Echinococcus multilocularis as an emerging public health threat in Canada: A knowledge synthesis and needs assessment

Emily Denstedt, BSc. DVM.

Master of Public Health Candidate,

University of Guelph

March 19, 2017

Summary

- *Echinococcus multilocularis* is a potentially emerging public health threat in Canada
- *E. multilocularis* is a zoonotic tapeworm previously identified as endemic in the Northern Tundra Zone and southern Alberta, Saskatchewan, and Manitoba
- Multiple domestic dogs were recently discovered to be infected in Ontario, the first ever documentation of this parasite as endemic in the province
- *E. multilocularis* in people can be severe, and locally-acquired cases in humans have been reported very rarely in Canada
- *E. multilocularis* was likely introduced into new Canadian regions via canine importation
- With urban wildlife changes, new environments in Canada may now be contaminated with the tapeworm
- Human cases may be underreported or going unrecognized
- The results of this review highlight the need for additional research on the parasite's geographic distribution in wildlife, policy changes for canine importation, and increased surveillance in the human population

Introduction

Echinococcus multilocularis is a zoonotic tapeworm known to be endemic in defined regions of Canada and many other countries around the world. With wild canids serving as the definitive hosts (ex: coyotes, foxes), this tapeworm is the agent responsible for alveolar echinococcosis (AE) in humans (1). Knowledge regarding its distribution among wild and domestic hosts, however, is seemingly lacking. The geographical range of *E. multilocularis* in Canada has been documented primarily in the Arctic and the North Central Region which

include the southern parts of Alberta, Saskatchewan, and Manitoba (1,2), but recent findings have brought forth concern that this range is expanding, or has long been wider than was initially thought. This poses a potential existing or emerging public health threat, one with substantial knowledge gaps and need for further assessment.

E. multilocularis in the adult form inhabits the intestines of wild canids (3). The definitive hosts shed eggs through feces that are then ingested by an intermediate host, typically a rodent. Alveolar hydatid cysts filled with larvae grow within the abdominal organs of the rodent (3). The rodent is then ingested by a wild canid, and the lifecycle starts once again. Deviations from this natural cycle can occur, however. Humans can become infected and develop severe AE by ingesting eggs shed by an infected domestic dog (3). Domestic dogs, despite being a definitive host, have been noted in the literature to suffer AE as well.

Several recent findings provide cause for concern. The first ever reported case of AE in Ontario in a domestic dog was confirmed in 2012 (4). Since that time, four additional cases in dogs have been reported (5,6,9). Prior to these reports, Ontario had not been considered an endemic region for *E. multilocularis*. Furthermore, the presence of a European strain causing AE in dogs was recently discovered in Canada (1,7). *E. multilocularis* has been shown to exist commonly in coyotes inhabiting urban areas of Alberta, possibly due to habitat impingement or coyotes simply encroaching on metropolitan areas (8). AE in humans has overall been considered very rare in Canada. Few reported cases of locally acquired AE in Canadian humans have been described (1). Interestingly, an analysis of Canadian hospital discharge data demonstrated that 242 patients were treated for echinococcosis between 2001-2014 (1). Perhaps the parasite has contaminated Canadian environments across a wider range than previously thought, previously foreign strains have established themselves, and the risk to the human

population has largely gone unrecognized for some time. In light of these recent findings, this review seeks to examine the current evidence surrounding this zoonotic parasite in Canada, highlight gaps in both knowledge and policy, and evaluate the public health risk.

Methods

A literature review was conducted evaluating articles from peer-reviewed journals written in English between 2004-2017. Using a search of keywords in web-based academic search tools, the article titles were screened for relevance. Abstracts of appropriate articles were then reviewed. Articles were chosen based on their relevance to the epidemiology of *Echinococcus multilocularis* in Canada and/or their applications to the public health of Canadians. Articles containing useful results from *E. multilocularis* research in other countries were also selected if they were deemed applicable to this knowledge synthesis. Additional details regarding specific search methods, keywords, and inclusion and exclusion criteria can be found in the Appendix. Article summaries are provided in the Appendix as well.

