



Internal Medicine For Pet Parents

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Immune-Mediated Polyarthritis (IMPA)

What is IMPA?

Your pet has been diagnosed with a condition called immune-mediated polyarthritis (IMPA). *Arthritis* means joint and *Poly-* means that many of the joints are affected. *Immune-Mediated* means that the inflammation is caused by the immune system attacking the joints.

Typically, IMPA involves an inflammatory condition within your pet's joints, most commonly the carpi (wrist joints) and tarsi (ankle joints). This arthritis is different than what we think of for traditional arthritis, which involves a degeneration of the cartilage and underlying bone in a joint.

Immune-mediated polyarthritis involves active inflammation in the joint capsule and joint fluid. This inflammation occurs when antigen-antibody immune complexes that are circulating in the blood get filtered by the joint capsule. Antigens are foreign substances that invade in to the body. Antibodies are part of the immune system involved in recognizing foreign substances and marking them for destruction by the immune system. These complexes can form big "globs" that float around in the blood stream. When these complexes get lodged in the joint capsule, instead of being filtered through, the immune system reacts within the joint resulting in inflammation in the joint. Depending on the severity of inflammation, this will lead to pain and often swelling of the joints. In severe cases, there will also be a fever and systemic malaise.

Clinical Signs



Symptoms of IMPA may begin as a reluctance or stiffness when trying to get up or starting to walk. They may be more painful on one leg or another at varying times, so often the stiffness or any limping may alternate legs. This can be referred to as 'shifting lameness'.

Sometimes all four legs will be painful and your pet may attempt to minimize pressure on the joints by appearing to walk higher on their toes, change their head carriage to distribute weight, or step gingerly appearing to be walking on "eggshells." Most dogs will have visible swelling of their joints that will become more prominent or "pouch out" when they are bearing weight.

Some dogs may have neck or back pain if the joints of the spinal column are affected.

Other times there will may be fever, lethargy, decreased appetite, or malaise and the joints are evaluated when no other cause can be identified.

Making the Diagnosis

To confirm an immune-mediated polyarthritis, a sample of the joint fluid needs to be evaluated by a pathologist. In order to get the sample, a mild sedative is given, a surgical preparation of the effected joint/s is performed, and a needle is inserted into the joint to aspirate the joint fluid. The fluid obtained is then placed on a microscope slide, a blood tube, and a culture medium.

These samples are evaluated for:

- Microscopic evaluation of the joint fluid to look for an increase in the number of neutrophil white blood cells in the fluid.
- Culture of the fluid to rule out an underlying bacterial infection causing the joint inflammation.

Prior to performing a joint tap, the veterinarian may perform radiographs of at least one affected joint to make sure that there is no degeneration or destruction of the cartilage or bone indicating a different disease.

With any potential immune-mediated disease a full health screening is recommended to look for any other concurrent diseases.

Lab Work:

Full biochemistries and complete blood count are recommended to look for any organ disease or changes in blood cells indicating infection or decreases in red blood cells and platelets indicating concurrent immune-mediated disease or tick-borne infections.

Tick-borne infection screening is important to rule out infections that need to be treated to prevent further immune stimulation.

Radiologic Evaluation:

Evaluation of the thorax (chest) is recommended to ensure no infections or neoplasia in the lungs and heart. An echocardiogram may be indicated if a murmur is noted on physical exam.

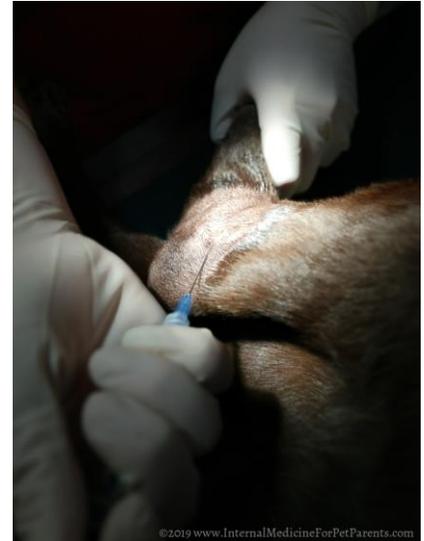
Evaluating the abdomen is also recommended, usually with an ultrasound, to screen for underlying causes.

Why Did This Happen?

When the immune system improperly attacks the body it can be an idiopathic reason (we don't know why, but it has happened) or it can be triggered by an underlying cause. These are defined as primary, idiopathic reason causing it, or secondary, another disease triggered the response. For the veterinarian to diagnose this as a primary immune-mediated disease other causes must be ruled out.

Diseases to rule out:

- Bacterial or fungal infections within the joint
- Systemic bacterial, fungal, viral, or parasitic infections such as:
 - tick-borne agents such as *Borrelia b.*, *Anaplasma*, *Rickettsia*, and *Ehrlichia*
 - heartworm disease



Joint tap of the hock Courtesy of Internal Medicine For Pet Parents

- chronic allergic skin disease
- dental disease
- Other systemic immune-mediated diseases such as:
 - systemic lupus erythematosus
 - immune-mediated hemolytic anemia or immune-mediated thrombocytopenia
- Cancer especially:
 - carcinoma, seminoma, Sertoli cell tumors, and leiomyoma.

Other potential triggers:

- Drugs: IMPA may develop after administration of any medications if an adverse reaction occurs, although certain drugs have been reported more often. Drugs such as antibiotics, human albumin, phenobarbital, and erythropoietin. Typically, symptoms can improve within 7 days of discontinuing the triggering medication.
- Vaccines: IMPA can be triggered by vaccines. The IMPA would present within 30 days of vaccine administration and the symptoms may resolve without immune suppression medications.
- Dog breeds predisposed to the development of IMPA include: Shar-Pei and Akita

Treatment Plan

Prognosis for IMPA depends on if an underlying cause can be identified and treated. These cases, secondary IMPA, have the best prognosis.

