Canine Immune-Mediated Hemolytic Anemia: Treatment and Prognosis*

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ABSTRACT: The treatment of primary immune-mediated hemolytic anemia involves short-term oxygen-carrying support and long-term immunosuppressive therapy. Therapeutic options include blood transfusion, standard and more speculative immunosuppressive agents, splenectomy, and prevention of thromboembolic disease. This article also discusses the prognosis and prognostic indicators.

Immune-mediated hemolytic anemia (IMHA) is one of the most common types of anemia in small animals. The diagnosis of primary (idiopathic or autoimmune) IMHA is one of exclusion of all potential underlying causes and identification of one or more of the following classic signs of the disease: anemia with a hematocrit less than 25% to 30%; evidence of hemolysis characterized by hemoglobinemia or hemoglobinuria; evidence of antibodies directed against red blood cells (RBCs), with autoagglutination, spherocytosis, or positive results from a direct antiglobulin (Coombs’) test; and an appropriate response to immunosuppressive therapy. The pathophysiology and diagnosis are discussed in depth in the companion article on page 217. This article discusses the treatment and prognosis of confirmed cases of IMHA.

Once a diagnosis of IMHA has been made, aggressive supportive therapy should be instituted. Most animals with severe RBC destruction initially require hospitalization to monitor, control, and treat continued hemolysis. The goal of treatment is stabilization of the packed cell volume (PCV) and resolution of clinical signs of anemia. Despite these apparently straightforward recommendations, treatment success ranges from 40% to 70% with frequent relapses. Patients rarely die from complications of anemia but do die from the hypercoagulable state and resultant disseminated intravascular coagulation (DIC) or thromboembolism.

SUPPORTIVE THERAPY

The average patient with IMHA presents with severe anemia with a hematocrit less than 15% to 20%. In these patients, supportive care is imperative to preserve normal tissue oxygenation, acid–base homeostasis, perfusion, hydration, and ventilation. The most important supportive therapy for patients with severe anemia is mainte-
nance of proper tissue oxygenation via blood transfusion (Figure 1). This is indicated when clinical signs such as tachypnea, dyspnea, and tachycardia indicate the presence of tissue hypoxia. To improve a patient’s oxygen-carrying capacity, clinicians may administer a transfusion of packed RBCs, whole blood, or bovine purified polymerized hemoglobin solution (Oxyglobin, Biopure Corporation). Approximately 70% to 90% of patients with IMHA require transfusion support, with a large percentage receiving multiple transfusions.\textsuperscript{1,2,6}

The type of blood product used for transfusion depends on product availability and patient need. Patients with hemolytic anemia are typically RBC depleted but not volume depleted, making transfusion with packed RBCs preferable. Hemoglobin-carrying solutions such as Oxyglobin also improve tissue oxygenation. The efficacy of Oxyglobin in dogs with IMHA is controversial, with reports of reduced survival rates in one study\textsuperscript{8} and no detectable reduction in outcome in other studies.\textsuperscript{6,9} In general, blood is considered the ideal product for transfusion, but Oxyglobin is warranted when blood is unavailable or crossmatching is difficult. Patients with concurrent thrombocytopenia and resultant blood loss may benefit from a transfusion of fresh whole blood or plasma as a means of replacing blood volume. However, clinicians should remember that blood transfusion has no significant effect on the platelet count.

In animals with hemolytic anemia, the decision to transfuse should be based on the clinical condition of the patient and the patient’s hematocrit. Although there is no specific PCV that dictates whether a transfusion is necessary, most dogs with a PCV of less than 12% to 15% need a transfusion. However, the ultimate determinant of the need for transfusion should always be the presence of anemia-related clinical signs, such as tachypnea, tachycardia, and weakness. The blood volume to transfuse can be approximated using the following equation:

\[
\text{Volume of blood for transfusion} = 90 \times \frac{\text{body weight (kg)}}{\text{PCV of donated blood}} 
\times \frac{\text{desired change in PCV}}{\text{PCV of donated blood}}
\]

This equation can be used for whole blood and packed RBCs by simply adjusting the PCV of donated blood.

