step that is often overlooked. If this step is not completed, the results will be inaccurate.
- Through capillary action, solution migrates up the membrane, revealing a control line and a line that represents the presence or absence of DEA 1 (for canine) or FEAs A, B, or AB (for feline).
- Even the weak appearance of a line is considered a positive result.
- This test is accurate even in the presence of agglutination or in samples with incredibly low PCV; however, the lower the PCV, the lighter the control appears.

QuickTest for Canine and Feline
Complete within 2 minutes in any clinical setting. The canine test is designed to identify only the DEA 1 antigen (**FIGURE E**). The feline test is designed to identify FEAs A, B, and AB (**FIGURE F**).
- For either test, add 3 drops of buffer (provided in the kit) and one single drop of blood into the provided well.
- Place a membrane strip previously treated with monoclonal antibodies into the solution.

**From top:** Courtesy RapidVet (4); Courtesy Alvedia (2).
determines whether there is an antibody reaction to antigens in the donor and is performed to determine compatibility or incompatibility between donor and recipient. Screening for compatibility maximizes patient safety by reducing the risk of immune-mediated hemolytic transfusion reactions and improving survival of the RBCs. Major crossmatching detects antibodies in the recipient’s serum that may agglutinate or lyse the donor’s RBCs. Minor crossmatching detects antibodies in the donor’s plasma directed against recipient RBCs.

Point-of-care testing can be performed manually or with affordable commercially available kits; therefore, crossmatching is considered the standard of care in transfusion medicine. It should be used in addition to blood typing, not as a substitute. Identification of the feline Mik and canine Dal, Kai 1, and Kai 2 antigens further supports the necessity of crossmatching all RBC transfusions.

A 2016 study evaluated the accuracy of a gel-based commercial crossmatching kit and compared it with the standard manual method in a private veterinary referral practice. The authors concluded that the gel-based test was 3x faster to perform; however, microagglutination and low-grade hemolysis made it difficult to interpret the test results, potentially leading to transfusion reactions. Standard manual crossmatching (BOX 3) remains the gold standard to determine compatibility.

Crossmatching is absolutely essential in patients that have been previously transfused with RBCs in the past 4 to 7 days, that have a transfusion reaction history, or for which the transfusion history is unknown. Although most dogs lack natural antibodies to DEA 1 and therefore may not react to an initial transfusion with DEA 1–positive blood, such an exposure puts them at risk for severe reactions to a second transfusion. One study found that 7 out of 9 dogs receiving DEA 1–positive RBCs became sensitized to other RBC antigens. Another study concluded that crossmatching incompatibility can exist even between first-time transfusion recipients and potential blood donors.

In the past, it was thought that pregnancy sensitized female animals to RBC antigens; however, this theory is no longer supported.

**Pretransfusion Preparation**

Treatment with steroids or antihistamines prior to transfusion is not recommended, as it may mask transfusion reactions. Initial vital signs should be recorded and the patient fully evaluated before beginning the transfusion. The presence of vomiting, facial edema, hemolysis, or pigmenturia before transfusion should be recorded on a form such as the one shown in the sample (BOX 4).
BOX 4

Sample Transfusion Record

Veterinary nurse name ___________________________ Date _______________________
Client ___________________________ Patient ___________________________ Weight ________ kg
Diagnosis ___________________________ Prior blood products ________ When ___________
Patient’s blood type ___________________________

1) Product ID # ___________________________ Crossmatch performed? ______________ 
2) Product ID # ___________________________ Crossmatch performed? ______________ 
3) Product ID # ___________________________ Crossmatch performed? ______________ 

Initial vitals: Temp ________ HR ________ RR ________ MM ________ PCV/TP ________ PT/APTT ________
Patient’s mentation: __________________________

Discontinue IV medications/dextrose/LRS if transfusion is not through a dedicated IV line ______________
Visible signs of bruising, swelling, vomiting, diarrhea prior to start? ______________
Administration rate 0.50–1 mL/kg/hr _15 minutes. Then increase rate as needed. Transfusion should be
completed within 4 hours. Total volume to be transfused: ________ mL

