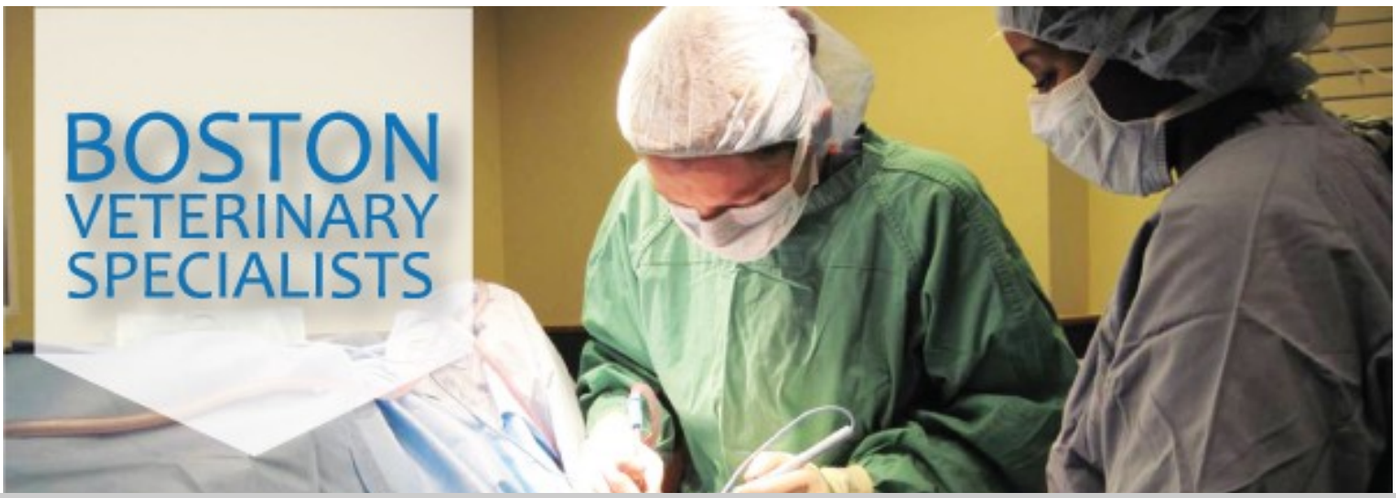

Monthly Update
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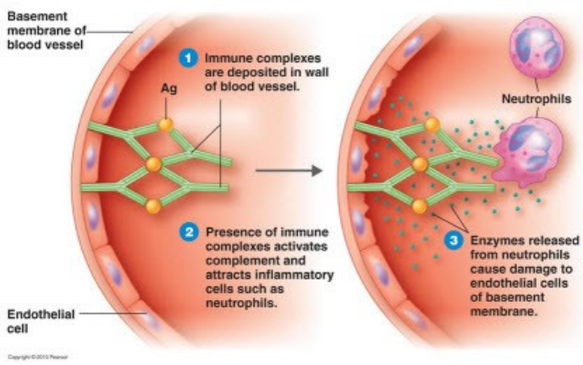
June 2013

Canine Immune Mediated Polyarthropathy

Kate Westcott, DVM and Louisa Rahilly, DVM DACVECC

Canine polyarathropy is a common disease, particularly in tick endemic areas. There are multiple presentations and etiologies of this condition and the astute veterinary practitioner should always have an index of suspicion for polyarthropathy in systemically ill or febrile dogs. We should also keep in mind that not all polyarthropathies in our area are caused by Lyme disease! Canine arthropathies are initially classified into inflammatory vs. non-inflammatory conditions. Inflammatory conditions are further subdivided into infectious/septic and non-infectious etiologies. Finally, non-infectious arthropathies are divided into erosive vs. non-erosive processes. Canine immune-mediated polyarthropathy (IMPA) is an inflammatory, non-infectious, non-erosive disease process.

