EMERGENCY MEDICINE/CRITICAL CARE

Hemolytic Crisis in Small Animals

***Andrew Linklater**, DVM, DACVECC*
Veterinary Specialists of the Rockies, Castle Rock, Colorado

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Abstract

Hemolysis can lead to a severe crisis, primarily resulting from loss of oxygen-carrying capacity of arterial blood. Hemolytic crisis can lead to signs of anemia, shock, and even death. Other signs, such as thrombosis and icterus, may result from the consequences of hemolysis. Several diagnostic steps are necessary to not only diagnose hemolysis but also to determine if an underlying cause of the hemolytic crisis exists.

Take-Home Points

- Confirm hemolysis by performing appropriate diagnostics along with additional confirmatory tests.
- Assess tissue oxygen delivery by evaluating perfusion parameters and recognizing clinical signs of inadequate oxygen delivery.
- Formulate a targeted differential list for acute hemolysis by considering infectious, immune-mediated, toxic, metabolic, and other etiologies.
- Implement treatment and monitoring for complications during a hemolytic crisis.

Anemia in small animals is defined as decreased circulating red blood cells (RBCs), which is practically defined as reduced PCV, hematocrit, hemoglobin concentration, or total RBC count below the reference interval.[1] Because breed differences, geographic location, and methods of measuring these values can alter the reference interval, a local, age- and breed-specific definition of anemia is recommended.

In response to anemia, rapid compensatory mechanisms result in increased cardiac output and redistribution of blood flow through autoregulation and altered systemic vascular resistance, usually resulting in constriction of blood vessels in nonessential or peripheral tissues. When anemia continues over a longer period, other compensatory mechanisms (which may take days) include increased blood flow, increased oxygen onloading and offloading from the hemoglobin molecule (through increased 2,3-diphosphoglycerate), and eventually, production of new RBCs under the influence of erythropoietin. When anemia is severe or acute enough, these mechanisms are insufficient and/or have a maximal level of compensatory ability, potentially leading to shock or death.

Anemia secondary to hemolysis can result in a state in which oxygen consumption becomes dependent on oxygen delivery (**FIGURE 1**). Tissue oxygen delivery is dependent on several physiologic concepts (**BOX 1**). Most of the oxygen in the blood is carried on hemoglobin, which is effective as an oxygen-carrying molecule only when it is in the tetrameric form, found inside RBCs. When hemoglobin is not present in sufficient quantities, the delivery of oxygen to tissues decreases. A small amount of oxygen is also dissolved in the plasma; however, that amount is trivial

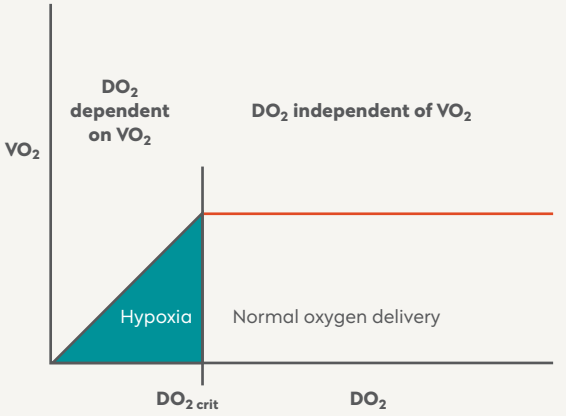

FIGURE 1. Oxygen delivery (DO_2) and oxygen consumption (VO_2) relationship curve. There are 2 portions of the relationship curve. The red flat line is the DO_2-independent portion of the VO_2 curve; in this portion of the curve, more oxygen is delivered to tissues than is required to meet physiologic needs and is the status for most healthy animals. In anemic patients, delivery of oxygen decreases (moving toward the left of the curve), depending on the severity of the anemia. If anemia (and DO_2) becomes severe enough, a critical point of oxygen delivery (DO_2crit), may be reached, where the amount of oxygen being delivered to the body matches the amount being consumed. Below this point (further toward the left), there is no longer enough oxygen being delivered to the tissues to meet physiologic demands, and VO_2 becomes dependent on the amount of oxygen being delivered, leading to tissue hypoxia and clinical signs of anemia.