Results and Discussion

Echinococcus multilocularis is a zoonotic tapeworm that has largely been absent from any widespread public health reporting in Canada. Until recently, the parasite was largely restricted to wild canids and their prey in the Northern Tundra Zone and the North Central Region of Canada. The level of concern has increased, however, after the parasite was discovered in a domestic dog in 2012. This formed the first evidence *E. multilocularis* had expanded its endemic range into Ontario (4).

In the last five years, five cases of AE have been confirmed in domestic dogs in Ontario (4,5,6,9), and two in non-human primates (9). Only one of these animals had previously spent

time outside Ontario, meaning the infections were locally acquired in all but one case. This new discovery has brought forth concern for the public's health and a need to reevaluate the nature of this parasite in Canada. Although human infections in Canada have been seemingly rare (1), the disease is severe and without treatment is often fatal (3,10). Multiple factors may have brought Canada to this point, and gaps in knowledge and policy will be discussed henceforth.

Canine importation

The environmental contamination of new Canadian regions may be the result of anthropogenic influences such as canine importation. Unlike other nations, Canada's regulations on dogs entering the country remain lenient with limited monitoring and control of animal imports (11). With increased globalization, large numbers of dogs are now moved into Canada from around the globe annually, none of which require deworming for foreign and potentially zoonotic parasites (11). This substantial gap in Canadian policy for the importation of domestic dogs and cats brings forth the ongoing risk of new pathogen introduction. A European strain of *E. multilocularis,* not previously known to exist in Canada, was identified in a domestic dog in British Columbia in 2009 (7). Interestingly, this was also the first report in the literature of a domestic canid with alveolar echinococcosis in North America, and the case had no travel history outside the province (12). This report, along with the recent findings of endemic *E. multilocularis* in Ontario, points to the possibility of these infections arising via infected imported dogs. Infected dogs from other countries can lead to significant environmental contamination with *E. multilocularis*, posing a potentially serious public health threat (11). For a dog to gain entrance into Finland, the UK, Ireland, or Norway, the animal must first be treated with praziquantel, the medication highly effective in the treatment of intestinal *E. multilocularis* infections (11, 13). In a risk assessment conducted by Torgerson and Craig, it was determined

that introduction of *E. multilocularis* into the UK would be nearly inevitable without the required praziquantel treatment as part of the Pet Travel Scheme policy (13). Without addressing the weaknesses of the current Canadian import requirements for foreign dogs, Canada remains at risk for continued introductions of new or rare pathogens. It is likely that Ontario became a newly endemic region of Canada due to the lack of tapeworm treatment requirements in foreign dogs at the time of entry (14,15).

Urbanization of wildlife

With the continued sprawl of human development and urbanization, the human-animal interface is changing. Humans now frequently share common physical environments with wild canids, with foxes and coyotes frequently occupying urban centres in Canada. *E. multilocularis* has been found to contaminate the metropolitan areas of Calgary and Edmonton (16). Urban parks in Calgary have since been studied, confirming the presence of a sylvatic *E. multilocularis* life cycle in Canadian urban settings frequented by people and domestic dogs (17). Other endemic countries with urban wild canids such as Switzerland have demonstrated a high degree of *E. multilocularis* contamination of periurban areas commonly used for recreational activity and gardening (ex: public parks) (18). Echinococcus eggs are known to survive well in the environment, potentially putting those who work outside and handle soil at increased risk (19).

In response to the newly identified domestic dog cases in Ontario, research is currently being conducted to determine the presence and extent of *E. multilocularis* in the fox and coyote populations. Fecal shedding from wild canids has been confirmed in both southern and eastern Ontario, and the data has yet to be published (20; oral communication, Andrew Peregrine, March 2017). Incidentally, a deceased chipmunk in Ontario was found recently by a passerby and confirmed to have AE, highlighting the importance of passive surveillance (9). Additional

research to improve knowledge on the geographical distribution and transmission ecology of this parasite, particularly in locations occupied by people and their pets, is imperative so we can better understand the level of risk faced by Canadians.