The main proposed pathophysiologic mechanism of canine IMPA is a Type III hypersensivity reaction. During a Type III hypersensitivity reaction, immune complexes are formed and deposited in the synovium of the joints. Those immune complexes then attract inflammatory mediators to the area which results in inflammation and subsequent clinical signs of canine IMPA.



Canine IMPA has been classically categorized into 4 groups:
Type 1: Idiopathic
Type 2: Reactive
Type 3: Enteropathic
Type 4: Neoplasia-associated

Type I IMPA:

Type I IMPA, or idiopathic IMPA, is an inflammatory condition of the joints that does not have an underlying etiology. Type I IMPA is the most common type of IMPA seen in dogs. Type I IMPA is most commonly seen in younger sporting and large breed dogs. Incidence of clinical disease usually peaks around 2-6 years of age in canine patients. Over-represented breeds include the German Shepherd, Doberman Pinschers, Collie breeds, Spaniel breeds, Retrievers, Terriers, and Poodles. There is no statistically shown sex predilection for IMPA.

CT Scan Diagnostics

CCVS CT Scan Hours:

8:00 AM-6:00PM 7 days a week. 1-800-457-4900

The breakdown of CT charges are as follows:

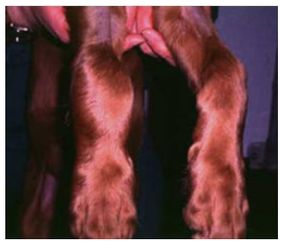
1. CT Scan, In patient $905.00 (case already hospitalized at CCVS or referred to CCVS for work up and treatment and has a CT scan)
2. CT Scan, Additional image (if you add an additional scan site $300.00)
3. CT Scan, Out patient $985.00 **(case sent to CCVS exclusively for a CT; this includes charges for doctor overseeing case, IV catheter, and fluids post CT).
4. CT "Met Check" $590.00
5. CT STAT fee, $50.00 (on top of whatever you are doing).

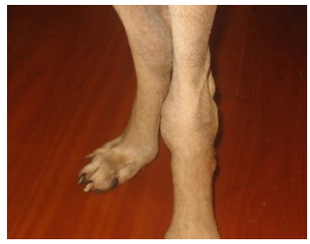
These charges cover the CT, the contrast, radiologists read, rapid infuser, sevo anesthesia, and technician fee if we need to call someone in for the CT. It does not cover injectable drugs, if needed for IV anesthesia; estimated additional cost $50.00-$75.00.

Visit Our Newsletter Archive

Read our March newsletter article - Endocrine Emergencies Part 2: Diabetic-ketoacidosis (DKA) and Thyrotoxicosis aka "Thyroid Storm" - by visiting our newsletter archive!
http://archive.constantcontact.com/fs032/1109892572426/archive/1110184841979.html

Clinical features of IMPA include lameness, "walking on eggshells" gait, joint swelling/effusion, painful joints, neck or spinal pain, fever, decreased appetite, vomiting, diarrhea, lethargy and lymphadenopathy. Multiple joints are usually affected, and it is the smaller, more distal joints such as the carpus, hock, and tarsus that are more frequently involved. It must also be noted that some dogs have absolutely no history or physical exam findings of joint disease and may only have systemic signs of illness at the time of presentation.

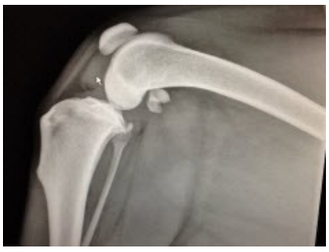




Diagnostics that should be considered in suspected cases of IMPA include baseline blood work (CBC, chemistry, 4DX), urinalysis with possible culture, joint radiographs, and arthrocentesis with joint cytology and culture.

Blood work for Type I cases of IMPA is usually non-specific, but can show a leukocytosis with neutrophilia, regenerative anemia, hyperglobulinemia, hypoalbuminemia, azotemia, increased ALKP, or be normal. The animal should be negative for tick -borne disease, and urinalysis is often normal. There may be mild proteinuria due to systemic inflammation.