Slow or stop transfusion if the following parameters are reached:
Temp = Initial + 1.5 °F ______________ HR = Initial × 1.5 ________ RR = Initial × 1.2 ________

<table>
<thead>
<tr>
<th>Time</th>
<th>Time Lapse</th>
<th>Rate</th>
<th>Volume Completed</th>
<th>Temp</th>
<th>Heart Rate</th>
<th>Respiration</th>
<th>Reaction</th>
<th>Reaction Treatment</th>
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<td>3.5 hours</td>
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</tbody>
</table>

Total volume administered: ________ mL
2-hour post-transfusion PCV/TP ________ 2-hour post PT/APTT ________
Additional notes: __________________________________________________________
___________________________________________________________
___________________________________________________________
Ideally, a separate large-bore catheter should be aseptically placed for administration of blood products. If additional venous access is not feasible, fluid therapy and medications should be discontinued during transfusion.

**ADMINISTRATION OF RED BLOOD CELL PRODUCTS**

RBCs should be stored in a refrigerator designated specifically for the hospital’s blood supply at a temperature of 2 °C to 6 °C. Units should never be frozen or microwaved. Once spiked, a unit of RBCs should be transfused immediately or placed in the refrigerator and used within 24 hours.

An end-user log should be maintained for all units to track their source, draw date, expiration date, and recipient. Units should not be used after their expiration date.

Administration rates should start slowly (0.5 mL/kg/hr) for 15 to 30 minutes, with hands-on patient monitoring every 10 to 15 minutes to ensure there is no evidence of transfusion reactions. Vital statistics that should be recorded immediately prior to and throughout the transfusion include temperature, heart rate, pulse rate and quality, respiration rate, mucous membrane color, urine color, and capillary refill time. An increase of 1.5 °F in initial temperature, 1.5× the initial heart rate, or 1.2× the initial respiratory rate is an indication to slow or stop the transfusion.

A veterinary transfusion guide smartphone app is available from BodeVet (Veterinary Transfusion Guide; bodevet.com). It offers information on product selection, administration rates, and dosages that can be useful; however, all decisions for individual patients are at the discretion of the doctor and depend on the patient’s condition, diagnosis, and response.

**BOX 5** lists some specific precautions to take during the transfusion procedure.

**TRANSFUSION REACTIONS AND THEIR TREATMENT**

Transfusion reactions can vary from mild to life-threatening. Severe, acute reactions result in hemolysis, disseminated intravascular coagulation (DIC), shock, and renal failure. Cats receiving mismatched transfusions and dogs with a second exposure to an...
incompatible blood type are at risk for severe reactions. Most reactions can be avoided with proper typing, crossmatching, monitoring, and storage practices.

Early detection of transfusion reactions and appropriate intervention are key to positive outcomes. Use of a transfusion monitoring worksheet is recommended.

Transfusion reactions are classified as immunologic, delayed immunologic, nonimmunologic, and delayed nonimmunologic. Clinical signs of transfusion reactions are listed in TABLES 1 AND 2.

Immunologic Reactions

Hemolytic Reactions
Hemolytic transfusion reactions are caused by hemolysis of transfused RBCs by preexisting antibodies in the recipient’s plasma. These are immediate, dramatic, life-threatening reactions. The severity of the reaction is determined by the amount of incompatible blood that is transfused.

Hemolytic reactions are rare in dogs receiving a first transfusion due to the low prevalence of naturally occurring RBC alloantibodies. Antibody synthesis after an initial transfusion can result in a potentially fatal hemolytic reaction to subsequent transfusions. This occurs in DEA 1–negative dogs transfused with DEA 1–positive RBCs and can be prevented with typing for the DEA 1 antigen. Cats often have natural RBC alloantibodies, making hemolytic reactions more likely. Therefore, blood typing is essential in cats, even before the first transfusion.

Treatment for hemolytic reactions may include discontinuation of the transfusion; fluid therapy; or administration of antihistamines, glucocorticoids, and vasopressors at the veterinarian’s discretion.

Hypersensitivity Reactions
Hypersensitivity reactions are allergic reactions triggered by proteins and other substances in the donor plasma. These reactions range from mild to life-threatening. They are minimized by use of component therapy (i.e., blood products without plasma). Treatment depends on the severity of the reaction. Slowing the rate of transfusion; administration of antihistamines, corticosteroids, or vasopressors; or discontinuation of the transfusion may be considered.