BOX 1
Aspects of Oxygen Delivery to Tissues

$DO_2 = CO \times CaO_2$

$CO = HR \times SV$

$CaO_2 = (SaO_2 \times Hgb \times 1.37) + (PaO_2 \times 0.003)$

- DO_2 is the delivery of oxygen to the tissues.
- CO is cardiac output, which is dependent on heart rate (HR) and stroke volume (SV). SV is subsequently dependent on preload, afterload, and contractility.
- CaO_2 is the arterial content of oxygen and is dependent on the arterial oxygen hemoglobin saturation (SaO_2), the amount of hemoglobin (Hgb) in the blood, and a factor of 1.37, which is how much oxygen hemoglobin can carry. There is also a small amount of oxygen dissolved in the plasma (0.003 times the partial pressure of arterial oxygen [PaO_2]).

compared with the amount attached to the hemoglobin molecule.

Clinical Signs

In the presence of hemolysis, hemoglobin is no longer an effective oxygen-carrying molecule. The clinical signs of poor oxygen delivery are the same as those of most states of shock. In this context, poor oxygen delivery is from anemia (low hemoglobin resulting from oxygen delivery to the tissues falling below the critical point). Signs of anemia can include tachycardia; tachypnea; weakness; lethargy; pale mucous membranes (**FIGURE 2**) with prolonged capillary refill time; altered mentation; cool extremities/skin; collapse; and, if severe enough, death. Patients exhibiting these clinical signs often need rapid intervention, not only to treat the anemia (e.g., transfusions) but also for diagnostics to investigate the underlying cause of the anemia.

In addition to poor delivery of oxygen, RBC lysis can lead to the following consequences:

- Fragments of RBCs in the circulation can initiate the inflammatory and coagulation cascades (which may result in thrombosis).
- Circulating hemoglobin can result in vasoconstriction and potentially pigment-related injury to the kidneys.
- Overwhelming the body's ability to process free hemoglobin can result in icterus, which may result in signs of illness.

When anemia is caused by hemolysis, along with signs of impaired oxygen delivery, additional signs of circulating free hemoglobin or by-products of hemoglobin may be evident (e.g., icterus [**FIGURE 3**], hemoglobinemia, bilirubinemia, bilirubinuria, hemoglobinuria [**FIGURE 4**], potentially thrombosis).

FIGURE 2. Pale mucous membranes in a dog with anemia.

FIGURE 3. Icteric mucous membranes in a dog, secondary to severe hemolytic anemia.

FIGURE 4. Urine being withdrawn from a urethral catheter in a dog, exhibiting hemoglobinuria secondary to rapid and severe hemolysis.

FIGURE 5. Venous lingual thrombosis, resulting in discoloration and decreased function of the tongue.

In patients with immune-mediated hemolytic anemia (IMHA), the pathogenesis of thrombosis is complex; it may occur at any location and may be either venous or arterial.

- Venous thrombosis will result in tissues that are swollen, painful, usually darkly discolored (**FIGURE 5**), and dysfunctional.
- Arterial thrombosis will result in pain, dysfunction, and tissues that are pale and cold.
- Arterial or venous thrombosis of the neurologic system results in acute and severe neurologic deficits, including acute death.

Differential Diagnoses

There are many differential diagnoses for the etiology

TABLE 1 Causes of Hemolytic Anemia

CATEGORY	CAUSES
Infectious diseases	Bacterial infection (e.g., mycoplasmosis, leptospirosis, bartonellosis), viral infection (e.g., feline leukemia virus, feline immunodeficiency virus, feline infectious peritonitis), rickettsial disease (e.g., ehrlichiosis, anaplasmosis), protozoal disease (e.g., babesiosis, cytauxzoonosis), and dirofilariasis
Toxins	Heavy metal intoxication (e.g., zinc, lead), *Allium* intoxication (e.g., onions, garlic), rodenticides (e.g., zinc phosphide), acetaminophen (in cats), naphthalene, propylene glycol, snake venom, skunk musk, NSAIDs, and steroid use (rare)
Prescription drugs	Penicillins, cephalosporins, sulfonamides, methylene blue, propofol, and benzocaine
Metabolic derangement	Hypophosphatemia, which can be secondary to diabetes (in particular, newly diagnosed diabetes or diabetic ketoacidosis, when treatment with insulin is initiated); refeeding syndrome; hepatic lipidosis; and, less commonly, alkalosis, hypovitaminosis D, malabsorptive disorders, inadequate intake, diuretic use, hemolytic–uremic syndrome, osmolarity changes, and eclampsia
Microangiopathic disease	Disseminated intravascular coagulation, circulatory disease (e.g., valve disease, organ torsion, caval syndrome), and vasculitis. Systemic illness may include any causes of systemic inflammatory response syndrome (e.g., pancreatitis, neoplasia including histiocytic disease and hemangiosarcoma). Heritable conditions are uncommon (e.g., phosphofructokinase deficiency, pyruvate kinase deficiency).