Arthrocentesis is paramount in a definitive diagnosis of canine IMPA. Dogs with IMPA have a neutrophilic, non-septic synovial fluid. There should be no infectious agents identified on cytology and all cultures should be negative. Total nucleated cell count (TNCC) is usually increased with >5k WBC/uL and >80% neutrophils.



Joint radiographs in cases of IMPA usually only show joint and soft tissue inflammation and swelling. Radiographs of the joint are important in distinguishing erosive vs. non-erosive types of arthropathies.

Glucocorticoids are the cornerstone of treatment for Type I Canine IMPA. It has been shown that treatment with prednisone results in remission of 50% of cases with Type I IMPA. Immunosuppressive doses are used for the initial 2 weeks. The dose is subsequently tapered over 3-6 weeks depending on clinical response to treatment and joint fluid evaluation prior to each taper if possible. Response to prednisone therapy usually occurs in the first 48-72 hours, and is important to remind clients that therapy needs to be continued for at least two weeks prior to drug taper to avoid relapse. Many animals require multi-drug therapy for successful treatment of Type I IMPA.

Additional immunosuppressive medications that have been used in the treatment of Type I IMPA include azathioprine, cyclophosphamide, cyclosporine, levamisole, and leflunomide. Additional management of IMPA includes pain control management with opioids and/or NSAIDs. If animals are refractory to treatment, particularly if more than one immunosuppressive agent is being used, the animal should be reevaluated for a co-existing disease process causing a Type II IMPA or an alternate diagnosis.

The prognosis for Type I IMPA is fair to excellent. Relapses can occur, so it is important to educate clients as to the clinical signs to watch for at home.

Type II IMPA:

Type II IMPA, or "Reactive" IMPA is a polyarthropathy that is associated with infectious/inflammatory disease remote from the joints. Type II IMPA accounts for about 25% of all IMPA cases. The drug-induced and vaccine-induced polyarthropathies also fall into this category. Examples of inflammation or infection remote from the joints include Lyme disease, pancreatitis, infections of the oral cavity and respiratory tract, urinary tract infections, pyoderma, endocarditis, and diskospondylitis.

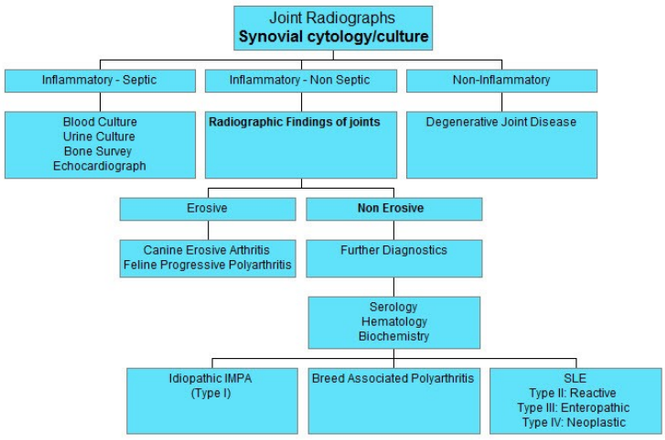
Drugs more commonly associated with causing a secondary polyarthropathy include sulfadiazine, phenobarbital, erythropoietin, penicillin, and ephalexin. Vaccines that have been associated in a similar fashion include calicivirus and canine distemper vaccines. Diagnostic results and prognosis of Type II IMPA cases is largely dependent on the underlying etiology of the polyarthropathy. Vaccine and drug-associated IMPA usually resolves within 7-10 days of vaccination and after discontinuation of the inciting drug. Additional diagnostics that should be considered include additional imaging such as abdominal ultrasound, abdominal and thoracic radiographs, echocardiography, serology, infectious disease testing, blood cultures, and CSF taps. Remember that Type II IMPA has an underlying etiology.