Often, the most difficult decision related to transfusion is when to give the blood, but another important issue to consider is the target PCV after therapy. Patients with a normal regenerative response that receive a transfusion should have a resultant PCV of less than 25% to 30%. In dogs, a transfusion resulting in a PCV of more than 30% can increase the risk of volume overload, dampen the regenerative response, and ultimately delay recovery.

Ideally, all animals that require RBC products should be crossmatched before a transfusion. Unfortunately, autoagglutination is common in patients with IMHA and can make accurate crossmatching difficult or impossible because of an inability to differentiate autoagglutination from incompatible crossmatch agglutination. Antibodies to foreign blood group antigens develop approximately 5 days after an animal has received a transfusion. Dogs that have a history of transfusion and require another transfusion at least 5 days after their first one are at increased risk for acute and life-threatening reactions and should, therefore, never receive a transfusion without a crossmatch. Dogs with a history of transfusion that need an immediate transfusion or cannot be crossmatched because of autoagglutination should receive blood negative for dog erythrocyte antigen 1, universal donor blood, or bovine polymerized hemoglobin solution. It is important to realize, however, that transfusion reactions to the dog erythrocyte antigen 4 component of universal donor blood have been documented and pose a risk to animals that have not been crossmatched before transfusion.\textsuperscript{10}

Additional supportive therapies to consider in patients with hemolytic anemia include fluid and oxygen therapies. Intravenous fluids can help maintain adequate volume and acid–base homeostasis. Hemoglobin-related nephropathy has not been definitively identified in dogs but is frequently mentioned as a risk in patients with intravascular hemolysis and can be minimized with fluid therapy. Care should be taken to ensure that fluid ther-
apy does not contribute to volume overload, particularly in patients with concurrent kidney or heart conditions. When whole blood is used instead of packed RBCs, volume overload can be minimized by using conservative transfusion rates or splitting the transfusion into two, with each half given over 4 hours to slow the transfusion rate. Oxygen therapy is of little benefit for most anemic patients but may be helpful in animals with significant pulmonary disease, especially those with pulmonary thromboembolism. RBC oxygen saturation in anemic patients is typically maximized and improves very little with additional oxygen therapy. In severely anemic patients, additional oxygen-carrying support via transfusion is usually far more beneficial than oxygen therapy.

**STANDARD IMMUNOSUPPRESSIVE THERAPY**

Numerous studies have attempted to determine the appropriate pharmacologic therapy for the management of IMHA. Unfortunately, the results have primarily caused confusion. We have attempted to summarize the results of many of these studies and list the immunosuppressive drugs in order of preference, understanding that opinions may differ.

Despite the controversy, it is agreed that short- and long-term management of IMHA involves the judicious use of immunosuppressive agents to reduce the rate of antibody-mediated RBC destruction.

### Table 1. Relative Potency of Corticosteroids

<table>
<thead>
<tr>
<th>Drug</th>
<th>Relative Antiinflammatory Potency</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hydrocortisone (cortisol)</td>
<td>1</td>
</tr>
<tr>
<td>Prednisolone</td>
<td>4</td>
</tr>
<tr>
<td>Prednisone</td>
<td>4</td>
</tr>
<tr>
<td>Methylprednisolone</td>
<td>5</td>
</tr>
<tr>
<td>Triamcinolone</td>
<td>5</td>
</tr>
<tr>
<td>Betamethasone</td>
<td>25</td>
</tr>
<tr>
<td>Dexamethasone</td>
<td>30</td>
</tr>
</tbody>
</table>

*a* If doses are adjusted for potency, the dosing intervals remain the same. For example, if the adjusted 0.25-mg/kg dose of dexamethasone is administered instead of 2 mg/kg, the dosing interval remains the same. If doses are not adjusted for potency, the dosing intervals need to be extended.

