IMMUNE-MEDIATED ANEMIA
(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
• Isolated families of dogs have been documented to be affected (breeds include the Old English sheepdog, Vizsla, Scottish terrier, cocker spaniel, and miniature schnauzer)
• No genetic basis has been established

SIGNALMENT/DESCRIPTION of ANIMAL

Species
• Dogs
• Cats

Breed Predilections
• Dog breeds—Old English sheepdog, Vizsla, Scottish terrier, cocker spaniel, and miniature schnauzer; other commonly affected dog breeds include the miniature poodle, Irish setter, English springer spaniel, Doberman pinscher, and collie
• Cat breed—domestic shorthair

Mean Age and Range
• In dogs, mean age, 5 to 6 years; reported range of 1 to 13 years of age
• In cats, mean age, 3 years; reported range of 0.5 to 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 ANIMAL
• Collapse
• Weakness
• Sluggishness (lethargy)
• Lack of appetite (known as "anorexia")
• Eating of nonfood items (known as "pica") in cats
• Exercise intolerance
• Difficulty breathing (known as "dyspnea")
• Rapid breathing (known as "tachypnea")
• Vomiting
• Diarrhea
• Occasionally increased urination (known as "polyuria") and increased thirst (known as "polydipsia")
• 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 "lymphadenopathy")
• Heart murmur and "gallop" sound on listening to the heart with a stethoscope
• Bruising or dark, tarry stools due to the presence of digested blood (condition known as "melena") possible in animals with coexistent low platelet counts (known as "thrombocytopenia") or a blood-clotting disorder ("disseminated intravascular coagulopathy" or "DIC")
• Skin lesions may be seen
• Other generalized (systemic) signs possible (such as joint pain and kidney disease) if immune-mediated hemolytic anemia (IMHA) is a component of systemic lupus erythematosus (autoimmune disease in which body attacks its own skin and other organs)

CAUSES

Primary Immune-Mediated Hemolytic Anemia (IMHA)
- Autoimmune hemolytic anemia, where the body's immune system attacks its own red-blood cells
- Systemic lupus erythematosus (autoimmune 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
- Abnormal immune system
- Infectious agents (such as bacteria and viruses) and medications
- Unknown cause (known as "idiopathic immune-mediated anemia")

Secondary Immune-Mediated Hemolytic Anemia (IMHA)
- Infectious causes (such as *Mycoplasma*, *Babesia*, *Leptospira*, *Ehrlichia*, feline leukemia virus [FeLV], feline infectious peritonitis [FIP])
- Heartworm disease
- Cancer
- Medications (such as cephalosporins, propylthiouracil, and methimazole)

RISK FACTORS
- Exposure to infectious agents, vaccination, chemicals or drugs, surgery, hormonal change, or other stress events within the previous 30 to 45 days may act as a potential trigger for immune-mediated hemolytic anemia (IMHA)

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 animal has complications such as development of a blood-clotting disorder (disseminated intravascular coagulopathy or DIC); blood clots to the lungs (known as "pulmonary thromboembolism"); low platelet counts (thrombocytopenia); bleeding into the gastrointestinal tract; and heart failure and/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 patient is not exhibiting clinical signs secondary to the low red-blood cell count (anemia)
- Fluid therapy to maintain vascular volume and correct dehydration; use caution with administering fluids to patients with long-term (chronic) low red-blood cell counts (anemia) because volume overload (that is, too much fluid) is a concern
- Address underlying cause (such as infection or medications), if secondary immune-mediated hemolytic anemia (IMHA) 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 after 4 to 6 weeks of treatment

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.

- Cross-matched, packed red-blood cells for transfusion or oxyhemoglobin in cases with severely low red-blood cell counts (severe anemia)
- Supportive treatment for animals with blood-clotting disorder (disseminated intravascular coagulopathy or DIC), such as heparin or ultra-low dose aspirin along with azathioprine and steroids significantly improve survival
- 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 "autoagglutination") or very sudden breakdown of red-blood cells (known as "peracute hemolysis") exists or if the response to prednisone is poor after 14 to 21 days; drugs include azathioprine, cyclophosphamide, or chlorambucil (for cats)

• Studies have shown no increased effectiveness with combination therapy of cyclophosphamide and prednisone versus using prednisone alone
• Lefluomide may be useful in cases that do not respond to medical treatment
• Cyclosporine—decreases the immune response
• Danazol—for dogs; not recommended in cats as drug may cause liver damage
• Human γ-globulin

FOLLOW-UP CARE

PATIENT MONITORING
• 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 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 ("PCV," 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 to 4 times per year; rechecks may need to be more frequent if patient is on long-term medication
• A complete blood count (CBC) 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
• Blood tests (such as reticulocyte count and Coombs' test) can be monitored if the packed cell volume ("PCV," a means of measuring the percentage volume of red blood cells as compared to the fluid volume of blood) is not rising as expected

POSSIBLE COMPLICATIONS
• Blood clots in the lungs and other organs (known as "pulmonary and multiorgan thromboembolism") have been identified in up to 80% of all cases at necropsy
• Blockage of the portal vein by a blood clot; the portal vein is the vein carrying blood from the digestive organs to the liver (condition known as "portal vein thrombosis")
• Blood-clotting disorder (disseminated intravascular coagulopathy or DIC); has been diagnosed in 32% of dogs with immune-mediated hemolytic anemia (IMHA)
• Irregular heart beats (known as "cardiac arrhythmias"); 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 and inflammation/infection of the heart (known as "endocarditis")
• Death

EXPECTED COURSE AND PROGNOSIS
• Immune-mediated hemolytic anemia (IMHA) and its complications (such as a blood-clotting disorder [disseminated intravascular coagulopathy or DIC] and blood clots to the lungs [pulmonary thromboembolism]) can be fatal
• Very sudden (known as "peracute") disease usually caused by clumping together of red-blood cells due to the presence of antibodies (autoagglutination) or breakdown of red-blood cells within blood vessels (known as "intravascular hemolysis")
• Sudden (acute) disease usually caused by breakdown of red-blood cells within blood vessels (intravascular hemolysis) or outside of blood vessels (extravascular hemolysis)
• Long-term (chronic) disease usually caused by breakdown of red-blood cells outside of blood vessels (extravascular hemolysis) or cold-reacting antibodies (as identified in the laboratory)
• Increased levels of bilirubin (a bile pigment formed from hemoglobin) in the blood (known as "hyperbilirubinemia") measured at greater than 5 mg/dL on blood work; clumping together of red-blood cells due to the presence of antibodies (autoagglutination); 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
• Overall mortality 33.3% in dogs; reported as 23.5% in cats
• Clumping together of red-blood cells due to the presence of antibodies (autoagglutination) is associated with up to 50% mortality
• Very sudden (peracute) breakdown of red-blood cells (hemolysis) is associated with up to 80% mortality
• Warm-reacting immune-mediated hemolytic anemia (IMHA) has a guarded prognosis; of patients who survive hospitalization (up to 71%), long-term prognosis is relatively good
• Cold-reacting immune-mediated hemolytic anemia (IMHA) is more resistant to drugs to decrease the immune response (known as "immunosuppressive drugs") than warm-reacting IMHA
• Response to treatment may take weeks to months; immune-mediated hemolytic anemia (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 (IMHA) and its complications (such as a blood-clotting disorder [disseminated intravascular coagulopathy or DIC] and blood clots to the lungs [pulmonary thromboembolism]) can be fatal

• Life-long treatment may be needed, and the disease may recur

• Side effects of treatment may be severe