Treatment for Type II IMPA is directed at the underlying etiology. Once the underlying etiology is treated the polyarthropathy usually resolves without further treatment. Short-term, anti-inflammatory dose corticosteroids can be used to help treat the synovitis and pain/inflammation associated with reactive IMPA, but do not need to be used at immunosuppressive doses. In the face of the current Doxycycline shortage, Minocycline can be used to treat Lyme disease.

Type III IMPA:

Type III IMPA, or "Enteropathic" IMPA is a polyarthropathy that develops secondarily to gastrointestinal or hepatic disease. It is uncommonly reported in veterinary medicine and has been associated with ulcerative colitis and Crohn's Disease in humans.

As with Type II IMPA, diagnostic findings, treatment, and pronosis are all dependent on the underlying etiology. Supportive treatment for the pain and inflammation associated with the polyarthropathy can be treated as directed previously, and definitive treatment of the underlying etiology usually results in cessation of the polyarthropathy.



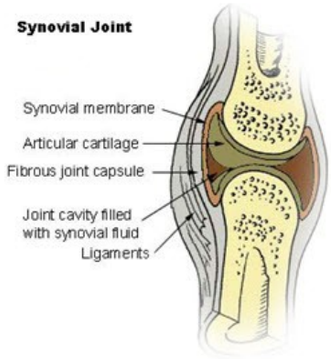
Type IV IMPA:

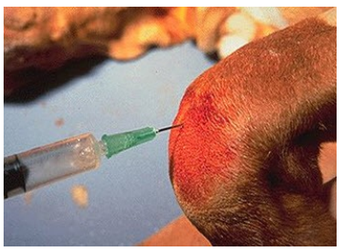
Type IV IMPA, or "Arthritis of Malignancy" is a polyarthropathy that arises secondary to neoplasia remote from the joints. More commonly associated neoplasms include squamous cell carcinoma (SCC), heart base tumors, leiomyoma, and mammary adenocarcinoma, although any neoplastic process can be involved.

Diagnostic results, treatment, and overall prognosis are largely dependent on the underlying etiology.

Arthrocentesis

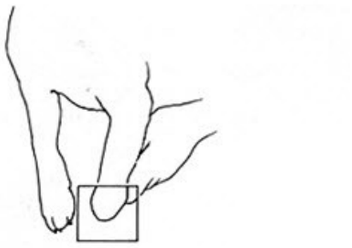
Arthrocentesis is the corner stone of confirmation of canine IMPA and should be considered in all patients with systemic disease and/or fever. It is usually performed under sedation or general anesthesia. The joint area should be clipped and a sterile preparation performed. Sterile technique including sterile gloves should be worn during this procedure to avoid inadvertently causing a septic arthritis and/or sample contamination! Depending on the size of the patient, a 22 or 25-gauge needle attached to a 3mL syringe can be used for procedure and sample collection. Larger dogs may require a longer needle for stifle sampling.

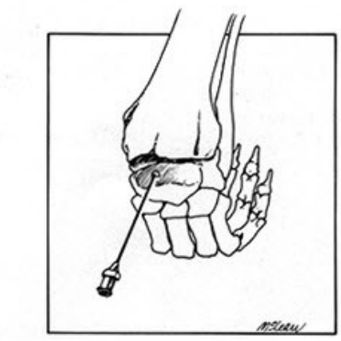




Fluid collected should be submitted for both cytology and culture. The following are diagrams of how to perform arthrocentesis of the most commonly sampled joints with specific descriptions of the procedure.

Carpal Arthrocentesis:



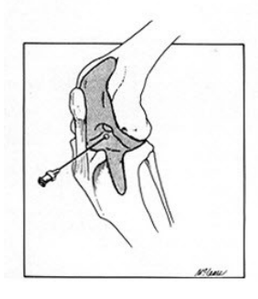


For carpal arthrocentesis the joint is placed in flexion.

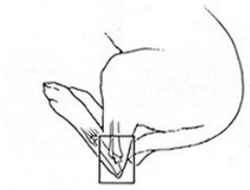
The needle should be inserted into the joint between the carpal bones just medial or lateral to the mid-sagittal plane, approaching from the dorsal aspect.