### Table 2. Drugs Used to Treat IMHA

<table>
<thead>
<tr>
<th>Drug</th>
<th>Recommended Dosage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Prednisone</td>
<td>2 mg/kg PO q12–24h</td>
</tr>
<tr>
<td>Azathioprine</td>
<td>2 mg/kg PO q24h</td>
</tr>
<tr>
<td>Cyclosporine</td>
<td>10 mg/kg PO q12–24h</td>
</tr>
<tr>
<td>Immunoglobulin</td>
<td>0.5–1.5 g/kg IV over 6–12 hr</td>
</tr>
<tr>
<td>Unfractionated heparin</td>
<td>250 U/kg IV or SC q6h or 10–25 U/kg/hr constant-rate infusion</td>
</tr>
<tr>
<td>Low-molecular-weight heparin</td>
<td>Dalteparin 150 U/kg SC q12h</td>
</tr>
<tr>
<td></td>
<td>Enoxaparin 0.8 mg/kg SC q6h</td>
</tr>
<tr>
<td>Low-dose aspirin</td>
<td>0.5 mg/kg/day PO</td>
</tr>
</tbody>
</table>

**Glucocorticoids**

Glucocorticoids such as prednisone and dexamethasone are the mainstay of therapy for IMHA. For many patients, single-agent glucocorticoid therapy is the only treatment necessary. Corticosteroids reduce the destruction of RBCs by inhibiting phagocytosis of antibody-covered RBCs and decreasing cytokine and immunoglobulin production. The use of adequately immunosuppressive doses of glucocorticoids is imperative. Prednisone is typically dosed at 2 mg/kg PO q12–24h. Dexamethasone can also be used, particularly in animals that cannot take oral medication. Because dexamethasone is seven to eight times more potent than prednisone, the dose of dexamethasone should be reduced accordingly (Table 1).11

Unless unacceptable side effects occur, the glucocorticoid dose should not be reduced until the patient’s PCV is stable and near normal reference ranges. Once remission has been maintained for 1 to 2 weeks, the glucocorticoid dose can be reduced by 25% to 50% every 2 to 4 weeks.12 Treatment can generally be stopped once the prednisone dose has been reduced to 0.25 to 0.5 mg/kg PO q48h. Complete withdrawal of steroids should take a minimum of 2 to 4 months.12 Patients that relapse at decreased doses likely need to be maintained on some degree of immunosuppressive therapy (prednisone or another drug) for sustained periods or even, in rare cases, for life.

Immunosuppressive doses of glucocorticoids have significant side effects that can limit their use and frustrate owners. Typical side effects, such as polyuria, polydipsia,
polyphagia, incontinence, and panting, can be expected at initial dose rates and are especially evident in large-breed dogs. Owners should be warned that these side effects are expected for the first few weeks of therapy. More serious complications include secondary infections, steroid myopathy, and gastric ulceration, especially if the glucocorticoid is given in combination with an NSAID.11

Other Immunosuppressive Agents
Additional immunosuppressive agents should be administered if glucocorticoids fail to induce remission, cause unacceptable side effects, or cannot control the disease unless they are given at persistently high doses. Other therapies should also be considered in patients that relapse when steroids are tapered or stopped. Additional immunosuppressive therapy should be included in the initial treatment protocol in patients with autoagglutinating, intravascular, hemolytic, or nonregenerative forms of IMHA and in patients that are transfusion dependent. Because many cases of IMHA meet one or more of these criteria, many clinicians start all patients on early aggressive therapy. The most common additional immunosuppressive agents used in patients with IMHA are azathioprine and cyclosporine (Table 2). These agents are rarely used as a substitute for glucocorticoids, especially during initial treatment; rather, they are given in addition to standard glucocorticoid therapy and frequently permit more rapid reduction of steroid doses in the event of unacceptable corticosteroid side effects.

