

Nat Whitley**Head of Medicine, Davies Veterinary Specialists
BVMS, CertVC, DAVCIM, DECVIM, FRCVS
RCVS and European Specialist in Small Animal Medicine****What is IMHA?**

IMHA is a form of anaemia that occurs when the immune system starts attacking the red blood cells (sometimes called an autoimmune disease). This can occur in dogs of any breed, gender or age, but is more common in older dogs and may be more common in females. Some breeds are clearly predisposed, notably Cocker Spaniels. IMHA is an uncommon condition in dogs. It is even less common in cats and in man.

What are the symptoms of IMHA?

This depends on the severity of the disease. Sometimes signs of anaemia predominate – dogs may be lethargic, pale, weak and wobbly or even collapse. Some dogs breathe more quickly. Many dogs with IMHA become jaundiced – the tissues are stained a yellow colour – this is often noticed when looking at the gums, the whites of the eyes or areas where bare skin is visible (such as on the belly). The colour of the urine may change too, typically becoming deep yellow or brown, occasionally red. In contrast with other forms of anaemia, many dogs with IMHA feel quite unwell – they may have a fever, loss of appetite, vomiting or diarrhoea. These signs are associated with the body's significant inflammatory response that is part of the disease and a reaction to red blood cells being destroyed. A few patients suffer severe breathing difficulties due to blood clots developing in the lungs. Often the symptoms of IMHA come on quite suddenly – a dog can seem fine in the morning, then very ill a few hours later, but some cases have a more gradual onset of signs. Sometimes the immune system attacks other body tissues as well as the red blood cells. If the platelets in the blood are attacked, bleeding may develop. The joints, skin and kidneys are other possible targets but this is extremely rare.

What causes IMHA?

This is not fully understood and is the subject of ongoing research and debate. Most immune diseases occur due to a combination of an individual's genetic makeup and environmental factors, lifestyle and general health. Infectious disease and infections (especially those carried by ticks), drugs (including flea prevention, wormers and vaccines), toxins and pollutants and diet all fall under scrutiny. Other disease conditions that the dog has suffered from recently or may have at the same time as IMHA (ranging from severe dental disease to intestinal problems to cancers) can be relevant as possible "trigger" factors that could have upset the balance of the immune system and led to IMHA developing in a genetically predisposed dog. The exact trigger factor can be very difficult to identify. When no trigger factor can be found, the disease is referred to as "Idiopathic" IMHA. Where a trigger factor is found the disease is referred to as "secondary" IMHA. Flatcoated Retrievers do not seem to be at increased risk from Idiopathic IMHA compared with other breeds of dog. However, due to their propensity for cancer, Flatcoated Retrievers may present with secondary IMHA more often than some other breeds – cancer often has effects of the immune system.

Investigations

It is normally straightforward to confirm whether anaemia and jaundice are present by simple blood tests. Establishing whether the anaemia is caused by the immune system can be trickier – in IMHA, cells of the

immune system produce antibodies which bind to the outer membrane of the red blood cells, labelling them for destruction. The antibodies can make adjacent cells stick together in clumps (agglutination) and some red blood cells lose parts of their membrane and change shape rather than being completely destroyed. Clumping and cells whose shape has changed can be seen under the microscope, and additional tests (such as a Coombs test) are sometimes useful to “unmask” red blood cells that are coated with antibodies. X-rays of the chest and abdomen and an ultrasound of the abdomen, along with analysis of the urine, are routinely performed to see how the body is coping and look for other conditions that could have triggered or mimic IMHA. These “imaging” tests are particularly important in Flatcoated Retrievers to help rule out cancers. In some cases, blood tests for infectious disease may be appropriate. Occasionally a bone marrow sample gives additional useful information regarding possible triggers.

How is IMHA treated?

