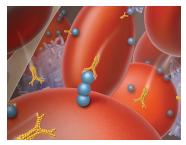
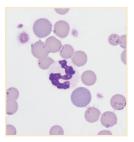


Hemotropic Mycoplasma spp

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Mycoplasma haemofelis. Photo courtesy of Jennifer Neel, DVM, DACVP (Clinical), North Carolina State University.

Overview

Hemotropic *Mycoplasma* spp of the cat

- M haemofelis
- Candidatus M haemominutum
- Candidatus M turicensis

Hemotropic Mycoplasma spp of the dog

- M haemocanis
- Candidatus M hematoparvum
- Note: Experimental data are not available on the need or efficacy of treatment of hemotropic Mycoplasma spp infections in dogs.

Pradofloxacin

Cats: 5 or 10 mg/kg PO once a day for 14 consecutive days¹

Contraindicated in cats with hypersensitivity to quinolones²

Dogs (extralabel, based on anecdotal evidence): 5 or 10 mg/kg PO once or twice a day for 14 consecutive days

• Although in some countries pradofloxacin is licensed for use in dogs, it is only available extralabel in the United States because of safety concerns (eg, marrow suppression with neutropenia/thrombocytopenia²).

Pradofloxacin, a fluoroquinolone antibiotic, disrupts bacterial replication by inhibiting DNA gyrase (thereby preventing DNA replication) and by blocking topoisomerase IV. In

an experimental infection model in cats, pradofloxacin administered at 5 or 10 mg/kg showed efficacy similar to doxycycline against *M haemofelis* and appeared to provide more effective long-term clearance of *M haemofelis* organisms than did doxycycline administered at 5 mg/kg twice a day for 14 days.¹

• To date, there are no experimental data on treatment efficacy of pradofloxacin in dogs.

Marhofloxacin

Cats only: 2.75 mg/kg PO once a day for 14 days³⁻⁵

Marbofloxacin is a carboxylic acidderivative fluoroquinolone antibiotic that disrupts bacterial replication by inhibiting DNA gyrase and thereby preventing DNA replication. Following experimental infection of cats with *M haemofelis*, marbofloxacin was safe and resulted in rapid hematologic improvement but did not consistently eliminate infection.³⁻⁵

Enrofloxacin

Cats: 5 mg/kg PO once a day6

- Cats at risk for retinal lesions
- Caution: 5 mg/kg is upper end of dosing for this indication, and because other efficacious and safer fluoroquinolones are available, pradofloxacin or marbofloxacin is recommended for treating hemotropic *Mycoplasma* spp infections in cats.

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Dogs (based on anecdotal evidence): 5 or 10 mg/kg PO once a day for 14 days

Enrofloxacin, a fluoroquinolone antibiotic, disrupts bacterial replication by inhibiting DNA gyrase and thereby preventing DNA replication. Treatment with enrofloxacin at 5 mg/kg was well tolerated by cats and was equally or more effective than doxycycline administered at 5 mg/kg PO once a day for 14 days. However, enrofloxacin use in cats has been linked to a risk for retinal lesions.

 No experimental data to date for treatment of hemotropic Mycoplasma spp infections in dogs

Doxycycline

Cats: 10 mg/kg P0 twice a day for 14-28 days⁶

 Neither a lower dose of 5 mg/kg twice a day nor higher dose of 10 mg/kg twice a day consistently eliminates Mycoplasma spp infections in cats.

Dogs (based on anecdotal evidence): 10 mg/kg PO once a day for 14-28 days⁷

Doxycycline is a tetracycline class antibiotic that inhibits protein synthesis by binding of aminoacyl-tRNA synthetase to the 30S ribosomal subunit in the mRNA translation complex. Historically, tetracycline derivatives were considered the drugs of choice for treating hemotropic *Mycoplasma* spp infections.

Based on laboratory studies, fluoroquinolones are of equal or superior efficacy for treating *M haemofelis* as compared with doxycycline. Administration of doxycycline rarely clears *M haemofelis* from the body and can be ineffective at controlling clinical signs of disease. In addition, oral administration of capsules has been associated with esophageal strictures in cats. Therefore, administration of a fluoroquinolone antibiotic has become the treatment of choice.^{6,8}

 No published data available for treatment of Mycoplasma spp infections in dogs

Minocycline

Cats (extralabel): 8.8 mg/kg PO once a day for 14 consecutive days⁹

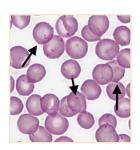
Dogs (extralabel, based on anecdotal evidence): 10 mg/kg P0 twice a day for 14 consecutive days

Minocycline is also in the tetracycline class of antibiotics. Recently, increased cost and decreased availability of doxycycline have sparked an interest in using minocycline as an alternative antibiotic in cats and dogs. However, there are no controlled studies involving the use of minocycline for treatment of hemotropic *Mycoplasma* spp infection (or any tick-borne disease) in cats or dogs.