Azathioprine
Azathioprine, a purine analogue antimetabolite that preferentially suppresses T-cell function, is frequently used as an additional immunosuppressive agent in dogs with IMHA. Azathioprine is relatively inexpensive, and several studies1,6,13–15 report a good response or an improved overall prognosis in patients receiving the drug. Azathioprine is used in dogs at a dose of 2 mg/kg PO q24h. The dose is often given on alternate days when prednisone therapy is decreased to every other day.12 Because azathioprine has a slow onset of action (7 to 14 days), it should not be used as a sole therapy during initial treatment, but it is ideal when used alone for long-term management. Infrequent side effects of azathioprine therapy include anorexia, vomiting, diarrhea, myelosuppression, hepatopathy, and pancreatitis. Complete blood counts should be checked weekly during initial treatment because of the myelosuppressive activity of azathioprine. In recent years, azathioprine has become the primary additional therapy for patients with IMHA.

Cyclosporine
Cyclosporine is an immune modulator that was originally used to prevent transplant rejection but is now used as an immunosuppressive agent for a variety of other conditions, including perianal fistulae, granulomatous meningoencephalitis, and inflammatory bowel disease.16–19 It inhibits T-cell function by preventing T-cell production of the cytokine interleukin-2, a necessary step in T-cell activation. The original vegetable oil formulation was found to have poor and unpredictable oral bioavailability, but the current microemulsified formulations (cyclosporine modified or microemulsi-
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Primary IMHA requires aggressive immunosuppressive therapy, whereas secondary IMHA is less likely to respond to immunosuppressive therapy alone.

Intravenous Immunoglobulin

Intravenous immunoglobulin is a conglomeration of purified and concentrated immunoglobulin derived from human donors that has significant immunosuppressive effects in dogs. Intravenous human immunoglobulin binds to macrophage Fc receptors, preventing binding to antibody-coated RBCs and subsequent removal from circulation. Intravenous human immunoglobulin appears to be well-tolerated and has been associated with rapid recoveries in dogs with IMHA with refractory and severe anemia, although improvements in overall survival rates have not been demonstrated. The recommended intravenous human immunoglobulin dosing regimen in dogs is a single dose of 0.5 to 1.5 g/kg infused over 6 to 12 hours. The safety of multiple infusions to treat chronic or refractory disease has not been ascertained. Intravenous human immunoglobulin is expensive, and its availability is often limited, but its use has been strongly advocated in several retrospective and laboratory studies.

Leflunomide and Mycophenolate Mofetil

Because of the significant expense of leflunomide and mycophenolate mofetil, these immunomodulators are generally reserved for refractory cases. Leflunomide is an inhibitor of pyrimidine biosynthesis that has historically been used to prevent renal allograft rejection in dogs. Anecdotal reports are available regarding the use of leflunomide to treat dogs with histiocytic disease as well as immune-mediated disorders such as IMHA, but scientific evidence to support efficacy of the drug is lacking. The standard recommended oral dose of leflunomide is 4 mg/kg/day. Mycophenolate mofetil inhibits an enzyme needed for purine synthesis, leading to suppression of both B- and T-lymphocyte function.