of hemolytic anemia.[2] Broad categories include nonassociative IMHA, infectious diseases, toxins and drugs, metabolic derangements, microangiopathic disease, neonatal isoerythrolysis, severe systemic illness, heritable conditions, and neoplasia (**TABLE 1**).

For immune-mediated hemolysis, a recent American College of Veterinary Internal Medicine (ACVIM) consensus statement recommended updating the nomenclature to associative IMHA, meaning there is a comorbid condition that may or may not have been a trigger for the immune response, or nonassociative IMHA, in which comorbid conditions are not identified in the diagnostic workup.[3]

Diagnostics

Determining the cause of a hemolytic crisis depends on astute history collection, physical examination findings, and appropriate diagnostics. As mentioned, IMHA may be either nonassociative, for which no underlying etiologies or comorbidities are evident, or associative, for which comorbid conditions (or an underlying potential etiology) are identified. Examples of etiologies that may result in associative IMHA include disseminated intravascular coagulation (DIC), feline immunodeficiency virus infection, neoplasia, and *Mycoplasma* infection. To determine if IMHA is associative or to rule out other causes, many routine screening tests are usually recommended when hemolytic anemia is diagnosed (**BOX 2**). Recently, the ACVIM published its diagnostic criteria for nonassociative IMHA (**BOX 3**).[3]

Treatment

Calm Handling and Provision of Sedatives, Oxygen, and Fluids

For unstable patients, the first step is minimizing additional stress and providing calm and supportive handling as stress can increase oxygen demand and shift the critical point of oxygen delivery to the right (**FIGURE 1**). Oxygen may be administered through

BOX 2
Routine Diagnostics to Screen for Hemolysis Etiology (and/or Associative Versus Nonassociative Category)

1. Routine blood work (CBC, chemistry, electrolyte, blood gasses, thyroid level); may include pathologist review of the blood smear to examine for infectious disease (e.g., red blood cell parasites); saline agglutination
2. Urinalysis +/- culture
3. Abdominal radiography (particularly to rule out metallic gastric foreign objects [**FIGURE A**])
4. Abdominal ultrasonography
5. Thoracic radiography
6. Specific testing for infectious diseases (e.g., feline leukemia virus or feline immunodeficiency virus infection, dirofilariasis, mycoplasmosis, babesiosis) and additional infectious diseases endemic to where the animal is living or has lived[3]
7. Fecal testing
8. Systemic evaluation of coagulation for disseminated intravascular coagulation and other severe illness
9. Other tests usually specific to clinical signs, preventive care, physical examination findings, or geographic region (e.g., fungal diseases)

FIGURE A. Lateral whole-body radiograph of a puppy with a metallic gastric foreign body made of zinc, which led to a hemolytic crisis.

several techniques (e.g., cage, hood, flow-by, nasal prongs). Although oxygen supplementation will only minimally increase oxygen delivery to the tissues, increasing the oxygen partial pressure (**BOX 1**) may be lifesaving for some patients. Nonessential procedures (e.g., radiography, ultrasonography) should be delayed until the patient is stable. Intravenous fluids (e.g., crystalloids) should be administered cautiously to severely anemic patients as fluids may dilute the RBC volume, further reducing oxygen delivery. Mild sedatives, such as butorphanol (0.2 to 0.4 mg/kg IV or IM), may be beneficial for some patients.

