INTRODUCTION

_Echinococcus multilocularis_ is a zoonotic tapeworm that occurs in central Europe, much of northern, central and eastern Eurasia, and parts of North America. Adult parasites reside within the small intestine of definitive hosts, which are primarily wild canids (e.g., foxes, coyotes, wolves). However, in some areas, domestic dogs, and to a lesser extent cats, may act as definitive hosts. Eggs shed in the feces of these species are morphologically indistinguishable from *Taenia*-type eggs and are immediately infective for intermediate hosts which include various species of wild rodents. Subsequent to ingestion, a hexacanth embryo is released from the egg, travels to the liver via the hepatic portal circulation and develops into alveolar hydatid cysts. This larval stage of the parasite is comprised of numerous small vesicles lined with a germinal epithelium from which multiple protoscolices develop, undergoes exogenous budding, and behaves like an invasive tumour. The resultant disease, alveolar echinococcosis (AE), is associated with extensive damage to the liver and occasionally spread to other locations within the intermediate host. When an infected intermediate host is ingested by a definitive host the life cycle is completed; development to the mature tapeworm takes approximately 4-5 weeks. Lastly, ingestion of eggs by people may also result in AE, a potentially severe, fatal disease that is currently an emerging issue in parts of central Europe.

In North America, _E. multilocularis_ has historically been considered to occur in two distinct geographic regions: the Northern Tundra Zone that extends from the west coast of Alaska to parts of the Canadian arctic, and the North Central Region that includes the southern parts of 3 Canadian provinces (Alberta, Saskatchewan, Manitoba) and 13 neighbouring USA states (North/South Dakota, Iowa, Minnesota, Montana, Wyoming, Nebraska, Illinois, Wisconsin, Indiana, Ohio, Missouri, Michigan). Within this latter region, red foxes and coyotes are considered the primary definitive hosts; the most significant intermediate hosts include voles and mice. Strangely, despite this large geographic distribution, there are very few reports of _E. multilocularis_ intestinal infections in dogs or cats in the USA and Canada. Outside Alaska, patent intestinal infections in dogs appear to have been described only once; using molecular methods, _E. multilocularis_ was identified in the feces of 1/218 dogs in 2014 in Alberta. Similarly, only 5 cats have been reported with intestinal infections; 3 in 1971 in Saskatchewan, and 2 in 1972 in North Dakota. Likewise, only 3 cases of alveolar echinococcosis in people are described that appear to have been acquired in the USA or Canada; one in 1937 in Manitoba, one in 1979 in Minnesota, and one in 2014 in Alberta.

Information concerning dogs as definitive hosts for _E. multilocularis_ is contained in veterinary parasitology textbooks. However, what is missing in almost every book is the fact that since the late 1980s, cases of AE, primarily involving the liver, have been described in dogs in Switzerland, Germany, France and Belgium. These cases are thought to occur as a result of either ingestion of large numbers of eggs or by autoinfection in association with the presence of adult tapeworms in the small intestine.

CASES OF CANINE ALVEOLAR ECHINOCOCCOSIS IN NORTH AMERICA

Prior to 2009, _E. multilocularis_ had never been diagnosed in a dog in Canada. However, in that year hepatic AE was diagnosed in a 3-year old dog that had lived permanently in British Columbia; _E. multilocularis_ was identified on histology and direct immunofluorescence of hepatic tissue; sequence data for the mitochondrial 12S rRNA gene, and RFLP analysis of the mitochondrial NADH dehydrogenase 1 and 12S rRNA genes, confirmed the diagnosis. In 2012, a second case was similarly diagnosed in a 2-year old dog that resided in southern Ontario; a third case was diagnosed in a 4-year old dog that lived in Alberta and Manitoba. Between 2013 and 2015, three additional cases were diagnosed in southern Ontario. None of the 6 dogs were related; all 6 dogs had never travelled outside Canada; 4 of the dogs had lived their entire lives in provinces where _E. multilocularis_ had never been diagnosed prior to the occurrence of these cases.

CLINICAL PRESENTATION AND DIAGNOSIS

Corsini and others recently published a retrospective analysis of twenty confirmed (n = 18) or probable (n = 2) cases of canine AE in Europe. The median age at diagnosis was 3.1 years (range = 1.1-10.7 years) and the most common clinical signs included abdominal distension, lethargy, anorexia and vomiting; less common clinical signs included diarrhea, weight loss, polypnea, fever and polyphagia. Most dogs had lived all their adult lives in areas where foxes occurred and were exercised outdoors.

