# Top 5 Transplacental Parasitic Infections in Dogs

**Dwight D. Bowman, MS, PhD** Cornell University



 Tissue press of murine brain tissue showing an infective third-stage larva of *Toxocara canis*

In dogs, parasites that infect the fetus transplacentally may cause life-threatening disease in the fetus and newborn. Transplacental transmission also allows vector-borne diseases to cycle when vectors are not active or present in a geographic area and can contribute to introduction and establishment of parasites where they previously did not occur. This mode of transmission is well-known for some parasites (eg, Toxocara canis) and more recently shown to occur with others (eg, Leishmania infantum).

# Toxocara canis

Puppies infected in utero by massive numbers of reactivated T canis larvae in the bitch sometime after the 42nd day of pregnancy are at risk for obstruction and rupture of the intestine.1 Rupture can lead to peritonitis that may be exacerbated by continued release of eggs into the peritoneal cavity. Puppies can be presented with inappetence, depression, diarrhea, weakness, ascites, failure to thrive, cachexia, and signs similar to those of rickets (eg, difficulty rising, bowed limbs, stiff gait). Young adult worms may be found in the peritoneal cavity, bile ducts, and even the liver parenchyma. The typical pressure-sensitive, drum-shaped abdomen may occur as well. Puppies with large numbers of prenatal T canis will have decreased erythrocyte numbers, mostly caused by severe internal bleeding from preadults

# TOP 5 TRANSPLACENTAL PARASITIC INFECTIONS IN DOGS

- 1. Toxocara canis
- 2. Neospora caninum
- 3. Babesiosis
- 4. Leishmaniasis
- 5. Dirofilarial microfilariae



 Tissue press of brain tissue from a naturally infected dog showing a cyst (arrow) containing bradyzoites of Neospora caninum

migrating through the liver and intestinal rupture; when only moderately infected, puppies will show an increase in erythrocytes from the fifth week of life onward.<sup>1</sup> Eosinophilia is observed in prenatally infected puppies beginning 7 days postpartum.<sup>1</sup> Liver enzymes (ie, glutamate dehydrogenase [GLDH] and alanine transaminase [ALT]) are elevated at birth.<sup>1</sup> Enzyme levels return to normal values 1 to 2 weeks postpartum.<sup>1</sup> Prenatal infection almost guarantees that puppies will be infected with *T canis* at birth.

### Management

No anthelmintics are registered in the United States for prevention of transplacental transmission of *T canis*. Macrocyclic lactones have demonstrated efficacy against reactivated larvae in pregnant dogs.<sup>2</sup> Moxidectin reliably prevents *T canis* infections in puppies after 2 SC applications on days 40 and 55 of pregnancy.<sup>3,4</sup> Ivermectin and doramectin can also be efficacious at high dosages. Fenbendazole is labeled in the United Kingdom for prevention of transplacental transmission of *T canis* but only when administered daily from day 40 of pregnancy until parturition.<sup>5</sup>

### Neospora caninum

When prenatally acquired, infection with Neospora caninum (ie, neosporosis) can result in a progressively worsening polyradiculitis, often leading to fatal paralysis.<sup>6-8</sup> Signs can begin at 3 to 9 weeks of age and typically appear in dogs younger than 6 months of age presented with ascending paralysis of the limbs. Neosporosis is characterized by ascending paralysis associated with gradual muscle atrophy and stiffness that usually affects the pelvic limbs more than the thoracic limbs. Paralysis progresses to rigid contracture of the muscles of the affected limb. Occurring arthrogryposis is caused by scar formation in the muscles from lower motor neuron damage and myositis. Some puppies may develop joint deformation and genu recurvatum. Cervical weakness, dysphagia, megaesophagus, and death can occur. Dogs do not develop severe intracranial manifestations and maintain alert attitudes. They can survive for months with hand-feeding and care but remain paralyzed with associated complications.

Suppositions are that during gestation, the chronically and subclinically infected bitch develops parasitemia, which spreads transplacentally to the fetus, and successive litters may be born infected. However, transplacental transmission alone is unlikely to propagate *N caninum* infection in dogs in nature.<sup>9</sup> Most puppies in a litter have clinical manifestations; others may carry the infection subclinically, with reactivation occurring later in life because of immunosuppressive illnesses, administration of modified live virus vaccines, or glucocorticoids.