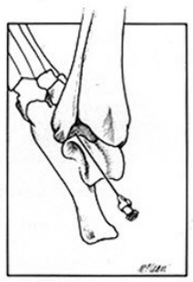
Stifle Arthrocentesis:

Place the stifle joint in flexion for proper exposure of the joint space. The needle should enter the joint either just medial or just lateral to the patellar ligament. The most exposed joint space is usually between the distal end of the patella and the proximal articular surface of the tibia. The needle should pass obliquely and caudally into the joint.

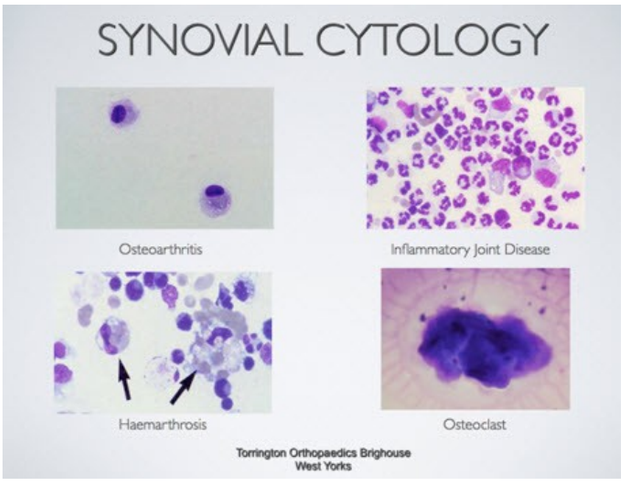


Hock (Talocrural) Arthrocentesis:
Place the joint in flexion, and approach from the caudal aspect of the joint. The needle should enter the joint from the plantar-lateral aspect and should be advanced in a dorsomedial and distal direction.





Normal Joint Fluid Analysis and Culture:
Normal joint fluid should be clear, colorless, and viscous. A cloudy or turbid appearance to the joint fluid is usually indicative of an increase in total nucleated cell count (TNCC). A thin or watery consistency to the joint fluid is usually due to breakdown of the normal polymerized hyaluronic acid (HA) found in joint fluid. This breakdown of HA can be due to dilution from serum, degradation from intra-articular inflammation or breakdown by proteases from bacteria. The normal cellular population of joint fluid should be a mix of large and small mononuclear cells with <10% of the cells being neutrophils. Joint fluid culture should be negative in cases of IMPA.



Evaluating joint fluid to direct tapering of drug therapy is very important in cases of Type I IMPA. Evaluating joint fluid every 2 weeks to guide treatment is ideal. A decrease in TNCC <4k/uL and mostly mononuclear cells is a good prognostic indicator for remission. Generally speaking, 3-5 mononuclear white blood cells per high power field (100X) is normal.

TECH TIP

ISOFLURANE OR SEVOFLURANE - DOES IT REALLY MATTER?

With the removal of halothane from the US veterinary market, veterinarians who hadn't already transitioned to use of isoflurane or sevoflurane are faced with selecting between them. The question of whether a practice should switch from isoflurane to sevoflurane or have both is also frequently raised. We currently use both depending on the patients age, general health, length of the surgical procedure, and surgeon's preference. The following discussion may help you understand the differences between the two gas anesthetics we have available and commonly use.

Blood Gas Solubility
Speed of anesthetic onset and recovery and the ability to change anesthetic depth precisely and rapidly are directly related to the agent's blood gas solubility. When all other factors are equal, changes occur faster when blood gas solubility decreases and so is most rapid for sevoflurane and slowest for halothane. Changes occur more rapidly with sevoflurane than with isoflurane. Clinically this impact is most notable in patients being anesthetized with an inhalant agent in the absence of other drugs (less common approach in today's practice except perhaps with small mammals and birds). While efficiency may be improved with a more rapid onset, offset and change in anesthetic depth, patient monitoring is critical to avoid an anesthetic overdose.

