Immune-Mediated Anemia (IMHA)

(Destruction of Red Blood Cells Caused by an Immune Response)

Basics

OVERVIEW

- Accelerated destruction or removal of red blood cells related to an immune response, in which the body produces antibodies against red blood cells
- Also known as "immune-mediated hemolytic anemia" or IMHA
- "Anemia" is a low red blood cell count; "hemolytic" refers to hemolysis; "hemolysis" is the destruction of red blood cells, which allows the release of hemoglobin (the compound in the red blood cells that carries oxygen to the tissues of the body)
- "Antibody" is a protein that is produced by the immune system in response to a specific antigen (in this case, on the red blood cells); two groups of antibodies have been identified that are involved in immune-mediated anemia, based on characteristics identified in the laboratory: warm-reacting antibodies and cold-reacting antibodies

GENETICS

- Cocker spaniels are more likely to develop immune-mediated anemia than other breeds; absence of dog erythrocyte antigen (DEA) 7 is associated with increased risk in this breed

SIGNALMENT/DESCRIPTION OF PET

Species
- Dogs
- Cats

Breed Predilections
- Dog breeds—the cocker spaniel is the breed that is most likely to develop immune-mediated anemia; other commonly affected breeds include the miniature poodle, Irish setter, English springer spaniel, Old English sheepdog, Doberman pinscher, collie, bichon frise, miniature pinscher, and Finnish spitz
- Cat breed—domestic shorthair

Mean Age and Range
- In dogs, mean age, 5–6 years; reported range of 1–13 years of age
- In cats, mean age, 2 years; reported range of 0.5–9 years of age

Predominant Sex
- Females may have a higher risk than males in dogs
- Males have a higher risk than females in cats

SIGNS/OBSERVED CHANGES IN THE PET

- Sluggishness (lethargy)
- Weakness
- Collapse
- Lack of appetite (known as "anorexia")
- Exercise intolerance
- Difficulty breathing (known as "dyspnea")
- Rapid breathing (known as "tachypnea")
- Vomiting
- Diarrhea
- Dark red urine
- Eating of non-food items (known as "pica") in cats
- Pale gums and moist tissues of the body (tissues known as "mucous membranes"); rapid heart rate (known as "tachycardia")
- Enlarged spleen (known as "splenomegaly") and enlarged liver (known as "hepatomegaly")
- Yellowish discoloration to gums and moist tissues of the body (known as "icterus" or "jaundice") and dark urine (known as "pigmenturia") due to the presence of hemoglobin (a breakdown product of red blood cells) or bilirubin (a bile pigment that is in increased levels with icterus)
- Fever and enlarged lymph nodes (known as "lymphadenomegaly")
- Heart murmur
- Bruising or dark, tarry stools due to the presence of digested blood (condition known as "melena") possible in pets with coexistent low platelet counts (known as "thrombocytopenia") or a blood-clotting disorder (known as "disseminated intravascular coagulopathy" or DIC)
- Other generalized (systemic) signs possible (such as joint pain and kidney disease) when immune-mediated hemolytic anemia is a component of systemic lupus erythematosus (auto-immune disease in which body attacks its own skin and other organs)
- Death of tissues (known as "necrosis") involving the legs and ear tips in cold-type immune-mediated hemolytic anemia (rare)

CAUSES

Primary IMHA
- Auto-immune hemolytic anemia, where the body's immune system attacks its own red blood cells

Secondary IMHA
- Infectious causes (such as *Mycoplasma*, *Ehrlichia*, *Anaplasma*, *Babesia*, *Leishmania*, feline leukemia virus [FeLV], feline infectious peritonitis [FIP], long-term (chronic) bacterial infection)
- Heartworm (*Dirofilaria immitis*) disease
- Cancer (such as lymphoma and hemangiosarcoma)
- Medications (such as cephalosporins, propylthiouracil, and methimazole, sulfa drugs)

Miscellaneous Causes
- Systemic lupus erythematosus (auto-immune disease in which body attacks its own skin and other organs)
- Breakdown of red blood cells due to the presence of antibodies from the mother in the milk (condition known as "neonatal isoerythrolysis")—queen (mother cat) with blood type B; kitten with blood type A
- Breakdown of red blood cells (hemolysis) due to an incompatible blood transfusion

- Exposure to infectious agents, vaccination, chemicals or drugs, surgery, hormonal change, or other stressful events is suggested as a potential trigger for immune-mediated hemolytic anemia

Treatment

HEALTH CARE
- Inpatient during the sudden (acute) hemolytic crisis, during which the body is destroying red blood cells; outpatient when the packed cell volume (PCV, a means of measuring the percentage volume of red blood cells as compared to the fluid volume of blood) has stabilized, ongoing breakdown of red blood cells (hemolysis) has been controlled, and clinical signs of low red blood cell count (anemia) have resolved
- Inpatient if pet has complications such as development of a blood-clotting disorder (disseminated intravascular coagulopathy); blood clots to the lungs (known as "pulmonary thromboembolism"); low platelet counts (thrombocytopenia); bleeding into the gastrointestinal tract; or the need for multiple transfusions
- Long-term (chronic), low-grade breakdown of red blood cells outside of the blood vessels (known as "extravascular hemolysis") can be treated on an outpatient basis, if the pet is not exhibiting clinical signs secondary to the low red blood cell count (anemia)
- Fluid therapy to maintain vascular volume and correct dehydrationAddress underlying cause (such as infection or medications), if secondary immune-mediated hemolytic anemia is diagnosed