### Management

Treatment will likely not lead to improvement in puppies already showing advancing paralysis or muscle contracture. However, if 1 puppy in a litter is diagnosed with infection, it is prudent to treat the entire litter with

ALT = alanine transaminase GLDH = glutamate dehydrogenase clindamycin, sulfadiazine, and pyrimethamine, alone or in combination.<sup>10</sup> At this time, potential benefits of ponazuril on affected neonates are unclear.

# **Babesiosis**

Both Babesia canis and Babesia gibsoni are known to be transmitted transplacentally in dogs.<sup>11</sup> B canis, the species with a large intracellular trophozoite, was diagnosed in a litter of 3-week-old mastiffs that came from a tick-infested kennel housing  $\approx 30 \text{ dogs.}^{12}$  Clinical signs seen in the puppies included lethargy, poor body condition, pale and icteric mucous membranes, splenomegaly, tachycardia, heart murmur, anemia, and thrombocytopenia. The puppies responded well to treatment with intramuscular diminazene aceturate at 3 mg/kg. Organisms were not seen in the blood of the mother, although she was seropositive on an immunofluorescent assay.

B gibsoni, the species with the small intracellular trophozoite, has been transmitted experimentally to puppies in Japan.<sup>13</sup> An adult female dog that had been experimentally infected 2 years before mating gave birth to 1 stillborn puppy and 4 living puppies, which died of congenital babesiosis between 14 and 39 days postpartum.

# Management

Puppies typically respond well to treatment with antibabesial drugs (eg, imidocarb dipropionate, diminazene aceturate).<sup>14</sup> An atovaquone and azithromycin combination reportedly is more effective for B gibsoni infections.15



# Leishmaniasis

*Leishmania infantum (L chagasi)* infection was identified in several thousand foxhounds throughout 18 US states and 2 Canadian provinces.<sup>16</sup> Efficient sandfly vectors were not found, and transplacental transmission for canine leish-



parasitized by Babesia gibsoni (arrows)



smear from canine splenic tissue showing a macrophage (red arrow) with numerous amastigotes (blue arrows) of Leishmania infantum

maniasis was suspected.<sup>16-24</sup> Infected puppies can be presented with nonregenerative anemia, mild thrombocytopenia, mild hyponatremia, and signs of hepatocellular injury. Infected dogs typically have hyperproteinemia attributed to hypergammaglobulinemia. Urinalysis will often show proteinuria.



▲ Giemsa-stained microfilaria of *Dirofilaria immitis* in a peripheral blood smear

### Management

Sodium stibogluconate can suppress and sometimes cure infection. However, although clinical improvement may occur, relapses are common, and chemotherapeutic elimination of *L infantum* has not been consistently achieved with any drug tested to date.

### Dirofilarial microfilariae

Puppies born to mothers with patent infections of the heartworm *Dirofilaria immitis* or heartworm's subcutaneous relative *D repens* outside North America will often have circulating microfilariae in their blood at birth.<sup>25-28</sup> Although these infections in puppies are without direct medical significance, they can often be detectable at the time of a microfilarial test 6 months after birth. These microfilariae do not develop further and expire in 1 to 2 years if not first cleared by microfilaricidal therapy. Theoretically, these microfilariae could develop further if ingested by a mosquito and serve as of reservoir of infection for other dogs.

### Management

Microfilariae-positive neonatal puppies should be started on heartworm preventive therapy and monitored to ensure the microfilariae clear as expected.

### Conclusion

The infections discussed are common in the United States. Although few parasites infect dogs transplacentally, vertical transmission may allow for more widespread prevalence of these infections.

### References

- Vossman T, Stoye M. Klinische, hämatologische und serologische befunde bei welpen nach pränataler infektion mit *Toxocara canis* WERNER, 1782 (Anisakidae). *Zentralbl Veterinarmed B.* 1986;33(8):574-585.
- Kramer F, Hammerstein R, Stoye M, Epe C. Investigations into the prevention of prenatal and lactogenic *Toxocara canis* infections in puppies by application of moxidectin to the pregnant dog. *J Vet Med B Infect Dis Vet Public Health*. 2006;53(5)218-223.
- Epe C, Pankow, WR, Hackbarth H, Schnieder T, Stoye M. A study on the prevention of prenatal and galactogenic *Toxocara canis* infection in pups by treatment of infected bitches with ivermectin or doramectin. *Appl Parasitol.* 1995;36(2)115-123.
- Schnieder T, Kordes S, Epe C, Kuschfeldt S, Stoye M. Investigations into the prevention of neonatal *Toxocara canis* infections in puppies by application of doramectin to the bitch. *Zentralbl Veterinarmed B*. 1996;43(1):35-43.
- 5. Panacur Small Animal 10% Oral Suspension. MSD Animal Health. http://www.msd-animal-health.co.uk/products\_ public/panacur\_10\_\_suspension/090\_product\_datasheet. aspx. Accessed February 2016.