Abdominal ultrasound and clinical pathology

In dogs with clinical AE, abdominal ultrasound typically reveals the presence of multiple, large, heterogeneous, poorly limited, cavitated hepatic masses. Usually, there is a hyperechoic thick periphery, an irregular inner surface, and a centrally located cavity filled with corpuscular fluid. Extension to neighbouring organs is observed in approximately one third of cases; free abdominal fluid is present in a similar proportion. In many dogs, ultrasound-guided fine-needle aspirates of intralesional or peritoneal fluid generates samples with cytological morphology consistent with AE; calcareous corpuscles and folded membranous structures. While the former indicates the presence of any cestode, the latter has only been described with _E. multilocularis_.

Histopathology
In dogs with hepatic AE, there is typically extensive involvement of the liver with a multinodular firm pale-tan mass that grossly has the appearance of a neoplasm. Histological examination of hepatic biopsies is extremely helpful as the morphology is characteristic for *E. multilocularis*; hepatic architecture is replaced by multi-loculated coalescing cystic structures surrounded by fibrosis. Lining individual cysts is a hyaline membrane ("laminated layer") that stains with Periodic acid-Schiff (PAS) stain. The inner lining of the hyaline membrane typically comprises a basophilic matrix that contains occasional calcareous corpuscles. Intraluminal protoscolices are sometimes observed. A prominent chronic eosinophilic and granulomatous inflammation is also typically present.

**Serology and PCR**

Positive serology to the *E. multilocularis* Em2-antigen is observed in most dogs with AE. However, at the present time this diagnostic method is only available at the University of Bern, Switzerland. In addition, some dogs will seroconvert, but not develop AE due to abortive infections. As a result, examination of intralesimal or abdominal fluid, or hepatic tissue, using an *E. multilocularis*-specific PCR provides confirmatory diagnostic information.

**MANAGEMENT**

Historically, dogs with AE have been managed with surgery and/or treatment with albendazole at 10 mg/kg bodyweight, daily, for life. In the aforementioned case series from Europe, dogs that received any intervention (i.e. only albendazole, or surgery and albendazole combined) were shown to survive significantly longer than dogs with no intervention. However, no significant difference in survival time was observed between these two intervention groups. While low numbers of dogs limited the statistical power of the study, the authors concluded that there was no evidence that debulking surgery (cytoreduction) followed by treatment with albendazole resulted in a superior outcome compared to treatment with albendazole alone. As a result, debulking surgery could not be recommended at the present time; as in people, surgery should only be attempted if complete resection is possible. Thus, ideally, investigation of potential cases requires advanced imaging (CT-Scan) to assess whether surgical excision is possible. In non-resectable cases with a centrally located fluid cavity, a pigtail retention catheter can be placed attached to a sealed collection system to provide temporary relief. Lastly, it has historically been assumed that medical management of dogs with AE is associated with short-term survival. However, 4 of 6 dogs managed with only daily albendazole were alive 0.5, 0.5, 2.6 and 9.5 years after the initial diagnosis and were considered to be in remission. Medical management of dogs with AE can therefore be associated with long-term survival; however, daily treatment with albendazole is required.

**PUBLIC HEALTH CONCERNS**

The intermediate (larval) stage of *E. multilocularis* in the abdomen of dogs constitutes no risk to public health. However, some dogs with hepatic AE may also have patent intestinal infections and therefore may constitute a zoonotic threat. Thus, as soon as a presumptive diagnosis of hepatic AE is made, dogs should be treated with praziquantel at 5 mg/kg bodyweight to eliminate intestinal *E. multilocularis* infection; treatment should be repeated 24 hours later to ensure the correct dosage is administered. In areas endemic for *E. multilocularis*, monthly administration of praziquantel at 5 mg/kg bodyweight is required to prevent patent intestinal infections, and may be effective at preventing canine AE; a risk assessment should be carried out to determine if such preventive treatment is necessary.

If exposure of people to *E. multilocularis* eggs is a concern, serological testing at 3, 6 and 12 months following exposure using three different ELISAs (EgHF-ELISA, Em2-ELISA and Em18-ELISA) is recommended.

**CONCLUSION**

In dogs with hepatic masses, travel to areas endemic for *E. multilocularis* should be evaluated. If hepatic lesions are first detected during an exploratory laparotomy, it should be recognised that the gross appearance of hepatic AE in dogs is very similar to that of hepatic neoplasia. Thus, histological examination of hepatic biopsies should be carried out to confirm tentative gross diagnoses, particularly in young dogs. Management of AE involves daily treatment with albendazole for life, with or without surgery; due to the late stage at which infections are diagnosed, the prognosis for long-term survival is typically poor.

**References**