Cyclophosphamide

Cyclophosphamide is an alkylating agent with potent myelosuppressive effects that was originally widely advocated for use in patients with severe IMHA. Cyclophosphamide, unlike azathioprine, has not been proven to improve clinical outcome in patients with IMHA and has been associated with reduced survival rates in several studies. The side effects associated with cyclophosphamide therapy include anorexia, vomiting, diarrhea, and potent myelosuppressive effects that can lead to leukopenia, neutropenia, and thrombocytopenia. Cyclophosphamide can result in sterile hemorrhagic cystitis, which previously necessitated discontinuation of therapy. In the rare situations in which cyclophosphamide must be used, recommendations have been made to combine cyclophosphamide with furosemide to prevent sterile hemorrhagic cystitis. Because other immunosuppressive agents with less serious side effects and better bioavailability and attain more consistent and predictable therapeutic blood levels. Unlike cyclophosphamide and azathioprine, cyclosporine is not myelosuppressive and is suitable for use in patients with nonregenerative forms of IMHA. Cyclosporine is considerably more expensive than azathioprine and cyclophosphamide and requires regular monitoring of blood levels to ensure appropriate dosing. The recommended immunosuppressive starting dose of oral microemulsified cyclosporine is 10 mg/kg q12–24h. To reduce oral cyclosporine doses in large dogs, ketoconazole can be added to the drug regimen. Several studies have found that this drug combination resulted in financial savings of 40% to 70% compared with the use of cyclosporine alone. Unfortunately, few clinical studies have reported on the efficacy of cyclosporine in small animals with IMHA, and the use of the drug in treating IMHA is purely anecdotal. We have had success with cyclosporine in managing refractory IMHA, but no scientific data exist at this time to support its use.
efficacy are available, cyclophosphamide is no longer recommended in treating IMHA.

**Splenectomy**

The spleen has a central role in the pathogenesis of IMHA. The spleen is typically the major site of mononuclear phagocytic system removal of IgG-coated RBCs in patients with IMHA and has an integral role in antigen presentation and autoantibody production. Removal of the spleen can eliminate a major contributor to the pathogenesis of RBC destruction in patients with IMHA but is reserved for patients that do not respond to standard immunosuppressive therapy or that experience adverse effects associated with drug therapy. A recent preliminary study in a relatively small group of dogs described the use of early splenectomy to treat patients with acute IMHA and found that dogs treated with glucocorticoids and azathioprine as well as splenectomy within 48 hours of presentation had shorter recovery times and higher survival rates than dogs treated with glucocorticoids and azathioprine alone. Based on these preliminary results, further investigation into early splenectomy is warranted, but we cannot advocate this procedure because of its high risk. Risks associated with splenectomy include complications associated with anesthesia and surgery and an increased predisposition to infectious diseases (bacterial sepsis, blood-borne parasitemia) that would normally be controlled by the spleen.

**Therapeutic Efficacy Studies**

Given the wide array of drugs and therapies that have been suggested as possible treatments for IMHA, it can be difficult for veterinarians to determine which medications to choose when treating their patients. A number of recent retrospective studies on relatively large groups of dogs have attempted to address this important issue. A retrospective study of 70 dogs with IMHA reported median survival times of 974 days in dogs that received prednisone and azathioprine; 57 days in dogs that received prednisone alone; 28 days in dogs that received prednisone and cyclophosphamide; and 15 days in dogs that received prednisone, cyclophosphamide, and azathioprine, although there were not enough dogs in each group to allow statistical comparison between specific treatment groups. Another retrospective study of 88 dogs with IMHA evaluated differences in survival rates associated with various treatments, including prednisone, dexamethasone, azathioprine, danazol, cyclosporine, cyclophosphamide, Oxyglobin, and intravenous human immunoglobulin. This study did not find a significant difference in mortality rates between animals given single and multiple immunosuppressive drugs but did find an increased relative risk for death associated with the use of cyclophosphamide and Oxyglobin. In addition, a recent retrospective study of 151 cases reported improved survival rates in
dogs treated with a combination of glucocorticoids, azathioprine, and ultra–low-dose aspirin compared with dogs treated with glucocorticoids and azathioprine alone. Despite the evaluation of relatively large treatment groups, the retrospective nature of all of these studies is a significant limitation. Retrospective studies can be particularly affected by clinician case selection biases in that the most critically ill patients tend to receive treatments of last resort that attending veterinarians may perceive as speculative, expensive, or overly aggressive.

Based on anecdotal experience and the relatively limited concrete information available from current retrospective and prospective studies, it is reasonable to conclude that prednisone alone or prednisone and azathioprine in combination (with or without ultra–low-dose aspirin) is the best initial treatment in most dogs with IMHA; that cyclophosphamide is not indicated in most patients with IMHA; and that it is uncertain whether early splenectomy will further improve survival rates. It is hoped that future prospective canine IMHA studies involving larger case numbers will further evaluate promising treatment options, such as cyclosporine, early splenectomy, and leflunomide.

