





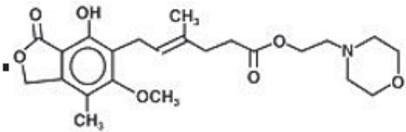




# A Newer Immunosuppressive Drug and Its Increased Use in Our Critical Care Unit: Mycophenolate Mofetil (MMF)



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➤ Mycophenolate Mofetil (MMF).

Mycophenolate mofetil (MMF) is a pro-drug whose metabolite inhibits guanine (a purine) nucleotide synthesis. Both B- and T-cells rely on this pathway

for proliferation. The drug has been used to treat rheumatoid arthritis, lupus, vasculitis, IBD, myasthenia gravis, immune-mediated hemolytic anemia (IMHA), and immune-mediated thrombocytopenia, and to prevent renal allograft transplant rejection in human patients. Its use has also been reported in veterinary literature. A recent journal article, by Dr. Bacek et al.,<sup>1</sup> describes the use of MMF in two cats with primary IMHA. This was the first report in the literature that described the use of oral MMF as an adjunctive treatment in cats with primary IMHA.<sup>2</sup> Both cats survived and no adverse effects from the drug were reported. In addition, this drug's use has been described in an abstract of eight dogs with IMHA, in a dog with immune-mediated glomerular disease, a dog with pemphigus vulgaris, and dogs with canine myasthenics.<sup>3,4</sup>



➤ "Spaulding" was treated with MMF and remains in remission.

Mycophenolate mofetil comes in the following formulations: pills, capsules, liquid, and injectable. In dogs the recommended dose ranges from 7 to 20 mg/kg PO BID, with the usual starting dose around 10 mg/kg. It can be given intravenously and has been given at 15–20 mg/kg diluted in 500 mL of 0.45% saline and 2.5% dextrose over four hours or 16 mg/kg IV over two hours.<sup>4</sup> It is thought that MMF may

achieve immunosuppression before azathioprine, since a positive clinical effect may take several weeks<sup>3</sup> with the latter medication. In fact, some papers report rapid inhibition to occur within two to four hours after dosing of MMF.<sup>5</sup> Potential adverse side effects in people include bone-marrow suppression, leukopenia, sepsis, infection, gastrointestinal upset (nausea, vomiting, diarrhea), and hypertension. In dogs the most commonly seen adverse side effect is gastrointestinal upset, though in my experience it is not too severe except perhaps at the highest doses. Mild suspected

allergic reactions have been reported with the parenteral preparation.<sup>5</sup> This medication has not been extensively reviewed in the veterinary literature and so its use and therefore efficacy remain controversial. Routinely, it is not a first-line immunosuppressive agent, and it is a fairly expensive drug. However, unlike some other immunosuppressive agents, blood levels need not be monitored to ensure efficacy.

Last year, MMF was used in our hospital to treat "Spaulding," who was managed by one of our emergency critical care residents, Dr. Roxanna Khorzad. "Spaulding" is a one-year-old CM Dachshund who was presented to Angell Animal Medical Center's Emergency service for labored breathing, not eating for two days, and vomiting. His physical exam and bloodwork were classic for IMHA. He had pale gums, icteric sclera, lethargy, and a II/VI heart murmur. Full bloodwork showed +2 spherocytes, autoagglutination, and polychromasia. His tick panel was negative. Whole-body radiographs and abdominal ultrasound did not reveal any abnormalities; therefore his diagnosis was primary IMHA. He was started on prednisone, cyclosporine, gastrointestinal protectants, and an anticoagulant. He needed four packed red blood transfusions prior to starting mycophenolate. After a few days on mycophenolate his red-blood-cell count stabilized and he was discharged from the hospital. His medications were tapered over a period of eight months, with mycophenolate as the sole agent keeping him in remission. All medications were stopped seven months ago and he remains in remission. Though it cannot be proven that the mycophenolate was the sole cause of his stabilization, clinically it seems like we have seen success with this medication.

The MMF used to treat "Spaulding" was ordered from outside pharmacies. However, recently our pharmacy has begun to stock MMF. We have Cellcept,<sup>®</sup> which can be given intravenously, and oral formulations (500 mg tablets, and a suspension that comes in 200 mg/ml). With these forms of medication, all of our patients can be dosed appropriately. A double-blind, placebo-controlled, prospective clinical study needs to be conducted to see if this drug decreases the length of hospital stay, and time to remission, in our patients with primary IMHA and other immune-mediated, small-animal diseases.