Many, but not all, cases of IMHA require a blood transfusion to improve the anaemia whilst initial investigations are underway and to “buy some time” to wait for drug therapies to take effect. In cases of “aggressive” or “fulminant” IMHA, more than one blood transfusion may be required. All blood transfusions carry a small risk of a “transfusion reaction” but these risks are small compared with the consequences of not giving a transfusion to a pet that really needs one. Best practice involves determining the dog’s blood type first to reduce the chances of transfusion reactions. If more than 4 days have elapsed from the first transfusion, a procedure called cross-matching should be done to ensure good compatibility between the blood donor and the recipient before giving further transfusions. Often other supportive and symptomatic treatments are appropriate for IMHA patients, such as intravenous fluids and antiemetic/antinausea and anticoagulant medications. In cases of secondary IMHA, if the trigger that has caused the disease can be removed or addressed, that may help get the IMHA under control more quickly. However, most cases of IMHA require drugs to suppress the immune system (immunosuppressant drugs).

Nearly all dogs with IMHA are started on glucocorticoid drugs, commonly called “steroids” (such as prednisolone) to suppress the immune system. IMHA is such a serious illness that it can be difficult to be patient whilst waiting for steroids to work, but in many cases steroids will bring the immune system under control within 7 days. Typically the dog remains hospitalised during this period. There is considerable debate and controversy about whether outcomes are improved by starting a second type of immunosuppressant drug alongside the steroids in the first 7 days, if the disease has not yet come under control. These additional drugs include azathioprine, ciclosporin, mycophenolate or leflunomide. Most vets agree that these drugs can be useful to allow the steroid dose to be reduced more quickly once the disease is under control. They are generally more expensive than steroids and require additional monitoring for side effects.

How long is immunosuppressant drug treatment required?

Drug treatment is usually required for between 3 and 6 months. Once it is clear that disease has been under good control for at least 2 weeks, the dose of drugs is gradually reduced (every 2-3 weeks) until the dog is off treatment. The risk of the disease relapsing and taking hold again is increased if the immunosuppressant drug dose is reduced too quickly. This has to be balanced against the cost and side effects of the drugs. Of all the drugs used, side effects of steroids are often the most problematic, but rarely life-threatening. They include increased appetite, thirst, lethargy, panting and muscle wastage. A few dogs that have been successfully weaned off drugs suffer a recurrence of IMHA months or years later. These unlucky patients will then require much longer courses of drugs or sometimes lifelong medication.

Can IMHA be fatal?

Yes. Unfortunately some dogs have such aggressive disease that it can prove impossible to keep up with their needs for transfusions or for owners to meet the costs of such high levels of care. Some dogs succumb to complications of the disease (such as blood clots) or the immunosuppressant drugs (such as infections). Although many of the early papers in the veterinary literature suggested high fatality, a large recent survey of dogs with idiopathic IMHA treated at select veterinary referral centres in UK was more encouraging: of 276 cases, 74.3% cases survived to discharge from the hospital and 67.7% of all cases were alive 30 days after admission.

Is there anything new on the horizon for IMHA in dogs?

Whilst onset of IMHA is very hard to predict or avoid, constant efforts are underway to establish the most effective immunosuppressant drugs regimes, and develop and evaluate potential new drugs. Results of a recent study (performed by referral centres in East Anglia) on use of human intravenous immunoglobulin with steroids for IMHA are eagerly awaited. The first veterinary licensed monoclonal antibody therapy (for allergic skin disease) has just become available in UK. In human medicine, use of monoclonal antibodies for treating immune system disorders is the norm, and hopefully this technology will have something to offer for IMHA in the future. For IMHA patients that do not respond to existing drugs there is also interest in a technique such as plasmapheresis (replacing the dog's plasma with the plasma from healthy donors), and splenectomy (surgical removal of the spleen, which is an important part of the immune system). Our understanding of blood clotting, and the best drugs to prevent blood clots developing in IMHA, is also evolving.

Further information

<http://vetspecialists.co.uk/announcements/vets-urged-to-assist-research-to-help-improve-prognosis-for-imha-cases>

Goggs R, Dennis S et al (2015) Predicting Outcome in dogs with Primary Immune-Mediated Hemolytic Anemia: Results of a Multicenter Case Registry. Journal of Veterinary Internal Medicine 29: 1603 -1610
(open access journal article)

http://vetspecialists.co.uk/factsheets/Internal_Medicine/IMHA.html