 Although gastrointestinal upset can occur in both dogs and cats, a recent pharmacokinetic study found that one 50Therapeutic elimination of hemotropic Mycoplasma spp infections can be challenging, and reactivation after treatment is not uncommon.

DNA = deoxyribonucleic acid, mRNA = messenger ribonucleic acid, RNA = ribonucleic acid , tRNA = transfer ribonucleic acid





Mycoplasma haemocanis organims. Long arrows point toward dot-like forms nestled in the membrane on the outer edge of the cell; shorter arrow points to a more ring-shaped M haemocanis organism. Photo courtesy of Jennifer Neel, DVM, DACVP (Clinical), North Carolina State University.

mg capsule PO once a day would provide appropriate dosing for most cats.9

Prednisolone

Cats, Dogs: 1-2 mg/kg PO twice a day as needed to control secondary immunemediated hemolysis¹⁰

Prednisolone is a synthetic glucocorticoid and a derivative of cortisol that is used to treat a variety of inflammatory and autoimmune conditions. Concurrent administration of immunosuppressive corticosteroids with an antibiotic is only recommended in cats and dogs with a rapidly progressive, severe hemolytic anemia. Because the cause of hemolysis is an infection, suppressing and hopefully eliminating the infection with an antibiotic is the primary objective. In some instances, hemolysis is so severe and rapidly progressive that the immune system must be suppressed to keep the animal alive.

Azithromycin (Not Recommended)

Cats: Azithromycin is not recommended therapy for feline hemoplasmosis.

Azithromycin, an azalide, is a subclass of macrolide antibiotics. When administered at a dose of 15 mg/kg P0 twice a day for 7 days to cats experimentally infected with *M haemofelis* or *Candidatus* M haemominutum, azithromycin was not an effective treatment.¹¹

Cats (particularly feral, stray, and fleainfested animals) can also be co-infected with *Bartonella henselae*. Based on in vitro testing, *B henselae* isolates rapidly developed azithromycin resistance due to a homogenous single nucleotide substitution in the 23S rRNA gene.¹²

PCR = polymerase chain reaction, rRNA = ribosomal ribonucleic acid

Closing Remarks

Although cats can be infected with *Candidatus* M haemominutum and *Candidatus* M turicensis, *M haemofelis* is considered the agent most likely to cause hemolytic anemia. Hemoplasmosis often occurs in association with immunosuppression or a concurrent infectious or noninfectious disease process.

Therapeutic elimination of hemotropic Mycoplasma spp infections can be challenging, and reactivation after treatment is not uncommon. Similar to cats, hemoplasmosis in dogs most often occurs as a result of concurrent disease or coinfection with a more pathogenic microorganism. Few experimental studies have evaluated therapy for canine hemotropic mycoplasmosis; based on limited follow-up polymerase chain reaction (PCR) assay data, as demonstrated in experimentally infected cats, 10 dogs that recover from hemotropic mycoplasmosis probably have latent infections. The advent of PCR testing now allows clinicians to more accurately assess treatment efficacy for hemotropic Mycoplasma spp infections than was historically possible. 13

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- gastrointestinal disease. *JVIM*. 2001:15(1):26-32.
- 35. Ruaux CG, Steiner JM, Williams DA. Early biochemical and clinical responses to cobalamin supplementation in cats with signs of gastrointestinal disease and severe hypocobalaminemia. *JVIM*. 2005;19(2):155-160.
- 36. Plumb DC. Folic acid. In: Plumb DC, ed. *Plumb's Veterinary Drug Handbook*, 8th ed. Ames, IA: Wiley-Blackwell; 2015:636-638.
- 37. Plumb DC. Maropitant citrate. In: Plumb DC, ed. *Plumb's Veterinary Drug Handbook*, 8th ed. Ames, IA: Wiley-Blackwell; 2015:890-892.