- 6 Schnieder T, Laabs EM, Welz C. Larval development of
- Toxocara canis in dogs. Vet Parasitol. 2011;175(3-4):193-206.
   Dubey JP, Schares G. Neosporosis in animals: the last five years. Vet Parasitol. 2011;180(1-2):90-108.
- Dubey JP, Lindsay DS, Lappin MR. Toxoplasmosis and other intestinal coccidial infections in cats and dogs. *Vet Clin North Am Sm Anim Pract*. 2009;39(6):1009-1034.
- Legnani S, Pantchev N, Forlani A, et al. Emergence of cutaneous neosporosis in a dog receiving immunosuppressive therapy: molecular identification and management. Vet Dermatol. 2016;27(1):49-e14.
- 10. Lyon C. Update on the diagnosis and management of Neospora caninum infections in dogs. *Top Companion Anim Med*. 2010;25(3):170-175.
- Fukumoto S, Suzuki H, Igarashi I, Xuan XN. Fatal experimental transplacental Babesia gibsoni infections in dogs. *Int J Parasitol.* 2005;35(9):1031-1035.
- Harvey JW, Taboada J, Lewis JC. Babesiosis in a litter of pups. JAVMA. 1988;192(12):1751-1752.
- Dubey JP, Lappin MR. Toxoplasmosis and neosporosis. In: Greene C, ed. Infectious Diseases of the Dog and Cat. 4th ed. St. Louis, MO: Elsevier Saunders; 2012:806-827.

# ADVERTISERS INDEX

# The *Clinician's Brief* Advertisers Index is provided as a service to our readers. The publisher does not assume responsibility for any errors or omissions.

Abaxis | abaxis.com | page 64 | Abaxis

- AccuPlex 4 | ANTECHdiagnostics.com | page 19 | ANTECH Diagnostics
- ACVS Surgery Summit | acvssurgerysummit.org | page 86 | American College of Veterinary Surgeons Alicam | alicamvet.com | page 23 | Infiniti Medical
- Apoquel | apoquel.com | page 25 | inimit includer BLUE Natural Veterinary Diet GI | TrueBLUEVets.com |
- page 20 | Blue Buffalo
- BLUE Natural Veterinary Diet WU | TrueBLUEVets.com | page 21 | Blue Buffalo
- Boehringer Ingelheim Vetmedica Products | bi-vetmedica.com/longtermcare | page 54 | Boehringer Ingelheim Vetmedica
- Bravecto | BravectoVets.com | cover insert, inside front cover, page 4 | Merck Animal Health
- Bronchi-Shield ORAL | bronchi-shieldORAL.com | page 58 | Boehringer Ingelheim Vetmedica
- Claro | OneDoseZeroHomework.com | inside back cover, page 111 | Bayer Animal Health
- Clinical Notes: Probiotics & Intestinal Dysbiosis | nutramaxlabs.com | pages 73-76 | Nutramax Laboratories
- Clinician's Forum: Feline Sarcomas | biviultraduramune.com | outsert | Boehringer Ingelheim Vetmedica
- Companion Regenerative Therapies System | CompanionRegenerativeTherapies.com | page 61 | Companion Animal Health
- Convenia | recommend convenia.com | pages 81, 80 | Zoetis
- Dermoscent Essential 6 | BayerDVM.com | page 95 | Bayer Animal Health
- Douxo | douxo.us | page 6 | Ceva Animal Health FRONTLINE Gold | FRONTLINE.com | back cover | Merial HEARTGARD Plus | HEARTGARD.com | pages 79, 78 | Merial Hill's c/d | HillsVet.com | pages 30-31 | Hill's Pet Nutrition Hill's i/d | HillsVet.com | page 8 | Hill's Pet Nutrition Hill's Metabolic + Urinary Stress | HillsVet.com |
- page 85 | Hill's Pet Nutrition