Febrile Reactions
Nonhemolytic febrile reactions are one of the most common reactions and are thought to be due to white blood cell cytokine production in stored products. As white blood cells deteriorate, they initiate a negative cascade of events, releasing inflammatory products that induce a febrile reaction in the recipient. Leukoreduction, which is the process of removing white blood cells from whole blood before separating or storage, can reduce the incidence of febrile reactions.

These reactions may respond to slowing the rate of transfusion. Active cooling measures may be necessary for temperatures greater than 104 °F. In rare cases, the veterinarian may choose to use antipyretics.

TABLE 1 Common Clinical Signs of Transfusion Reactions

<table>
<thead>
<tr>
<th>IMMUNOLOGIC REACTIONS</th>
<th>IMMUNOLOGIC REACTIONS</th>
</tr>
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<tbody>
<tr>
<td>HEMOLYTIC</td>
<td>HYPERSENSITIVITY</td>
</tr>
<tr>
<td>Fever</td>
<td>Hives</td>
</tr>
<tr>
<td>Tachycardia or bradycardia</td>
<td>Edema</td>
</tr>
<tr>
<td>Hypotension</td>
<td>Redness</td>
</tr>
<tr>
<td>Dyspnea</td>
<td>Vomiting</td>
</tr>
<tr>
<td>Cyanosis</td>
<td>Diarrhea</td>
</tr>
<tr>
<td>Salivation</td>
<td>Tachypnea</td>
</tr>
<tr>
<td>Lacrimation</td>
<td>Tachycardia</td>
</tr>
<tr>
<td>Urination</td>
<td>Hypotension</td>
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<tr>
<td>Defecation</td>
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<tr>
<td>Emesis</td>
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<tr>
<td>Collapse</td>
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<tr>
<td>Opisthotonos</td>
<td></td>
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<tr>
<td>Cardiac arrest</td>
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<tr>
<td>Hemoglobinemia</td>
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<tr>
<td>Hemoglobinuria</td>
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</tr>
</tbody>
</table>
Delayed Immunologic Reactions

Delayed immunologic reactions are caused by the recipient developing antibodies in response to antigens on the donor’s red cells after an initial mismatched transfusion. Subsequent mismatched transfusions stimulate increased antibody production, resulting in hemolysis. These reactions occur 3 to 7 days after the transfusion.

Blood typing before the initial transfusion will decrease the risk of a delayed reaction. Crossmatching will not prevent a delayed hemolytic transfusion reaction because alloantibodies are at low levels until repeat exposure to the antigens occurs. Administering type-specific blood reduces the risk of these reactions.

Nonimmunologic Reactions

Sepsis

Sepsis is caused by bacterial contamination of the blood products. Because signs of sepsis may be similar to those of other transfusion reactions, examining a centrifuged hematocrit tube of donor blood for hemolysis or performing culture and sensitivity testing may be helpful in diagnosis.

Care must be taken to aseptically prepare the donor for collection, and a closed system must be used for transfusion. Blood can also be contaminated if the donor has bacteremia. Blood is an excellent medium for bacterial growth, so transfusions should be completed within 4 hours from start to finish. Treatment of sepsis includes antibiotics, fluid therapy, and discontinuation of the transfusion.

Circulatory Overload

Circulatory overload or transfusion-associated circulatory overload (TACO) is caused by excessive expansion of vascular volume. As natural colloids, blood products can cause a significant increase in circulating blood volume, potentially resulting in pulmonary edema. Small patients or those with underlying cardiac disease, renal disease, or chronic anemia may be more susceptible.

Carefully monitoring the rate and volume of transfusion decreases the risk of circulatory overload. Discontinuation of the transfusion, oxygen supplementation, or diuretics may be required for treatment.