ACTIVITY
- Cage rest, until stable

SURGERY
- Surgical removal of the spleen (known as "splenectomy") can be considered if medical management fails to control the disease

Medications

Medications presented in this section are intended to provide general information about possible treatment. The treatment for a particular condition may evolve as medical advances are made; therefore, the medications should not be considered as all inclusive
- Packed red blood cells typed or cross matched; blood should be cross matched for pets that have received prior transfusions Steroids—prednisone, initially at a high dose and then gradually tapered to the lowest effective dose; follow the dosage prescribed by your pet's veterinarian carefully; dexamethasone can be used instead of prednisone; follow similar tapering schedule
- Chemotherapeutic drugs, if clumping together of red blood cells due to the presence of antibodies (known as "auto-agglutination") or very sudden breakdown of red blood cells (known as "peracute hemolysis") exists or if the response to prednisone is poor after 14–21 days; drugs include azathioprine, cyclophosphamide, or chlorambucil (for cats)
- Heparin may be administered to prevent blood clots in the lungs (thromboembolism) in dogs
- Cyclosporine—decreases the immune response
- Human λ-globulin

Follow-Up Care

PATIENT MONITORING
- Careful monitoring for complications, such as blood clots in the lungs (known as "thromboembolism"), bleeding (especially involving the gastrointestinal tract), blood-clotting disorder (disseminated intravascular coagulopathy); infection
- Monitor heart rate, breathing rate, and body temperature frequently during hospitalization
- Monitor for adverse reactions to treatment (such as transfusion reactions and overhydration [that is, too much fluid])
- If blood clots to the lungs (pulmonary thromboembolism) are suspected, frequently monitor chest x-rays (radiographs) and arterial blood gases (measurements of oxygen and carbon dioxide levels in arterial blood)

- During the first month of treatment, check the packed cell volume (a means of measuring the percentage volume of red blood cells as compared to the fluid volume of blood) weekly until stable and then every 2 weeks for 2 months; if still stable, recheck PCV monthly for 6 months and then 2–4 times per year; rechecks may need to be more frequent if the pet is on long-term medication
- A complete blood count (CBC) and reticulocyte count should be rechecked at least monthly during treatment, especially if chemotherapeutic drugs are used; if the neutrophil count falls to below 3,000 cells/mL of blood, discontinue chemotherapeutic drugs until the count recovers and then start drugs at a lower dosage; "neutrophils" are a type of white blood cell that fight infection
- Coombs' test can be monitored to assist in tapering of medications

PREVENTIONS AND AVOIDANCE
- Consider need for future vaccination on a case-by-case basis in dogs in which immune-mediated hemolytic anemia developed after vaccination

POSSIBLE COMPLICATIONS
- Blood clots in the lungs and other organs (known as "pulmonary and multi-organ thromboembolism") have been identified in up to 80% of all cases at necropsy
- Blood-clotting disorder (disseminated intravascular coagulopathy)
- Death of tissues in the liver (known as "centrilobular hepatic necrosis"); and death of kidney tubules (known as "renal tubular necrosis") secondary to low levels of oxygen in the blood and/or tissues (known as "hypoxia")
- Secondary infection Gastrointestinal ulceration due to high doses of steroids
- Increased levels of steroids in the blood due to high doses of steroids (known as "iatrogenic hyperadrenocorticism" or "iatrogenic Cushing's syndrome")
- Death

EXPECTED COURSE AND PROGNOSIS
- Immune-mediated hemolytic anemia and its complications (such as a blood-clotting disorder [disseminated intravascular coagulopathy] and blood clots to the lungs [pulmonary thromboembolism], and secondary infections) can be fatal; mortality ranges from 30% to 80% in dogs and 25% in cats
- Increased levels of bilirubin (a bile pigment formed from hemoglobin) in the blood (known as "hyperbilirubinemia") measured at greater than 5 mg/dL on bloodwork; clumping together of red blood cells due to the presence of antibodies (auto-agglutination); breakdown of red blood cells within blood vessels (intravascular hemolysis); severely low platelet counts (thrombocytopenia); low levels of albumin, a protein, in the blood (known as "hypoalbuminemia") are associated with a poor prognosis
- Response to treatment may take weeks to months; IMHA in which the bone marrow does not respond adequately to produce more red blood cells (known as "nonregenerative anemia") may have a more gradual onset than typical IMHA and may be slower to respond to treatment
- Breakdown of red blood cells (hemolysis) may recur, despite previous or current treatment

Key Points
- Immune-mediated hemolytic anemia and its complications (such as a blood-clotting disorder [disseminated intravascular coagulopathy] and blood clots to the lungs [pulmonary thromboembolism]) can be fatal
- **Lifelong treatment may be needed, and the disease may recur**
- **Side effects of treatment are common**