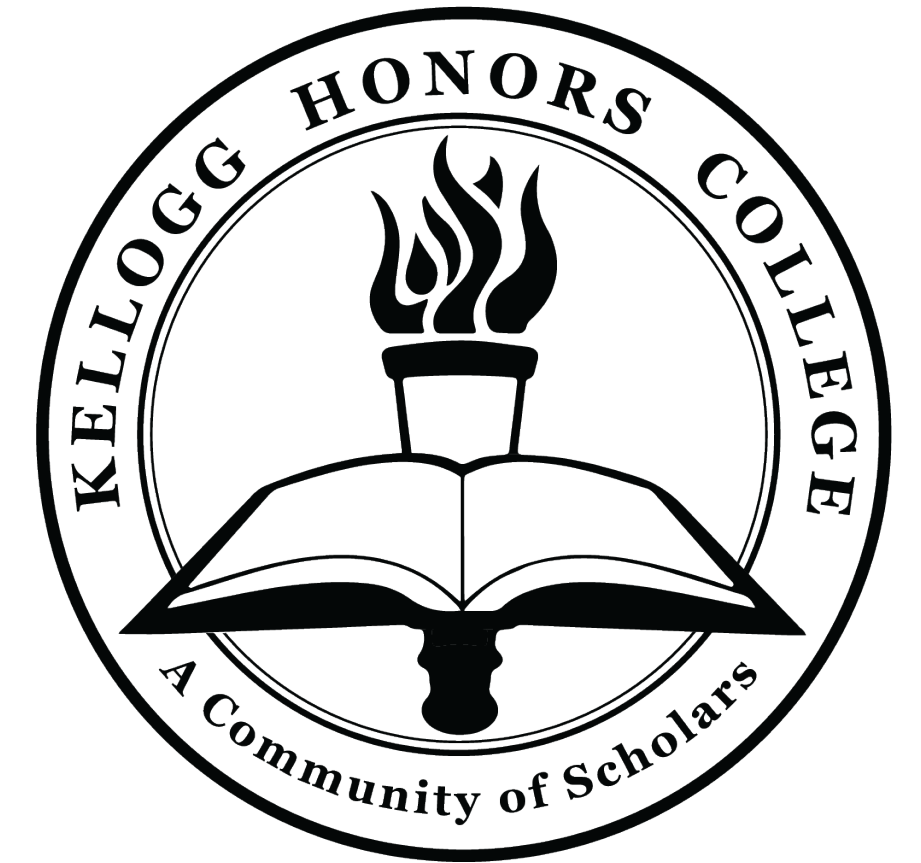# Diagnosis and Management of Autoimmune Hemolytic Anemia (AIHA) in Canines and Humans