Transfusing to Correct Oxygen Delivery

The next step for treating severe anemia is restoring oxygen delivery, most commonly achieved by increasing the RBC mass through packed RBC transfusions. Although type-specific and crossmatched species-specific RBCs are considered ideal,[4,5] there are often associated challenges (e.g., availability of allogeneic blood resources, agglutination interfering with the crossmatch). The Association of Veterinary Hematology and Transfusion Medicine transfusion guidelines and consensus statements provide additional information.[6-8]

Crossmatched blood may not be necessary for transfusion-naïve dogs but is recommended (if possible) for subsequent transfusions. Administration of DEA (dog erythrocyte antigen) 1 type-specific blood to dogs is strongly recommended.[7] Cats should always receive type-specific blood as preformed antibodies can lead to severe and potentially fatal consequences.[7] Crossmatching is generally recommended for cats.[7]

Xenotransfusion (canine blood administered to cats) is reportedly safe but the RBCs have a shorter lifespan; the complication rate is reportedly higher than that associated with allogeneic blood transfusion[7,9]; and xenotransfusion should not be repeated beyond 1 to 3 days due to antibody development, which could be fatal.[7,9,10]

Alternative solutions for increasing oxygen delivery with hemoglobin-based oxygen-carrying solutions have been reported; however, such solutions are not currently available in most countries.[11]

Treating the Underlying Cause

Describing treatment for all potential causes of hemolysis is beyond the scope of this article and should be based on the diagnosis and associative cause, if present. Patients with associative IMHA from infectious diseases (e.g., mycoplasmosis in cats) often require antibiotics (e.g., doxycycline, fluoroquinolones).

Arresting Hemolysis

Hemolysis is often arrested after the underlying disease is identified and treated. However, if there is an immune-mediated component of hemolysis (associative or nonassociative), immunosuppressive medications are the mainstay of therapy. Several methods for arresting the immune-mediated aspect of IMHA have been investigated.[12]

After diagnostic samples have been collected and the patient has been stabilized with transfusions, prednisone or prednisolone at immunosuppressive doses (2 to 3 mg/kg/day or 50 to 60 mg/m^2/day for dogs >25 kg [55 lb]) can be started. Until oral medications are started, dexamethasone (0.2 to 0.4 mg/kg/day IV) may be administered. A second immunosuppressive agent is recommended to help minimize the duration and adverse effects of high doses of steroids, most commonly one of the following medications (none have proven superior):

- Azathioprine at 2 mg/kg or 50 mg/m^2 q24h (after 2 to 3 weeks, the dosing interval may be increased to q48h)
- Cyclosporine at 5 mg/kg PO q12h with adjustments based on therapeutic drug monitoring
- Mycophenolate mofetil at 8 to 12 mg/kg PO q12h
- Leflunomide at 2 mg/kg PO q24h with adjustments based on therapeutic drug monitoring as indicated

Close patient monitoring is essential with long-term use of any immunosuppressive medication (e.g., monitoring for significant adverse effects, response to therapy, evidence of infection or other complications such as liver injury). The first drug to be tapered is prednisone, followed by other immunosuppressive agents when the patient is able to maintain normal RBC counts, usually for several weeks.

Alternative methods for arresting hemolysis remain more controversial, but there is some published or anecdotal support for the following treatments:

BOX 3
Diagnostic Criteria for Nonassociative Immune-Mediated Hemolytic Anemia (IMHA)[3]

The American College of Veterinary Internal Medicine consensus statement states that ≥2 signs of destruction with ≥1 sign(s) of hemolysis are consistent with IMHA. Findings that are supportive of IMHA are 1 sign of destruction with 1 sign of hemolysis or 2 signs of destruction with 1 sign of hemolysis. With only 1 sign of hemolysis, other diseases should be investigated; when there are no signs of destruction, IMHA is not likely.