- Plumb DC. Ondansetron. In: Plumb DC, ed. Plumb's Veterinary Drug Handbook, 8th ed. Ames, IA: Wiley-Blackwell; 2015:1071-1073.
- 39. Sartor RB, Muehlbauer M. Microbial host interactions in IBD: implications for pathogenesis and therapy. *Curr Gastroenterol Rep.* 2007;9(6):497–507.
- Bybee SN, Scorza AV, Lappin MR. Effect of the probiotic Enterococcus faecium SF68 on presence of diarrhea in cats and dogs housed in an animal shelter. JVIM. 2011;25(4):856-860.
- 41. Jergens AE. Traditional & nontraditional therapies for IBD: evidenced-based approach. In: Proceedings of the

- American College of Veterinary Internal Medicine (ACVIM) Forum, 2015; Indianapolis, IN.
- 42. Gieger T. Alimentary lymphoma in cats and dogs. *Vet Clin North Am Small Anim Pract*. 2011;41(2):419-432.
- 43. Kiselow MA, Rassnick KM, McDonough SP, et al. Outcome of cats with low-grade lymphocytic lymphoma: 41 cases (1995-2005). *JAVMA*. 2008;232(3):405-410.
- 44. Stein TJ, Pellin M, Steinberg H, Chun R. Treatment of feline gastrointestinal small-cell lymphoma with chlorambucil and glucocorticoids. *JAAHA*. 2010:46(6):413-417.



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REFERENCES

- 1. Dowers KL, Tasker S, Radecki SV, Lappin MR. Use of pradofloxacin to treat experimentally induced *Mycoplasma haemofelis* infection in cats. *Am J Vet Res.* 2009;70(1):105-111.
- 2. Bayer Healthcare Animal Health Division (2012). Veraflox (pradofloxacin, package insert). Shawnee Mission, KS.
- Tasker S, Caney SMA, Day MJ, et al. Effect of chronic FIV infection, and efficacy of marbofloxacin treatment, on Mycoplasma haemofelis infection. Vet Microbiol. 2006;117(2-4):169–179.
- 4. Tasker S, Caney SM, Day MJ, et al. Effect of chronic feline immunodeficiency infection, and efficacy of marbofloxacin treatment, on 'Candidatus Mycoplasma haemominutum' infection. Microbes Infect. 2006:8(3):653–661.
- 5. Ishak AM, Dowers KL, Cavanaugh MT, et al. Marbofloxacin for the treatment of

- experimentally-induced *Mycoplasma haemofelis* infection in cats. *JVIM*. 2008;22(2):288-292.
- Dowers KL, Olver C, Radecki SV, Lappin MR. Use of enrofloxacin for treatment of large-form Haemobartonella felis in experimentally infected cats. JAVMA. 2002;221(2):250–253.
- Greene CE. Hemotropic mycoplasmosis (hemobartonellosis). In: Greene CE, ed. Infectious Diseases of the Dog and Cat, 4th ed. St. Louis, MO: Elsevier Saunders; 2013:310-319.
- 8. Lappin MR. Treatment of *Mycoplasma* spp. infections in cats. *Vet Pract*. June:17-18, 2010.
- Tynan BE, Papich MG, Kerl ME, Cohn LA. Pharmacokinetics of minocycline in domestic cats. J Feline Med Surg. 2015 Apr 7, pii: 1098612X15579114. [Epub ahead of print].
- 10. Papich MG. Saunders Handbook of

- Veterinary Drugs: Small and Large Animal, 3rd ed. Philadelphia, PA; Saunders; 2011:642-644.
- 11. Westfall DS, Jensen WA, Reagan WJ, Radecki SV, Lappin MR. Inoculation of two genotypes of *Hemobartonella felis* (California and Ohio variants) to induce infection in cats and the response to treatment with azithromycin. *Am J Vet Res.* 2001;62(5):687-691.
- Biswas S, Maggi RG, Papich MG, Breitschwerdt EB. Molecular mechanisms of *Bartonella henselae* resistance to azithromycin, pradofloxacin and enrofloxacin. *J Antimicrob Chemother*. 2010;65(3):581-582.
- 13. Tasker S, Helps CR, Day MJ, Harbour DA, Gruffydd-Jones TJ, Lappin MR. Use of a Taqman PCR to determine the response of Mycoplasma haemofelis to antibiotic treatment. J Microbiol Methods. 2004;56(1):63-71.