Recognition and reporting of human alveolar echinococcosis

In Canada, only two human cases of locally-acquired *E. multilocularis* have been reported in the literature the last hundred years (1). Although human AE is seemingly very rare, these two individual reports may not paint the most accurate picture of the incidence of locally-acquired AE in Canadians.

Human alveolar echinococcosis is not a reportable disease in Canada, which may explain, at least in part, why cases in people have appeared to be so rare. These two human reports may be a substantial underestimate, as a recent evaluation of Canadian hospital discharge data revealed 242 patients classified as discharged with echinococcosis between 2001 and 2014 (1). Twelve of these 242 patients were categorized as being discharged with alveolar echinococcosis, and 191 patients were categorized as "unspecified echinococcosis" (1). What is missing from this data, however, is information on patients' travel or immigration history. It is therefore difficult to know how many of these infections were acquired within Canada (if any) versus another endemic country.

Alveolar echinococcosis can remain undetected in humans for years (21). Given the severe and often fatal nature of the disease if untreated (10), it is suggested by some that human AE should be classified as reportable in Canada (15). With listing it as a federally reportable disease, additional reports of locally-acquired alveolar echinococcosis may have emerged from this pool of discharged cases and the scope of this public health threat could be better understood. Furthermore, AE can appear grossly similar to hepatic neoplasia and perhaps, as a

result, be misdiagnosed in both humans (15) and domestic dogs (14). Listing human AE as reportable may therefore increase physician and veterinarian awareness and encourage improved surveillance of this pathogen within the Canadian population. The potential exists for additional human cases to arise in the coming years, and active reporting at the federal level should be strongly considered to avoid an underestimation of disease incidence.

Conclusions

It is evident that the scientific and public health community in Canada may be required to increase the level of preparedness to an emerging threat posed by *Echinococcus multilocularis*. In the limited literature currently available, there appears to be multiple contributing factors potentially playing a role in range distribution changes of this parasite and the contamination of the Canadian environment. Gaps in policy have been identified in the importation requirements of canines into Canada and in the reporting of human alveolar echinococcosis. In addition, gaps in knowledge and research on the distribution of *E. multilocularis* in wild hosts are apparent given its recent discovery in Ontario and British Columbia for the first time through positive identification of infected domestic dogs. These dogs may be sentinels and important red flags for what is to come, and the public health community should not ignore the emergence of the zoonotic and dangerous *Echinococcus multilocularis* tapeworm.

Additional surveillance efforts in wild hosts throughout Canada should begin in each province and territory to better estimate risk. Increasing awareness amongst Canadian physicians and improved reporting protocols of human alveolar echinococcosis is also recommended. In the face of increased globalization, stricter regulations on canine importation similar to other countries should be enforced to prevent further contamination or introductions of foreign *E.*

multilocularis strains into the Canadian ecosystems. This tapeworm may have posed a threat for some time now throughout Canada, but the present opportunity to enhance knowledge and improve management strategies should be acted upon.

Acknowledgements

The author would like to thank Dr. Andrew Peregrine for not only his assistance with this evidence review, but also for his fantastic teaching of countless veterinary students and professionals.

References

1. Massolo A, Liccioli S, Budke C, Klein C. *Echinococcus multilocularis* in North America: the great unknown. Parasite. 2014;21(73).

2. J. Eckert, M.A. Gemmell, F.-X. Meslin, Z.S. Pawlowski (Eds.). WHO/OIE Manual on Echinococcosis in Humans and Animals: A Public Health Problem of Global Concern. Office International des Epizooties, Paris; c2001.

3. Eckert J, Deplazes P. Biological, Epidemiological, and Clinical Aspects of Echinococcosis, a Zoonosis of Increasing Concern. Clinical Microbiology Reviews. 2004;17(1):107-135.