1. Anemia (measured by PCV, hematocrit, or CBC)
   - a. Regeneration may not be evident for several days and depends on normal marrow and iron stores.
   - b. Regeneration may be evidenced by anisocytosis, macrocytosis, reticulocytosis, or circulating nucleated red blood cells (RBCs).
2. Evidence of RBC destruction
   - a. Spherocytosis (dogs only), assessed in the blood smear monolayer
     - i. >3–5 spherocytes/high-power field is suggested to have high sensitivity and specificity.
   - b. Positive saline agglutination test
     - i. Mixing 4 drops of saline with 1 drop of blood is highly sensitive and specific (**FIGURE A**).
     - ii. With equivocal results, washing erythrocytes 3 times with 4:1 saline may help rule in nonassociative IMHA.
   - c. Antierythrocyte antibodies
     - i. Flow cytometry or Coombs test
3. Evidence of hemolysis
   - a. Erythrocyte ghost cells
   - b. Hyperbilirubinemia (in the absence of hepatobiliary disease)
     - i. Clinical icterus
     - ii. Serum bilirubin >2 mg/dL
     - iii. Bilirubinuria
   - c. Hemoglobinuria or hemoglobinemia
     - i. Visual examination, after eliminating artifacts from collection
     - ii. Ghost cells on blood smear

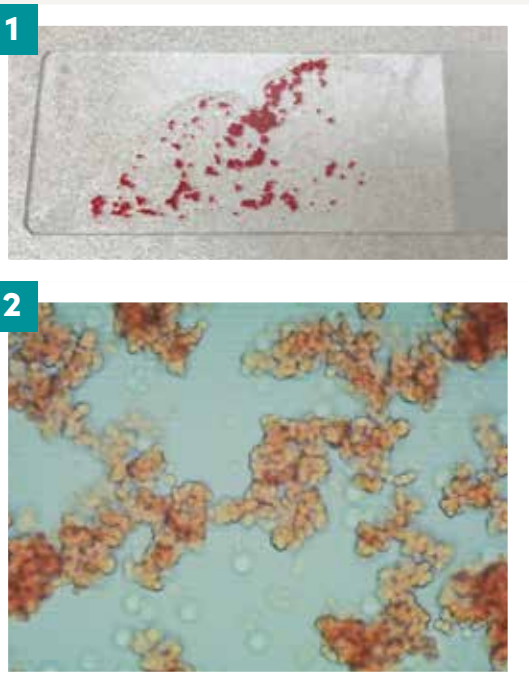

FIGURE A. Red blood cell agglutination. **(1)** Macroscopic agglutination on a microscope slide. **(2)** Microscopic agglutination (original magnification 40×); the cells appear as clusters of grapes and not stacks of coins.

intravenous immunoglobulins,[13] therapeutic plasma exchange or plasmapheresis,[14] surgical splenectomy,[15,16] and some additional methods (e.g., hyperbaric oxygen therapy, melatonin, liposomal clodronate). Alternative methods may be chosen on the basis of client resources, method availability, and disease progression.

Complications

Several complications have been associated with hemolytic crises. The most common and concerning is thrombosis; however, pigment-associated nephropathy and encephalopathy have also been reported. Other complications may be secondary to therapy (e.g., gastric or duodenal ulceration, infections).

The ACVIM consensus statement and the Consensus on the Rational Use of Antithrombotics and Thrombolytics in Veterinary Critical Care (CURATIVE) guidelines recommend using antithrombotics to treat IMHA.[3,17] The ACVIM consensus statement has the following recommendations[3]:

- **First line:** Unfractionated heparin (UFH; 150–300 U/kg SC q6h) with individual dose adjustment with or without addition of an antiplatelet agent (clopidogrel at 1–4 mg/kg PO q24h)
- **Second line:** Low–molecular-weight heparins (LMWH; dalteparin at 150–175 U/kg q8h or enoxaparin at 0.8–1 mg/kg q6–8h) or direct oral factor Xa inhibitor (rivaroxaban at 1–2 mg/kg PO q24h) are the next recommendations.
- **Third line:** If the previous options are not feasible, an antiplatelet drug alone (clopidogrel is favored over aspirin) is recommended.