**COMPLICATIONS**

Dogs with IMHA that receive appropriate transfusion support seldom die from anemia. According to several studies, thromboembolism, particularly pulmonary thromboembolism, is the most common complication in dogs with IMHA. Approximately 50% of dogs with IMHA are in a hypercoagulable state at the time of diagnosis. Major factors that influence the development of thrombus formation are described by Virchow’s triad of vascular endothelial injury, stasis of blood flow, and hypercoagulability, all of which can occur in patients with IMHA. Vascular injury in dogs with IMHA may occur secondary to the release of inflammatory cytokines triggered by RBC destruction and tissue hypoxia. Stasis of blood flow may be exacerbated in hospitalized patients because of cage confinement and the placement of intravenous catheters. Some veterinarians recommend avoiding the placement of jugular catheters in patients with IMHA and the prompt removal of all indwelling intravenous catheters as soon as is feasible. A recent study confirmed the hypercoagulable state of patients with IMHA by finding that their platelets express 8.1-fold greater P-selectin (a marker of platelet activation) than the platelets of healthy patients.

The presence of all the factors associated with Virchow’s triad predisposes patients with IMHA to thromboembolism and DIC. DIC is a systemic thrombohemorrhagic disorder that typically has a very poor prognosis. A provisional diagnosis of DIC is based on finding abnormalities by hematologic and hemostatic testing, including decreased platelet concentration, prolonged prothrombin and partial thromboplastin times, increased fibrin degradation product and D-dimer concentrations, decreased fibrinogen concentration, and increased numbers of schistocytes. Fourteen percent to 45% of dogs with IMHA have evidence of DIC during treatment. It may be difficult to conclusively identify true DIC in many patients with IMHA because pulmonary thromboembolism can cause many of the same clotting profile abnormalities reported in patients with DIC.

Current recommendations to prevent DIC and thromboembolic disease in patients with IMHA include the use of unfractionated heparin, low-molecular-weight heparin, or ultra–low-dose aspirin. Standard or unfractionated heparin binds to antithrombin, causing a conformational change that converts antithrombin from a slow anticoagulator to a rapid inhibitor of factors Xa and II. Unfractionated heparin can be administered at a starting dose of 250 U/kg IV or SC q6h or as a constant-rate infusion of 10 to 25 U/kg/hr. Heparin doses should then be titrated to prolong the partial thromboplastin time to one and one-half to three times the baseline. Unfortunately, however, unfractionated heparin has not been shown to reduce the incidence of pulmonary thromboembolism in dogs with IMHA. The use of low-molecular-weight heparins such as dalteparin and enoxaparin is becoming increasingly popular in human medicine because of their more predictable pharmacokinetic properties and ability to neutralize only factor Xa. Compared with unfractionated heparin, low-molecular-
weight heparins in humans have a more predictable effect with fewer complications, do not require the same extensive monitoring of clotting, and are less likely to cause overt bleeding. Recent research on low-molecular-weight heparins in dogs suggests using a starting dose of 150 U/kg SC q12h for dalteparin and 0.8 mg/kg SC q6h for enoxaparin. Administration of ultra–low-dose aspirin (0.5 mg/kg/day PO) in combination with prednisone and azathioprine has recently been reported to improve long-term survival in dogs with IMHA, but it was not determined whether this was due to decreased prevalence of thromboembolic disease.

**PROGNOSIS**

Unfortunately, the prognosis for dogs with IMHA is guarded. Complete response to treatment can take weeks to months, and some patients may require lifelong therapy. The condition can also recur despite previous or current therapy: one recent study found that 15% of dogs with IMHA that survived beyond 60 days relapsed when drugs were either discontinued or tapered.