## TOP 5 PARASITOLOGY CONTINUED FROM PAGE 108

- Birkenheuer AJ. Babesiosis. In: Greene C, ed. Infectious Diseases of the Dog and Cat. 4th ed. St. Louis, MO: Elsevier Saunders; 2012:771-784.
- Birkenheuer AJ, Levy MG, Breitschwerdt EB. Efficacy of combined atovaquone and azithromycin for therapy of chronic *Babesia gibsoni* (Asian genotype) infections in dogs. *JVIM*. 2014;18(4):494-498.
- Duprey ZH, Steurer FJ, Rooney JA, et al. Canine visceral leishmaniasis, United States and Canada, 2000-2003. Emerg Infect Dis. 2006;12(3):440-446.
- Mancianti F, Sozzi S. Isolation of *Leishmania* from a newborn puppy. *Trans R Soc Trop Med Hyg*. 1995;89(4):402.
- Rosypal AC, Troy GC, Zajac AM, Frank G, Lindsay DS. Transplacental transmission of a North American isolate of *Leishmania infantum* in an experimentally infected beagle. *J Parasitol.* 2005;91(4):970-972.
- Gibson-Corley KN, Hostetter JM, Hostetter SJ, et al. Disseminated *Leishmania infantum* infection in two sibling foxhounds due to possible vertical transmission. *Can Vet J.* 2008;49(10):1005-1008.
- Pangrazio KK, Costa EA, Amarilla SP, et al. Tissue distribution of *Leishmania chagasi* and lesions in transplacentally infected fetuses from symptomatic and asymptomatic naturally infected bitches. *Vet Parasitol.* 2009;165(3-4):327-331.

### JorVet Veterinary iPhone ECG & Lactate Meter

- JorVet.com | page 103 | Jorgensen Laboratories NAVTA/Merial Advertorial | navta.net; merial.us | pages 10-11 | Merial
- NexGard Chewables | NexGardForDogs.com; verticalmeasures.com/nexgard-merial-webinars | insert, pages 67, 66 | Merial
- Nutrition Exchange | PurinaVeterinaryDiets.com | insert | Nestlé Purina Company
- Plumb's Veterinary Drugs | plumbsveterinarydrugs.com | page 104 | Brief Media
- Proin | PRNpharmacal.com/urinaryhealth | page 52 | PRN Pharmacal
- Proviable-Forte | proviable-forte.com | page 2 | Nutramax Laboratories
- PureVax Feline Rabies | VaccinateYourPet.net | page 90 | Merial
- RapidBac Vet | rapidbacvet.com | page 69 | Silver Lake Research
- Revolution 4DC Dental X-Ray | im3vet.com | page 51 | iM3 Royal Canin Ultamino | ultamino.royalcanin.com | page 41 | Royal Canin
- Sentinel Spectrum | virbacvet.com | pages 29, 28 | Virbac
- Sileo | sileosoundsolution.com | pages 13-15 | Zoetis Tono-Pen AVIA VET | danscottandassociates.com |
- page 110 | Dan Scott & Associates
- Tresaderm | merial.us | page 42 | Merial VCA Animal Hospitals Recruitment | VCA Jobs.com |
- page 82 |VCA Animal Hospitals
- Veraflox | VerafloxOS.com | pages 71, 70 | Bayer Animal Health
- WSAVA Congresses | wsava2016.com; wsava2017.com | page 96 | World Small Animal Veterinary Association
- WSAVA Obesity Symposium | wsava-obesity.com | page 109 | World Small Animal Veterinary Association

## **Photo Credits**

© MDGstock.com pages 23, 39, 59 © Shutterstock.com pages 16, 18, 24, 49, 50, 53, 68, 75, 83, 90

- Freeman KS, Miller MD, Breitschwerdt EB, Lappin MR. Leishmaniasis in a dog native to Colorado. JAVMA. 2010;237(11):1288-1291.
- Boggiatto PM, Gibson-Corley KN, Metz K, et al. Transplacental transmission of *Leishmania infantum* as a means for continued disease incidence in North America. *PLoS Negl Trop Dis.* 2011;5(4):e1019.
- Naucke TJ, Lorentz S. First report of venereal and vertical transmission of canine leishmaniosis from naturally infected dogs in Germany. *Parasit Vectors*. 2012;5:67.
- Schantz PM, Steurer FJ, Duprey ZH, et al. Autochthonous visceral leishmaniasis in dogs in North America. JAVMA. 2005;226(8):1316-1322.
- 25. Mantovani A, Jackson, RF. Transplacental transmission of microfilariae of *Dirofilaria immitis* in the dog. *J Parasitol.* 1966;52(1):116.
- Henrikson DM, Anderson RA. Dirofilaria immitis microfilariae in amniotic fluid. J Parasitol. 1969;55(1):195.
- 27. Todd KS Jr, Howland TP. Transplacental transmission of *Dirofilaria immitis* microfilariae in the dog. *J Parasitol.* 1983;69(2):371.
- Manda JA. Transplacental migration of Dirofilaria immitis microfilariae. Comp Anim Pract. 1989;19 (6-7):18-20.