Use of UFH or LMWH is challenging due to the need for multiple injections per day, variable bioavailability, the need for regular monitoring (coagulation assessment), and the cost (for LMWH). Direct oral factor Xa inhibitors seem to be generally safe; they are currently expensive (in the United States); however, the FDA has recently approved a generic equivalent, which is likely to be less expensive and availability should therefore improve with time. The CURATIVE guidelines state that there is insufficient evidence to make strong recommendations as to the ideal anticoagulant.[18] Venous thrombosis seems to be more common in patients with IMHA, and the guideline examples suggest use of direct factor Xa inhibitors (e.g., rivaroxaban) or LMWH over UFH.[18] For arterial thrombosis in patients with IMHA, it is suggested that clopidogrel is favored over aspirin.[18]

Pigment nephropathy resulting in acute kidney injury has been reported for human patients but rarely for veterinary patients and most likely results from a combination of potential injury to the kidneys (e.g., local vasoconstriction, acute tubular injury, pigment casts [hemoglobin cast nephropathy], thrombosis, hypovolemia, dehydration).[19] Preventing pigment nephropathy or acute kidney injury by treating hemolytic disease and thromboprophylaxis and cautious IV fluid administration along with diligent patient monitoring are essential. Bilirubin encephalopathy has been reportedly successfully treated with plasmapheresis.[20]

Outcomes and Prognosis

Outcomes for patients that have experienced a hemolytic crisis are variable and depend highly on the underlying cause. Among dogs with nonassociative IMHA, prognosis has been quite variable. Recent data suggest survival rates of 72.6% to 84%.[21-24] Most deaths occur within the first 1 to 2 weeks. Some older studies reported that survival rates at 30 days ranged from 17% to 82%.[23] Recently, hematologic ratios (e.g., the neutrophil:lymphocyte ratio) have not been found to be associated with outcome for patients with IMHA.[25] Several additional variables have been negatively associated with prognosis, including but not limited to elevated bilirubin (icterus), decreased platelets or petechia, elevated blood urea nitrogen, elevated bands, prolonged coagulation times, and hypoalbuminemia.[26]

For cats with hemotrophic *Mycoplasma* infections resulting in anemia, 1 study reported the 1-year survival rate to be 65%, although frequency of hemolysis was not reported.[27]

Summary

Anemia can result in poor oxygen delivery to tissues and, when severe, can result in signs of shock and even death. Lysis of RBCs can also lead to initiation of the inflammatory and coagulation cascade, resulting in additional and often severe symptoms, such as thrombosis. The diagnosis of hemolytic anemia is often straightforward based on laboratory testing, guided by the ACVIM consensus statement; however, developing a differential diagnosis list and performing a thorough workup are recommended to determine if the hemolytic anemia is associative or nonassociative. The mainstay of nonassociative hemolysis treatment involves restoring the oxygen-carrying capacity (through transfusions), suppressing the immune system, and preventing complications. TVP

References

1. Couto GC. Anemia. In: Nelson RW, Couto CG, eds. *Small Animal Internal Medicine.* 5th ed. Elsevier Mosby; 2014:1201.
2. Cohn LA. Acute hemolytic disorders. In Silverstein DC, Hopper K, eds. *Small Animal Critical Care Medicine*. 3rd ed. Elsevier; 2023:633.
3. Garden OA, Kidd L, Mexas AM, et al. ACVIM consensus statement on the diagnosis of immune-mediated hemolytic anemia in dogs and cats. *J Vet Intern Med.* 2019;33(2):313-334. doi:10.1111/jvim.15441
4. McClosky ME, Brown DC, Weinstein NM, et al. Prevalence of naturally occurring non-AB blood type incompatibilities in cats and influence of crossmatch on transfusion outcomes. *J Vet Intern Med.* 2018;32(6):1934-1942. doi:10.1111/jvim.15334
5. Odunayo A, Garraway K, Rohrback BW, Rainey A, Stokes J. Incidence of incompatible crossmatch results in dogs admitted to a veterinary teaching hospital with no history of prior red blood cell transfusion. *JAVMA*. 2017;250(3):303-308. doi:10.2460/javma.250.3.303