For more information about Angell's Emergency service, please visit [angell.org/emergency](http://angell.org/emergency). Angell's Emergency service doctors are available for consultation via phone or e-mail ([emergency@angell.org](mailto:emergency@angell.org)) on weekends and after hours 7:00 a.m.–11:00 p.m. To reach an Angell criticalist by phone, please call **617 522-5011**. Dr. Megan Whelan of Angell's Emergency service can also be reached via e-mail at [mwhelan@angell.org](mailto:mwhelan@angell.org).

#### References:

- 1 Bacek et al. Treatment of Primary Immune-Mediated Hemolytic Anemia with Mycophenolate mofetil in Two Cats. *J Vet Emerg Crit Care* 21(1): 45–49, 2011.
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# Thoracoscopy at Angell



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It is hard to believe that it has been 13 years since I did my first thorascopic pericardectomy. Having completed over 100 cases, I thought it was time to summarize the Thoracoscopy program at Angell Animal Medical Center.

Thoracoscopy is the term for entry and exploration of the thorax using endoscopy which, when coupled with the use a video camera and monitor, facilitates VAT (video-assisted thoracoscopy). There are many indications for thoracoscopy but my main focus and experience have been in performing partial pericardectomy ("pericardial window") on dogs with recurrent pericardial effusion. The procedure eliminates future episodes of cardiac tamponade, which allows for less intensive recheck schedules. In addition, thoracoscopy provides some clues as to the etiology of pericardial effusion, particularly in those dogs that are "tumor-negative" on echocardiography. In these cases, the main differential diagnoses are occult right atrial (usually auricular) hemangiosarcoma, idiopathic fibrosing pericarditis (there are many other names for this non-neoplastic condition), and malignant mesothelioma. Malignant mesothelioma is a diffuse, malignant transformation of the lining cells of the pericardium, pleural space, or peritoneal cavity (and occasionally other mesothelial-lined spaces), resulting in persistent neoplastic effusion.

I prefer to hold off on thoracoscopy in tumor-negative dogs who present with a first-time effusion. The rationale for this is compound: first, the timing and pattern of recurrence is a helpful clue to the etiology (for example, most dogs with occult HSA will have a recurrent bleed, acutely within three weeks, whereas patients with a benign condition or mesothelioma are more likely to recur slowly and gradually). Second, although thorascopic pericardial biopsy is helpful in making a diagnosis of mesothelioma, the procedure will speed the spread of the disease from the pericardial space to the pleural cavity (if it is not present already). Many patients who are eventually diagnosed with malignant mesothelioma initially have long periods (months to years) between pericardial effusions. If the patients are tumor-positive on echocardiography, going ahead with a procedure is an individual decision. Most patients with a "heart base tumor" or a dense tumor adjacent to the aortic arch that is presumed to be a chemodectoma will have a favorable short- and long-term prognosis. These patients do tend to have recurrent pericardial effusion, and therefore often do quite well with a palliative thorascopic pericardial window. It is important to note that tumor location alone has been shown to be misleading when making a tentative diagnosis of a cardiac-associated tumor. If the tumor appears irregular, cavitory, or associated with the right

heart, the clinical suspicion for hemangiosarcoma rises significantly. If there is recurrent pericardial hemorrhage within days, our clinical suspicion climbs. Hemangiosarcoma carries a poor long-term prognosis and is considered metastatic at the time of diagnosis. Palliative thorascopic pericardial window can be done to eliminate episodes of cardiac tamponade, but the tumor bleeding will in all likelihood persist and can lead to significant hemothorax. I have had mixed results with these cases, with some patients doing well for months and others for only days to weeks.

To summarize the overall results of the Angell thoracoscopy program: looking at well over 100 cases, the results have been excellent. The procedure is generally quick (average of 30 minutes operative time). The recovery is very quick (generally discharged one day post-operatively) and the pets and clients generally are happy with the results. To date, no patient has had recurrent pericardial effusion or tamponade after a pericardial window. The main potential complication is hemorrhage. Four cases to date have experienced clinically significant bleeding: one patient did not require therapy, two patients received a single transfusion of packed red blood cells, and one patient required multiple transfusions as well as a thoracotomy to identify and address the source of the bleeding (a severed aberrant branch of the internal thoracic artery). One patient (a diabetic) developed steatitis at one of the port sites. The remaining cases have not had any complications.

Our other main focus for exploratory thoracoscopy is for diagnosis of idiopathic pleural effusion. These cases are quick, low-risk, and high-yield. No complications have been noted. Potential additional indications include canine idiopathic chylothorax, vascular ring anomalies, and lung biopsy.

