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Canine Immune-Mediated Hemolytic Anemia

What are red blood cells and what do they do?

Red blood cells are one of the main components of blood. Red cells carry oxygen from the lungs to the rest of the body. Oxygen is required for internal organs to function normally. Red cells are made in the bone marrow along with the other blood cells.

- *Hemoglobin* is the oxygen carrying molecule found in red cells. The *iron* in hemoglobin gives blood its red color
- *White blood cells* and *Platelets* are the other blood cells; white cells fight infection as part of the immune system; platelets help to clot blood and prevent bleeding
- *Plasma* is the fluid in which the red cells and other blood cells are suspended

What is immune-mediated hemolytic anemia (IMHA)?

IMHA is a disease in which the immune system reacts against red cells just as it would against a foreign bacteria or virus. When this happens, red cells are destroyed, *anemia* results, and oxygen delivery is greatly reduced. This leads to a number of common clinical signs and, if left untreated, death.

- *Anemia* is a low red cell count
- *Autoagglutination* is the clumping of red cells created by the IMHA immune reaction
- *Extravascular* IMHA occurs when red cells are destroyed within the organs of the immune system; this is the most common form
- *Intravascular* IMHA occurs when red cells are destroyed within the blood vessels
- *Evans' syndrome* is the combined immune mediated destruction of red blood cells and platelets

What causes IMHA?

The causes of IMHA are still not well understood. IMHA can result from a *primary* immune system problem or result *secondary* to some other condition. Primary IMHA is associated with certain breeds and is presumed to have a genetic component. Diseases that have been associated with IMHA include cancerous, inflammatory, and



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infectious disease. Vaccines and certain drugs have also been implicated as causes of IMHA. In most cases of IMHA the exact cause is not identified.

- Breeds predisposed to IMHA include the American Cocker Spaniel, Labrador Retriever, Miniature Schnauzer, and Shih Tzu
- Tick-borne infectious diseases have been associated with immune-mediated illness

What clinical signs does IMHA cause?

IMHA causes a number of clinical signs that will progress without treatment. Most of the clinical signs are associated with the destruction of red blood cells and lack of oxygen delivery. Complications, such as blood clots, can cause other more severe clinical signs.

Common signs include:

- Weakness
- Jaundice
- Anorexia
- Tachypnea
- Dark urine
- Vomiting
- Lethargy
- Pale gums

Less common clinical signs include:

- Dyspnea
- Sudden death
- Seizures

- *Jaundice* and *icterus* are the yellow discoloration of the skin, eyes, and plasma that occur when red blood cells are destroyed and *bilirubin* levels increase
- *Tachypnea* is increased respiratory rate
- *Dyspnea* is breathing difficulty or significantly increased respiratory effort
- *Anorexia* is the complete lack of appetite

What laboratory changes does IMHA cause?

IMHA can cause many changes on laboratory tests. Depending on the severity and duration of disease, the changes may be mild or extreme. Ultimately, laboratory tests are required to confirm the diagnosis of IMHA. Laboratory tests can also provide prognostic information.



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Common laboratory changes include:

- Anemia
- Autoagglutination
- Spherocytosis
- Leukocytosis
- Elevated bilirubin levels
- Increased liver enzymes
- Coagulation abnormalities
- Icteric plasma

- *Packed cell volume (PCV) and Hematocrit (HCT)* are measures of the relative amount of red blood cells present in the blood; normal is 40% to 60%
- *Spherocytes* are small rounded red cells typical of IMHA
- *Leukocytosis* is an increase in white blood cell numbers
- *Bilirubin* is a byproduct of the hemoglobin release that occurs with red cell destruction in IMHA; it can also be increased with liver or gall bladder disease

What testing is recommended for IMHA patients?

There are many goals in evaluating patients with IMHA. First, the diagnosis must be confirmed; secondly, other primary conditions that can cause IMHA and require specific treatment must be ruled-out; and finally, prognostic and complicating factors must be evaluated.

Most patients evaluated for IMHA will need the following tests:

- Chemistry profile
- Chest x-rays
- Complete Blood Count (CBC)
- Urinalysis
- Slide-agglutination test
- Coombs' test
- ANA titer
- Infectious disease titers
- Coagulation testing
- Abdominal ultrasound

- *The slide-agglutination test* is a quick test to evaluate for autoagglutination
- *Abdominal ultrasound* is a non-invasive test that uses sound waves to create images of internal organs and structures; this is performed along with x-rays to evaluate for underlying disease
- *Coombs' test* and *Anti-nuclear Antibody (ANA) titer* are tests that evaluate for immune response against red cells, and *DNA* (the genetic material of the cell), respectively.



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What complications can arise in patients with IMHA?

IMHA is notorious for causing secondary conditions in affected patients. The decreased oxygen delivery resulting from anemia can cause problems with internal organ functions, especially the liver and kidneys. In severe cases, increased bilirubin can be toxic to the kidneys and cause kidney failure. The most common complication in patients with IMHA, however, is *thromboembolic disease*. Blood clots can form within internal organs and cause severe respiratory difficulty, sudden death, or other clinical and laboratory changes.

- A *thrombus* is a blood clot that forms in a blood vessel; an *embolus* is a detached blood clot that is formed in one location and lodges in another; *thromboembolic disease* is the general term to describe both of these phenomena.

What treatment options are available for IMHA?

IMHA is considered a treatable condition. Aggressive medical care is required, however, to help dogs with IMHA and most require hospitalization. The immune response against the red cells must be controlled with immunosuppressive drugs. Blood clot formation must be prevented with *thromboprophylactic* medications. Anemia is treated with blood transfusion therapy. Oxygen and fluid therapy are often used for supportive care during the acute presentation. Other clinical signs, such as vomiting, diarrhea, or respiratory distress, are treated as needed. Because of how complex and variable IMHA is, the treatment of each patient is based on the individual disease presentation.

Long term treatment involves the use of immunosuppressive medications, thromboprophylaxis and other medications based on clinical signs. Animals are often on medications for 6-8 months after the time of presentation.

Any underlying diseases will also require treatment to help control the IMHA and reduce risk of future recurrence. Drugs or vaccinations given prior to illness should be avoided as should future immune stimulation (with vaccination, for example).

- *Thromboprophylaxis* is the prevention of blood clot formation; aspirin and heparin are used for this purpose



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- *Immunosuppressive* medications include steroids (prednisone, dexamethasone), azathioprine, cyclosporine A, and others; these medications are often used in combination and tapered slowly over time
- *Transfusion therapy* is provided with whole blood, concentrated red cells, or hemoglobin concentrates

What sort of long-term monitoring is recommended for IMHA patients?

General recommendations for patients with IMHA will depend on the individual case and what other primary or secondary conditions are identified. Generally, CBC/PCV evaluation is performed prior to and 7-14 days after reducing immunosuppressive medications. Depending on medications used, chemistry values may be monitored periodically. Slide-agglutination testing is also useful in assessing disease status. Monitoring is often patient-specific and unique recommendations may be made.

What is the prognosis with IMHA?

IMHA carries a fair prognosis in most cases, with published survival rates ranging from 50% - 80%. While anemia itself does not usually prove fatal, the complications of IMHA can be. Thromboembolic disease is the most life-threatening complication of IMHA, with survival rates dropping significantly in these patients. If a dog does well during the acute disease and treatment phase, they usually do very well over the long term. While many patients can be weaned from all medications, some patients may require life-long therapy. Regardless, they usually have an excellent quality of life.