6. Davidow EB, Blois SL, Goy-Thollot I, et al. Association of Veterinary Hematology and Transfusion Medicine (AVHTM) Transfusion Reaction Small Animal Consensus Statement (TRACS). Part 1: definitions and clinical signs. *J Vet Emerg Crit Care (San Antonio)*. 2021;31(2):141-166. doi:10.1111/vec.13044
7. Davidow EB, Bloids, SL, Goy-Thollot I, et al. Association of Veterinary Hematology and Transfusion Medicine (AVHTM) Transfusion Reaction Small Animal Consensus Statement (TRACS). Part 2: prevention and monitoring. *J Vet Emerg Crit Care (San Antonio)*. 2021;31(2):167-188. doi:10.1111/vec.13045
8. Odunayo A, Nash KJ, Davidow EB, et al. Association of Veterinary Hematology and Transfusion Medicine (AVHTM) Transfusion Reaction Small Animal Consensus Statement (TRACS). Part 3: diagnosis and treatment. *J Vet Emerg Crit Care (San Antonio)*. 2021;31(2):189-203. doi:10.1111/vec.13043
9. Elkin M, Amichay-Menasche N, Segev G, et al. Retrospective study of canine blood xenotransfusion compared with type-matched feline blood allotransfusion to cats: indications, effectiveness, limitations and adverse effects. *J Feline Med Surg*. 2023;25(7):1098612X231183930. doi:10.1177/1098612X231183930
10. Le Gal A, Thomas EK, Humm KR. Xenotransfusion of canine blood to cats: a review of 49 cases and their outcome. *J Small Anim Pract*. 2020;61(3):156-162. doi:10.1111/jsap.13096
11. Day TK. Current development and use of hemoglobin-based oxygen-carrying (HBOC) solutions. *J Vet Emerg Crit Care*. 2003;13(2):77-93. https://doi.org/10.1046/j.1435-6935.2003.00084.x
12. Swann JW, Garden OA, Fellman CL, et al. ACVIM consensus statement on the treatment of immune-mediated hemolytic anemia in dogs. *J Vet Intern Med*. 2019;33(3):1141-1172. doi:10.1111/jvim.15463
13. Kane B-K, Greer RM. Human intravenous immunoglobulin use for hematological immune-mediated disease in dogs. *JAVMA*. 2023;261(7):1004-1010. doi:10.2460/javma.23.01.0043
14. Francey T, Etter M, Schweighauser A. Evaluation of membrane-based therapeutic plasma exchange as an adjunctive treatment for immune-mediated hematologic disorders in dogs. *J Vet Intern Med*. 2021;35(2):925-935. doi:10.1111/jvim.16049
15. Horgan JE, Roberts BK, Shermerhron T. Splenectomy as an adjunctive treatment for dogs with immune-mediated hemolytic anemia: ten cases. *J Vet Emerg Crit Care (San Antonio)*. 2009;19(3):254-261. doi:10.1111/j.1476-4431.2009.00419.x
16. Bestwick JP, Skelly BJ, Swann JW, et al. Splenectomy in the management of primary immune-mediated hemolytic anemia and primary immune-mediated thrombocytopenia in dogs. *J Vet Intern Med*. 2022;36(4):1267-1280. doi:10.1111/jvim
17. Goggs R, Blais M-C, Brainard BM, et al. American College of Veterinary Emergency and Crucial Care (ACVECC) consensus on the rational use of antithrombotics in veterinary emergency and critical care (CURATIVE) guidelines: small animal. *J Vet Emerg Crit Care (San Antonio)*. 2019;29(1):12-36. doi:10.1111/vec.12801
18. Sharp CR, Goggs R, Blais M-C, et al. Clinical application of the American College of Veterinary Emergency and Critical Care (ACVECC) consensus on the rational use of antithrombotics in veterinary critical care (CURATIVE) guidelines to small animal cases. *J Vet Emerg Crit Care (San Antonio)*. 2019;29(2):121-131. doi:10.1111/vec.12804
19. Dvanajsack Z, Walker PD, Cassey LN, et al. Hemolysis-associated hemoglobin cast nephropathy results from a range of clinicopathologic disorders. *Kidney Int*. 2019;96(6):1400-1407. doi:10.1016/j.kint.2019.08.026
20. Chalifoux NV, Montague B, Rheingold C, Clarkin-Breslin R, Reineke EL. Resolution of canine acute bilirubin encephalopathy and immune-mediated hemolytic anemia following four plasmapheresis treatments. *JAAHA*. 2024;60(5):207-213. doi:10.5326/JAAHA-MS-7430
21. Piek CJ, Junius G, Dekker A, Schrauwen E, Slappendel RJ, Teske E. Idiopathic immune-mediated hemolytic anemia treatment outcome and prognostic factors in 149 dogs. *J Vet Intern Med*. 2008;22(2):366-373. doi:10.1111/j.1939-1676.2008.0060.x
22. Duclos AA, O'Sullivan L, McPhedran C, et al. Retrospective evaluation of hematological ratios in dogs with non-associative immune-mediated hemolytic anemia: 206 cases. *J Vet Intern Med*. 2025;39(3):e70101. doi:10.1111/jvim.70101
23. Weinkle TK, Center SA, Randolph JF, Warner KL, Barr SC, Erb HN. Evaluation of prognostic factors, survival rates and treatment protocols in immune-mediated hemolytic anemia in dogs: 151 cases (1993-2002). *JAVMA*. 2005;226(11):1869-1880. doi:10.2460/javma.2005.226.1869
24. Duclos AA, Bailén EL, Barr K, Le Boedec K, Cuq B. Clinical presentation, outcome and prognostic factors in dogs with immune-mediated haemolytic anaemia: a retrospective single-center study of 104 cases in Ireland (2002-2020). *Ir Vet J*. 2024;77(1):16. doi:10.1186/s13620-024-00277-w
25. Alaimo C, De Feo G, Lubas G, Gavazza A. Utility and prognostic significance of leukocyte ratios in dogs with primary immune-mediated hemolytic anemia. *Vet Res Commun*. 2023;47(1):305-310. doi:10.1007/s11259-022-09935-2
26. Mitchell K, Kruth S. Immune-mediated hemolytic anemia and other regenerative anemias. In: Ettinger SJ, Feldman EC, eds. *Textbook of Veterinary Internal Medicine*. 7th ed. Saunders Elsevier; 2010:768.
27. Nibblett BMD, Snead EC, Waldner C, Taylor SM, Jackson ML, Knorr LM. Anemia in cats with hemotrophic mycoplasma infection: retrospective evaluation of 23 cases (1996-2005). *Can Vet J*. 2009;50(11):1181-1185.