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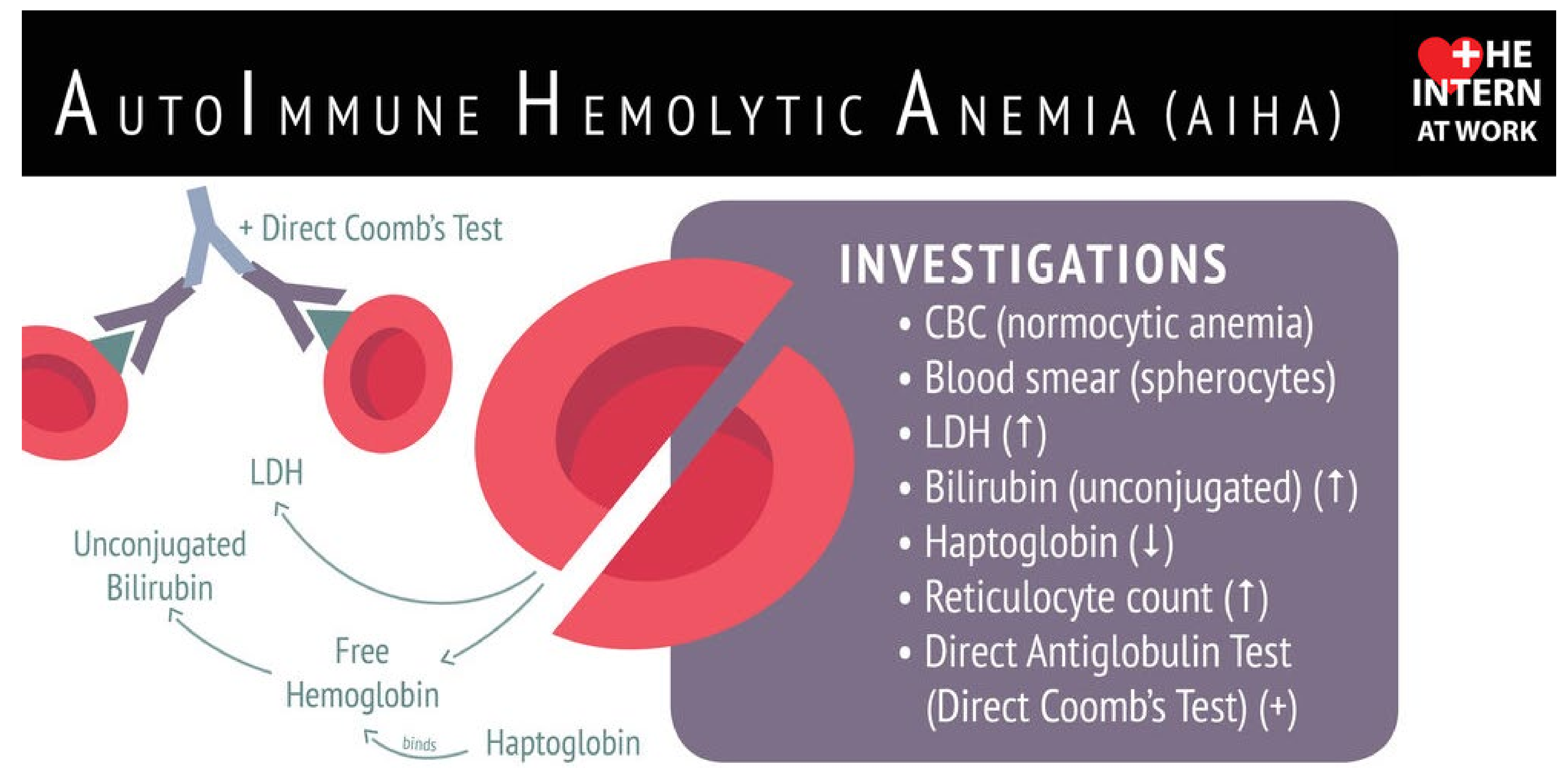Kellogg Honors College Capstone Project

Abstract: Autoimmune hemolytic anemia (AIHA) is an autoimmune disease that affects humans and animals. Although AIHA is found in both humans and animals, it is a more common disorder affecting all breeds of canine when compared to humans. The hallmark of AIHA is autoantibodies targeting red blood cells, and classification is based on pathophysiology of AIHA. Predisposing causes of AIHA are more identifiable in canines than humans, but idiopathic AIHA is the most common in both. The initial therapies for AIHA in both humans and canines are blood transfusions, but additional therapies such as splenectomies and immunosuppressive drugs, like Rituximab, are needed to treat AIHA. While some patients can be in remission for several years or even throughout the rest of their lives, many patients suffer from recurring AIHA.

Human Diagnosis and Treatment: With hemoglobin as the marker, a diagnostic test such as the direct antiglobulin test (DAT), or Coombs' test, serves as a conclusive laboratory tool to detect the presence of autoantibodies bound to RBCs (Hill et al., 2017; (Segel & Lichtman, 2014). Presence of autoantibodies may serve as indicators of varying diseases. A positive Coombs' test provides further insight and narrows the scope of potential diseases related to hemolysis of RBCs; also, this method of identifying positive IgG bound RBCs can differentiate between the forms of AIHA (Segel & Lichtman, 2014). While the Coombs' test is necessary in detecting AIHA in patients, the sensitivity of the test subjects it to errors in diagnosis (Bass et al., 2014). This may be due to low RBC bound antibody concentration and since the Coombs' test specifically detects IgG, there may be other immunoglobulins that have not been tested for in a patient with AIHA (Segel & Lichtman, 2014; Zanella & Barcellini, 2014). Detection of IgG is primary in a Coombs' test and other factors may play a role in why there may be a negative result. As a result of this, additional testing is required with a negative Coombs' test.