### (florfenicol, terbinafine, mometasone furoate) Otic Solution

Antibacterial, antifungal, and anti-inflammatory For Otic Use in Dogs Only

The following information is a summary of the complete product information and is not comprehensive. Please refer to the approved product label for complete product information prior to use.

**CAUTION:** Federal (U.S.A.) law restricts this drug to use by or on the order of a licensed veterinarian.

PRODUCT DESCRIPTION: CLARO<sup>™</sup> contains 15.0 mg/mL florfenicol, 13.3 mg/mL terbinafine (equivalent to 15.0 mg/mL terbinafine hydrochloride) and 2.0 mg/mL mometasone furoate. Inactive ingredients include purified water, propylene carbonate, propylene glycol, ethyl alcohol, and polyethylene glycol.

# INDICATIONS:

CLARO<sup>™</sup> is indicated for the treatment of otitis externa in dogs associated with susceptible strains of yeast (*Malassezia pachydermatis*) and bacteria (*Staphylococcus pseudintermedius*)

#### DOSAGE AND ADMINISTRATION:

CLARO<sup>™</sup> should be administered by veterinary personnel. Administration is one dose (1 dropperette) per affected ear. The duration of effect should last 30 days. Clean and dry the external ear canal before administering the product. Verify the tympanic membrane is intact prior to administration. Cleaning the ear after dosing may affect product effectiveness. Refer to product label for complete directions for use.

### CONTRAINDICATIONS:

Do not use in dogs with known tympanic membrane perforation (see **PRECAUTIONS**).

CLARO<sup>™</sup> is contraindicated in dogs with known or suspected hypersensitivity to florfenicol, terbinafine hydrochloride, or mometasone furoate, the inactive ingredients listed above, or similar drugs, or any ingredient in these medicines.

### WARNINGS:

<u>Human Warnings</u>: Not for use in humans. Keep this and all drugs out of reach of children. In case of accidental ingestion by humans, contact a physician immediately. In case of accidental skin contact, wash area thoroughly with water. Avoid contact with eyes. Humans with known hypersensitivity to florfenicol, terbinafine hydrochloride, or mometasone furoate should not handle this product.

### PRECAUTIONS:

Do not administer orally. The use of CLARO<sup>™</sup> in dogs with perforated tympanic

membranes has not been evaluated. The integrity of the tympanic membrane should be confirmed before administering the product. Reevaluate the dog if hearing loss or signs of

vestibular dysfunction are observed during treatment. Use of topical otic corticosteroids has been associated with adrenocortical suppression and iatrogenic hyperadrenocorticism in doos.

Use with caution in dogs with impaired hepatic function. The safe use of (LARO<sup>®</sup> in dogs used for breeding purposes, during pregnancy, or in lactating bitches has not been evaluated.

### ADVERSE REACTIONS:

In a field study conducted in the United States, there were no directly attributable adverse reactions in 146 dogs administered CLAR0  $^{\rm m}$ 

To report suspected adverse drug events and/or obtain a copy of the Safety Data Sheet (SDS) or for technical assistance, contact Bayer HealthCare at 1-800-422-9874.

For additional information about adverse drug experience reporting for animal drugs, contact FDA at 1-888-FDA-VETS or online at http://www.fda.gov/AnimalVeterinary/SafetyHealth.

## Bayer

Bayer (regd), the Bayer Cross (regd) and CLARO™ are trademarks of Bayer. ©2016 Bayer HealthCare LLC. Distributed by: Bayer HealthCare LLC Animal Health Division Shawnee

Distributed by: Bayer HealthCare LLC Animal Health Division Shawnee Mission, Kansas 66201 USA NADA 141-440, Approved by FDA.