Author

Andrew Linklater

Dr. Linklater grew up and graduated veterinary school in Canada, moved to the United States to complete his advanced training, and became a diplomate of American College of Veterinary Emergency and Critical Care in 2009. He has been the lead of the emergency department at a multispecialty hospital for more than 20 years in Wisconsin, mentoring over 100 interns and residents, serving in such roles as medical director, director of an emergency room internship and residency program and director of a Veterinary Emergency and Critical Care Society–certified and VetCOT-certified trauma center. He has authored more than 60 peer-reviewed publications, including 2 veterinary textbooks, and has provided hundreds of lecture hours at national and international conferences. Recently, he has moved to Colorado to join Veterinary Specialists of the Rockies. His professional interests include trauma, surgery, coagulopathies, and transfusions. In his free time, he enjoys traveling, skiing, curling, biking, hiking, and spending time with his family.

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CE Quiz Questions

1. **Which is the most important factor for delivery of oxygen to tissues?**
   a. The oxygen dissolved in plasma
   b. The oxygen attached to the hemoglobin molecule
   c. The cardiac output
   d. The stroke volume of the heart

2. **Which is not a sign of severe anemia?**
   a. Tachycardia
   b. Normal respiratory rate
   c. Weakness or collapse
   d. Tachypnea

3. **Clinical signs of hemolysis may include all of the following except:**
   a. Hemoglobinuria
   b. Icterus
   c. Thrombosis
   d. Straining to urinate

4. **Which of the following is not a pillar of the treatment of hemolysis?**
   a. Treatment of the underlying disease, if present
   b. Prevention of thrombosis
   c. Transfusions if the patient is demonstrating symptoms of anemia
   d. Immediate initiation of immunosuppressive agents in all patients

5. **Which of the following is a characteristic of all types of heparin (unfractionated or low molecular weight) used to prevent thrombosis in patients with immune-mediated hemolytic anemia?**
   a. Reliable bioavailability in veterinary patients
   b. No need for coagulation monitoring
   c. Once-per-day dosing
   d. Only available in injectable form