Vapor Pressure

The vapor pressure at a given temperature determines the maximum concentration of the inhalant. So for example, at sea level concentrations approximating 32% are possible for halothane and isoflurane, 21% for sevoflurane. Because these concentrations are well above the necessary anesthetic dose in human beings and animals, these drugs are administered using vaporizers calibrated to specifically administer clinically relevant concentrations. Agents with similar vapor pressures (e.g., halothane and isoflurane OR sevoflurane) have used interchangeably in the same vaporizer after thorough cleaning and recalibration. This has been historically used as a cost saving mechanism, but in today's environment manufacturers will frequently provide a vaporizer if the practice purchases sufficient inhalant agent.

While Mean Alveolar Concentration (MAC ie. the percentage of gas administered) vary slightly between species, for a specific agent they tend to be within a fairly tight numerical range. MAC is a good standard of comparison when evaluating physiologic effects (e.g., blood pressure, PaCO2) of a fixed concentration of the inhaled agents between species or effects at different concentrations within a species. While MAC may be used to guide anesthetic delivery in clinical patients, it is important to keep in mind that MAC is determined in healthy patients in the absence of modifying drugs. However, it does provide and indicator of drug potency; higher MAC values reflect a less potent drug or the need to get to a higher concentration to have a similar effect. Halothane is more potent than isoflurane which in turn is more potent than sevoflurane. This partially offsets the clinical effects of the differences in blood gas solubility observed for these agents. For example, the blood gas solubility for sevoflurane is approximately half that of isoflurane, but the MAC is approximately double. So while it takes less time for anesthetic uptake with sevoflurane, the concentration necessary to anesthetize a patient to a given depth is higher.

Cardiovascular and Respiratory Effects

Cardiovascular and respiratory depression occurs in a dose related manner with all the aforementioned inhaled agents. The magnitude of these changes at a given dose is both agent and species specific. Of the agents, halothane causes more cardiovascular depression, but less respiratory depression than isoflurane and sevoflurane which have roughly equivalent effects in the clinical dose range.

Other Considerations

Two other factors that should be considered when selecting between isoflurane and sevoflurane today are the reactivity of the compounds and their cost. Sevoflurane does react with carbon dioxide absorbents to form Compound A which has the potential, albeit limited or in extreme clinical circumstances, to be nephrotoxic. To minimize the level of Compound A present in the circuit, low flow or closed circuit anesthesia with sevoflurane is not recommended. This has an additional impact on the cost of using this agent which is while recently reduced in prices is still considerably more expensive than isoflurane. Example: Isoflurane @1liter of O2 per minute 1.4 %, costs 63 cent per hour; Sevoflourane @1 liter of O2 per minute 2.3%, cost $3.68per hour.

For many years, isoflurane has been the predominant inhalation agent in small animal practice in the US (vs. halothane). It offers greater cardiovascular stability, an ability to change depth more rapidly and is metabolized to a lesser degree than halothane. Veterinary patients unlike human patients do not seem to react adversely to isoflurane when administered by a mask. With the availability of the newer agent sevoflurane which like isoflurane is licensed for use in dogs, veterinarians have been faced with an additional choice of inhaled agent. The advocacy to switch to this agent has been largely driven by marketing of its rapid onset and offset. The literature is mixed in this regard and clinical impression suggests that in the presence of modifiers (premedications, injectable induction agents, analgesics, etc.) commonly used in peri-anesthetic patient management today, these potential advantages are less. The ability to quickly change anesthetic depth with sevoflurane can be an advantage as long as someone knowledgeable in its use is present during the anesthetic to monitor the patient. Cardiovascular and respiratory effects are very similar for the two agents. While likely not to be clinically important in the majority of patients the question of sevoflurane use in patients with renal compromise remains. The cost difference is not as substantial now as when sevoflurane was first introduced, but should be considered when choosing between the two agents.