Hemolysis

Nonimmunologic hemolysis is caused by improper storage and handling of blood products before and during transfusion. Following recommended guidelines for proper storage and administration techniques is necessary to prevent hemolysis. Several factors can lead to hemolysis before transfusion, including overheating, freezing, or repeatedly rewarming units; mixing RBCs with incorrect fluids; forcing RBCs through filters; and handling units roughly. Hemolysis can also occur as the product approaches its expiration date; therefore, transfusion of expired RBC products is never appropriate. When hemolysis occurs, the patient can develop hemoglobinuria and hemoglobinemia. It is important not to mistake this reaction for an immunologic reaction.

Sampling the blood from the donor bag and assessing it for hemolysis can be helpful to differentiate nonimmunologic hemolysis from other transfusion reactions. Treatments may vary based on the patient’s response to the hemolyzed product.

Citrate Intoxication

Massive transfusions may result in a variety of
Delayed Nonimmunologic Reactions

Storage lesions are progressive biochemical, biomechanical, and immunologic changes that occur while RBCs are in storage. These changes affect red cell viability, deformability, oxygen-carrying capacity, microcirculatory flow, and recipient response. Most human and veterinary literature supports the concept that storage lesions have deleterious effects, including decreased efficacy of transfusion, RBC lysis, increased inflammatory mediators, disruption of blood flow, decreased oxygen delivery, embolism, and excess free hemoglobin. The clinical signs vary and are poorly defined. Delayed nonimmunologic reactions should be considered in postransfusion patients developing complications that cannot readily be explained. Additional studies with improved experimental design are needed to identify compelling reasons to modify currently accepted duration of storage for blood products.

References
Blood Transfusions in Anemic Dogs and Cats

TOPIC OVERVIEW
This article provides an overview of transfusion medicine guidelines for anemic canine and feline patients. Areas of discussion include a brief review of anemia, canine and feline blood typing and crossmatching, proper administration of blood products, and monitoring for and recognizing transfusion reactions.

LEARNING OBJECTIVES
After reading this article, participants will be able to describe reasons for transfusion, supportive patient care before and during a transfusion, blood product selection, and how to acquire blood products. Participants will also be able to perform blood typing and crossmatching in canine and feline patients, administer and monitor a patient receiving a blood transfusion, recognize the different types of transfusion reactions, and prevent transfusion-associated complications.

1. The process of separating whole blood into individual fractions, effectively balancing clinical needs, reducing the risk of reactions, and efficiently using available blood products, is called
   a. Component therapy
   b. Therapeutic plasmapheresis
   c. Modality equality
   d. Leukoreduction

2. The process of determining compatibility between donor and recipient is called
   a. Biomarker identification
   b. Blood typing
   c. Crossmatching
   d. Autologous blood transfusion

3. Which is not a primary goal of an RBC transfusion?
   a. Normalize or attain a specific PCV value
   b. Improve oxygen delivery to tissues
   c. Decrease clinical signs of anemia
   d. Correct tissue hypoxia

4. Prior to starting a transfusion, it is not recommended to
   a. Pretreat with diphenhydramine
   b. Discontinue fluids such as lactated Ringer’s solution and dextrose
   c. Record initial heart and respiratory rates
   d. Perform blood typing

5. ___________ is thought to be due to white blood cell cytokine production in stored products.
   a. Transfusion-related acute lung injury
   b. A nonhemolytic febrile reaction
   c. Sepsis
   d. Circulatory overload

6. Nonimmunologic transfusion reactions include
   a. Sepsis
   b. Circulatory overload
   c. Citrate intoxication
   d. All of the above

7. The dog erythrocyte antigen (DEA) known to cause the more recognizable transfusion reactions is
   a. Kai 1
   b. Dal
   c. DEA 1
   d. Mik

8. Cats are more likely than dogs to have ___________ when incompatible blood types are transfused.
   a. Fatal reaction
   b. Increased body temperature
   c. Naturally occurring alloantibodies
   d. Transfusion not lasting as long as expected

9. Crossmatching should be performed
   a. For all feline and canine recipients
   b. When a dog has received a transfusion in the past 4 to 7 days
   c. When there is a history of transfusion reaction
   d. All of the above

10. Which of the following is not an indication for slowing or stopping an RBC transfusion?
    a. An increase in temperature of more than 1.5 °F
    b. Increased calcium levels
    c. Vomiting
    d. Development of increased lung sounds with a 1.5× increase in respiratory rate