For more information or to discuss referral of a patient for thorascopic surgery, please contact me (Dr. Nancy Laste) at [nlaste@angell.org](mailto:nlaste@angell.org) or 617 541-5038. For more information about Angell's Cardiology service, please visit [angell.org/cardiology](http://angell.org/cardiology). ■

## > Determination of Immunophenotype in Hematopoietic Neoplasms (Continued from Page 3)

For more information about Angell's Oncology service, please visit [angell.org/oncology](http://angell.org/oncology), e-mail [oncology@angell.org](mailto:oncology@angell.org), or call 617 541-5136. You may also e-mail Dr. Mahoney at [jmahoney@angell.org](mailto:jmahoney@angell.org).

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# Tips to Help Clients Brush Their Pets' Teeth



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It has been said that "prevention is the best medicine." This is certainly true when discussing periodontal disease in cats and dogs. The "gold standard" for prevention is brushing, but it has been estimated that less than 10% (Linick S., *Veterinary Economics*, February 1, 2010) of our clients brush their pet's teeth daily. Following are some tips to help your clients develop an effective, successful, less stressful brushing routine with their pets.

- Introduce brushing when the pet is young and more malleable. Include a discussion of why it is important to brush and how to brush during one of the puppy and kitten visits.
- Inform clients that the bacteria in the plaque film that forms on their pets' teeth cause gingivitis that can lead to gum and bone recession, eventually resulting in the loss of teeth. Brushing will remove the film before it turns into tartar, and may prevent tooth loss in the future.
- Focus the client's attention on the outside surfaces of the teeth. The tongue usually does a good job of keeping the inside surfaces clean, and most pets dislike having their mouth opened.
- Recommend lifting the pet's lips and brushing his/her mouth when it is closed. A lot of pets do not appreciate having their mouth forced open and the mandibular teeth that are obscured by the maxillary teeth when the mouth is closed do not tend to develop significant plaque deposition.
- Encourage clients to brush the pet's teeth at least once daily about the same time every day and follow the brushing with a reward.
- Show clients how to brush the pet's teeth. Show the client how to lift up the lip and what is involved with brushing. Once shown how to brush the teeth, people often are surprised at how easy it can be.



Additional tips for more resistant pets — frequently the small breed dogs that are very prone to developing significant periodontal disease:

- The client should move the brush in small circles or back and forth on the visible teeth (buccal surfaces) with the bristles angled towards the gum line and the mouth closed.
- Suggest smearing the toothpaste on the teeth after brushing, if they want. For some animals this can be their treat after getting their teeth brushed.
- Be sure to remind owners to only use a pet toothpaste because human toothpaste can be harmful when swallowed.

For more information about Angell Animal Medical Center's Dentistry service, please visit [angell.org/dentistry](http://angell.org/dentistry), e-mail [dentistry@angell.org](mailto:dentistry@angell.org), or call 617 524-5643. Additionally, Dr. Stiles can be reached at [cstiles@angell.org](mailto:cstiles@angell.org). ■

## > The Value of Orthogonal Views (Continued from Page 4)

Finally, I would like to emphasize the importance of radiograph quality control. Rotated, poorly centered radiographs are hard to interpret, do not contribute to a diagnosis, and can be a waste of money. Repeating a poorly executed radiograph with an appropriate technique is invaluable, enabling visualization of a lesion made inconspicuous by under- or overexposure, or poor positioning. If you cannot interpret the radiographs due to poor technique, a radiologist will likely have just as much difficulty as you. If you or your technicians find yourself struggling with a patient, only to obtain mediocre radiographs, do not give up in frustration. Repeating the exam after sedating the patient will help you to help your patient. Sedating a patient is invariably money well spent.

I cannot reiterate enough that it is worth the extra time and effort to obtain a good-quality, complete set of radiographs. Orthogonal views will help you determine an accurate, three-dimensional assessment of your patient. Your own diagnostic ability will improve dramatically. And, if you are still stumped, we are always happy to consult with you and put in our two cents' worth.

For more information about Angell's Diagnostic Imaging service, please visit [angell.org/diagnosticimaging](http://angell.org/diagnosticimaging), e-mail [diagnosticimaging@angell.org](mailto:diagnosticimaging@angell.org), or call 617 541-5139. You may also e-mail Dr. Basseches at [jbasseches@angell.org](mailto:jbasseches@angell.org). ■

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