Treatment using glucocorticoids, such as Prednisone, haves been shown to help influence hemolysis (Hill & Hill, 2018; Hill et al., 2017). Glucocorticoid treatment has been found to decrease the production of autoantibodies and improve hemolysis (Bass et al., 2014). One study found that the Coombs' test and antiglobulin test showed improvement of RBC survival rate and stabilization of hemoglobin levels after glucocorticoid treatment in patients with an 80% positive response rate to the treatment (Zanella & Barcellini, 2014). Patients who have had positive responses to the glucocorticoid treatment showed better RBC results on the Coombs' test and antiglobulin test. Once the stabilization of RBC count and hemoglobin levels occurs, the dosage of glucocorticoids can be reduced or discontinued if the patient displays clear and consistent clinical responses (Zanella & Barcellini, 2014). Patients who do not respond to glucocorticoid therapy may need to consider additional therapies.

Canine Diagnosis and Treatment: In veterinary medicine, there are several methods used to diagnose AIHA in canines. One of the most common and typically the most recommended tests for diagnosing AIHA in canines is the Coombs' test (Piek et al., 2008). Although, using the Coombs' test results in similar issues in diagnosing canines as are found in humans. The primary problem with the Coombs' test in diagnosing AIHA in canines and humans is false negatives, and in several cases, canines with AIHA test negative on the Coombs' test (Idalan et al., 2021). Therefore, the Coombs' test should be used in combination with other tests to ensure correct diagnosis. One such test is the saline agglutination test (SAT) which can be used in addition to the Coombs' test (Garden et al., 2019). Blood tests from canines with AIHA used for evaluation using the SAT haves reported around 95% to 100% specificity in agglutination. If agglutination continues as the blood is further diluted with saline solution, it decreases the chances of false negatives from occurring (Garden et al., 2019). This at would suggest strong evidence of AIHA since agglutination persists.

Immunosuppressive therapy is commonly used in canines following packed RBC transfusion (Ridyard et al., 2010). The use of glucocorticoids, such as Prednisone, is also has been the primary treatment in combating AIHA in canines (Richter et al., 2021). The use of glucocorticoids is effective at combating AIHA in canines. Glucocorticoids is commonly used in the treatment of AIHA in canines as positive outcomes have been shown (Swann et al., 2019; Swann & Skelly, 2016). Canines suffering from AIHA treated with glucocorticoids usually have a positive response rate of about 80% (Wang et al., 2013). Canine patients typically respond within two weeks of initial treatment and the dosage of glucocorticoids can be tapered off and eventually discontinued if the canines shows no signs of recurrence of hemolysis during the monitoring period of 90 days (Weingart et al., 2019). Some canines who recover after glucocorticoid therapy show no signs of AIHA throughout their lives, while others may have a recurrence of AIHA after remission (Swann et al., 2019; Swann & Skelly, 2016). Reaction to glucocorticoid therapy varies in canines, some may need to be on the immunosuppressive drug for the rest of their lives, while others may only need the treatment for a short time. Prednisone is the most common glucocorticoid used for AIHA treatment, but additional immunosuppressive drugs, such as Azathioprine, can be used in combination with Prednisone if the canines are showing little to no response towards the therapy (Piek et al., 2008).

INVESTIGATIONS
- CBC (normocytic anemia)
- Blood smear (spherocytes)
- LDH ($\uparrow$)
- Bilirubin (unconjugated) ($\uparrow$)
- Haptoglobin ($\downarrow$)
- Reticulocyte count ($\uparrow$)
- Direct Antiglobulin Test (Direct Coomb's Test) (+)

Discussion: There are many parallels with AIHA in canines and humans. Both canine and human patients with AIHA are affected by the aggression of autoantibodies attacking and destroying healthy RBCs, causing serious deteriorating health (Hill et al., 2017). In addition, their immunoglobins, mainly IgG, are producing these autoantibodies and typically the cause of this disease is unknown. The treatment of AIHA in both humans and canines also has some similarities, however treatment of AIHA in canines is limited. Treatment of AIHA in canines primarily relies on the use of immunosuppressive drugs, while splenectomies are one of the major therapies in humans following glucocorticoid treatment (Barros et al., 2011). The use of splenectomies for AIHA treatment could possibly be used in canines as well following additional clinical studies. Although, AIHA research is commonly studied in humans and canines separately, it is beneficial to note the similarities between the diagnosis and treatment of AIHA and illustrate that human and veterinary medicine share common issues. Information about diseases, such as AIHA, are shared and integrated amongst the field to find and understand groundbreaking studies that can help the quality of life for both humans and animals.

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