With either primary or secondary IMPA response to treatment is determined with aspiration of joint fluid (joint taps) to make sure that the inflammation has resolved microscopically. This is recommended as swelling and changes in the joints may not be evident on physical exam, but there may still be signs of immune reactivity within the joints.

Once there is no more evidence of inflammation, a slow tapering of the immunosuppressive medications can take place over 4-6 months. Ideally each time the dose is decreased, joint taps should be performed to make sure that the inflammation is not coming back.

If at any point the inflammation returns, higher doses of immunosuppression will have to be started again. These are usually then tapered down to the lowest dose that previously controlled the clinical signs and maintained there for a longer period of time before attempting to taper again. Alternatively, pets may continue a low dose life-long.

Treatment for IMPA involves a combination of treating the underlying source of the antigen along with suppression of the immune system to relieve the inflammation, swelling, and discomfort in the joints.

Tick-borne diseases are usually treated with antibiotics so even if no tick-borne disease is identified because these can be missed, a course of the antibiotic doxycycline may be recommended. Doxycycline also has some anti-inflammatory properties that can help joints to feel more comfortable more quickly.

If no underlying source can be identified, we are left with suppression of the immune system alone.

Immune Suppression

Corticosteroid hormones in high doses are the cornerstone of immune suppression. Prednisone and dexamethasone are the most popular medications selected.

Corticosteroids may well be the only immune suppressive medications the patient needs. The problem is that if they are withdrawn too soon, the inflammation will begin all over again. The patient is likely to be on high doses of corticosteroids for weeks or months before the dose is tapered down and there will be regular monitoring of the pet's joints. Expect your pet to require steroid therapy for at least 4 months.

If recurrence of the symptoms occurs during a tapering dose, the steroid is increased again and a secondary immune suppression agent may be prescribed.

Corticosteroids in high doses produce excessive thirst, re-distribution of body fat, thin skin, panting, predisposition for urinary tract infection and other signs that constitute Cushing's Syndrome. This is an unfortunate consequence of long-term steroid use but in the case of IMPA steroids are key to decreasing inflammation. It is important to remember that the undesirable steroid effects will diminish as the dosage diminishes.

Make sure to speak to your veterinary team if you have questions or concerns to help work together for the best solution for your pet. If your pet is experiencing extreme side effects from the steroids a quicker taper may be recommending with the addition of a secondary immune suppression drug.

Key Information:

- Give oral products with food.
- Goal is to find the lowest dose possible and use it for the shortest period of time.
- Many side effects are possible, especially when used long term. Most common ones are: greater appetite, thirst, and need to urinate.
- In dogs, stomach or intestinal ulcers, perforation, or bleeding can occur. If your animal stops eating, or you notice a high fever, black tarry stools or bloody vomit, contact your veterinarian immediately.
- Do not stop therapy abruptly without your veterinarian's guidance as serious side effects could occur.

Additional Immune Suppression

If minimal response is seen with corticosteroids or the side effects are extreme, supplementation with stronger immune suppressive agents is necessary.

Mycophenolate:

The most common medication used in cases of IMPA is mycophenolate. Typically, the mycophenolate dose does not change while tapering the steroids. Once the pet is on mycophenolate alone for several months with no sign of relapse a slow taper is recommended.

Key Information:

- Give medicine on an empty stomach; if animal vomits, try giving with a small treat to see if this helps.
- Diarrhea, vomiting, and lack of appetite are the most common side effects seen in dogs. Lack of energy and infection are possible while receiving this medicine. There has been limited use of this medication in animals (especially cats), so report any unusual signs to your veterinarian.

- **Pregnant women should use caution when handling this medication; this drug has a higher risk for causing birth defects.**

Leflunomide:

Leflunomide is an immuno-modulator that is meant for patients with immune mediated diseases when corticosteroids either do not work or cannot be used.

Key Information

- May be given either with food or on an empty stomach. Give with food if animal vomits or acts sick after getting a dose.
- Leflunomide has not been used much in animals, so side effects are not well known. Most likely side effects are vomiting and reduced appetite.
- **This drug has a very high risk for causing miscarriages or birth defects and it should NOT be used in households where pregnant women are present.**

Cyclosporine:

Cyclosporine is an immune-modulator, made popular by organ transplantation technology. It has the advantage over the two above medications of not being suppressive to the bone marrow cells.

Key Information

- Give on empty stomach (1 hour before or 2 hours after feeding). If your animal vomits or acts sick after receiving this drug on an empty stomach, try giving the next dose with food or a small treat. If vomiting continues, contact your veterinarian.
- May take up to 2 weeks to see if the drug is working. Cyclosporine level blood tests may be done if your animal is taking this medicine for immunosuppression.
- Vomiting, reduced appetite, and diarrhea are the most common side effects. These signs usually get better on their own, but if they are severe or persistent, contact your veterinarian.
- Contact your veterinarian immediately if you notice signs indicating an infection (eg, fever, low energy, poor appetite).
- **Pregnant women should handle this drug very carefully.**

Prognosis

A rapid response to immune suppressant therapy is expected in around 90% of cases. Some pets can be tapered off of all medications completely.

Of the 10% that do not respond quickly they may require secondary immune suppression and may be on lifelong medications. It is important to minimize side effects from the medications, so if these are seen speak to your veterinary team to help your pet have the best quality of life possible.

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