The overall mortality rate for primary canine IMHA varies in the literature from as low as 26% to as high as 70%. Despite this variability, most of the literature on IMHA agrees that the number-one cause of death is thromboembolic disease. A recent publication found that all necropsies of patients with IMHA showed evidence of thromboembolism. The mortality rates will undoubtedly decline dramatically once a reliable means of preventing thromboembolic disease has been established.

Many attempts have been made to link clinical pathologic changes with the prognosis in patients with IMHA, and although individual studies have detected associations between specific laboratory criteria and outcomes, few prognostic indicators are consistently reproducible in multiple studies. For example, the mortality rate has reportedly been higher with nonregenerative forms of IMHA, however, this observation was not reproducible in subsequent clinical studies. Clinical pathologic abnormalities that have been linked to increased acute or long-term mortality rates, albeit inconsistently in all clinical studies, include persistent autoagglutination, thrombocytopenia, leukocytosis with a left shift, hyperbilirubinemia, hypoalbuminemia, and elevated serum alkaline phosphatase activities.

A recent report that identified the presence of activated platelets in 75% of patients with IMHA determined that quantification of platelet P-selectin expression may be a more sensitive method than routine coagulation testing in detecting prothrombotic tendencies in dogs with IMHA. Because thrombosis is such a common cause of death in patients with IMHA, this test may help identify at-risk patients, allowing earlier detection and treatment and potentially improving the prognosis.

The lack of consistency in determining the prognosis for patients with
IMHA based on a single clinical or laboratory finding has resulted in the recent development of a prognostic scoring scheme. Scoring schemes are routinely used in human medicine to predict patient outcome and compare treatment protocols. A similar grading scale called the canine hemolytic anemia objective score (CHAOS) was recently developed to predict the survival of dogs with hemolytic anemia and found that the median CHAOS of the survivors was significantly lower than that of nonsurvivors. This may indicate that similar scoring protocols that account for multiple physical examination and clinical pathologic findings may more adequately predict the prognosis of patients with IMHA. It is hoped that the identification of at-risk patients will allow early intervention and improve the outcome of this frustrating and common disease.

REFERENCES
ARTICLE #3 CE TEST

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1. In anemic patients, ______________ does not significantly improve oxygen-carrying capacity.
   a. transfusion with Oxyglobin c. transfusion with packed RBCs
   b. provision of intranasal oxygen d. transfusion with whole blood

2. On average, approximately how long after a transfusion does an animal develop antibodies to foreign blood group antigens?
   a. 1 day c. 14 days
   b. 5 days d. 30 days

3. Which is not an appropriate indication for transfusion in a patient with IMHA?
   a. tachycardia c. weakness
   b. tachypnea d. jaundice

4. The standard immunosuppressive dose of prednisone in dogs is approximately _____ mg/kg/day PO.
   a. 0.25 c. 2
   b. 0.5 d. 6

5. Which drug is an antimetabolite that suppresses T-cell function?
   a. prednisone c. cyclosporine
   b. azathioprine d. danazol

6. The most common complication in patients with IMHA is
   a. renal failure. c. acute hemorrhage.
   b. thromboembolism. d. pulmonary edema.

7. Prevention of thromboembolism and DIC does not include administration of
   a. low-molecular-weight heparin. c. aspirin.
   b. an NSAID. d. heparin.

8. Intravenous immunoglobulin slows RBC destruction by
   a. inhibiting pyrimidine biosynthesis.
   b. inhibiting T-cell function.
   c. inhibiting purine synthesis.
   d. binding to Fc receptors on macrophages.

9. Administration of __________ requires monitoring of blood levels for adequate dosing.
   a. cyclosporine c. prednisone
   b. azathioprine d. cyclophosphamide

10. When unfractionated heparin is used to prevent thrombus formation, the partial thromboplastin time should be prolonged to __________ times the baseline.
   a. three to five c. five to seven
   b. two-tenths to one-half d. one and one-half to three