4. Skelding A, Brooks A, Stalker M, Mercer N, deVilla E, Gottstein B et al. Hepatic alveolar hydatid disease (*Echinococcus multilocularis*) in a boxer dog from southern Ontario. Canadian Veterinary Journal. 2014;55, 551–553.

5. Brouwer E, Peregrine A, Vince A. Update on *Echinococcus multilocularis* in Ontario [Internet]. Guelph: AHL Newsletter; 2015 p. 33. Available from: http://www.guelphlabservices.com/ahl/content/companion-animals-5

6. Oscos-Snowball A, Tan E, Peregrine A, Foster R, Bronsoiler J, Gottstein B et al. What is your diagnosis? Fluid aspirated from an abdominal mass in a dog. Veterinary Clinical Pathology. 2014;44(1):167-168.

7. Jenkins EJ, Peregrine AS, Hill JE, Somers C, Gesy K, Barnes B et al. Detection of European strain of *Echinococcus multilocularis* in North America. Emerging Infectious Diseases. 2012;18:1010–1012.

8. Liccioli S, Catalano S, Kutz S, Lejeune M, Verocai G, Duignan P et al. Gastrointestinal parasites of coyotes (*Canis latrans*) in the metropolitan area of Calgary, Alberta, Canada. Canadian Journal of Zoology. 2012;90(8):1023-1030.

9. Ontario Animal Health Network. Emerging Risk: *Echinococcus multilocularis* in Ontario [Internet]. 2016 [cited 14 March 2017]. Available from: http://oahn.ca/resources/companion-animals/emerging-risk-echinococcus-multilocularis-in-ontario-infographic/

10. Torgerson P, Schweiger A, Deplazes P, Pohar M, Reichen J, Ammann R et al. Alveolar echinococcosis: From a deadly disease to a well-controlled infection. Relative survival and economic analysis in Switzerland over the last 35 years. Journal of Hepatology. 2008;49(1):72-77.

11. Anderson M, Douma D, Kostiuk D, Filejski C, Rusk R, Weese S et al. Report of the Canadian National Canine Importation Working Group [Internet]. Canine Importation Working Group; 2016. Available from: https://www.canadianveterinarians.net/documents/canadian-canine-importation-working-group-report

12. Peregine A, Jenkins E, Barnes B, Johnson S, Polley L, Barker I et al. Alveolar hydatid disease (*Echinococcus multilocularis*) in the liver of a Canadian dog in British Columbia, a newly endemic region. Canadian Veterinary Journal. 2012;53(8):870-874.

13. Torgerson P, Craig P. Risk assessment of importation of dogs infected with *Echinococcus multilocularis* into the UK. Veterinary Record. 2009;165(13):366-368.

14. Peregrine A. Alveolar echinococcosis in dogs: an emerging issue?. Veterinary Record. 2015;177(22):567-567.

15. Trotz-Williams L, Mercer N, Walters J, Wallace D, Gottstein B, Osterman-Lind E et al. Public Health Follow-up of Suspected Exposure to *Echinococcus multilocularis* in Southwestern Ontario. Zoonoses and Public Health. 2016.

16. Catalano S, Lejeune M, Liccioli S, Verocai G, Gesy K, Jenkins E et al. *Echinococcus multilocularis* in Urban Coyotes, Alberta, Canada. Emerging Infectious Diseases. 2012;18(10):1625-1628.

17. Liccioli S, Kutz S, Ruckstuhl K, Massolo A. Spatial heterogeneity and temporal variations in *Echinococcus multilocularis* infections in wild hosts in a North American urban setting. International Journal for Parasitology. 2014;44(7):457-465.

18. Stieger C, Hegglin D, SchwarzenbachG, Mathis A, Deplazes P. Spatial and temporal aspects of urban transmission of *Echinococcus multilocularis*. Parasitology. 2002;124:631-640.

19. Scott W, Anderson M. Echinococcus: For Pet Owners [Internet]. Worms & Germs Blog. 2013 [cited 10 March 2017]. Available from: http://www.wormsandgermsblog.com/files/2013/08/M2-Echinococcus1.pdf

20. Ontario Animal Health Network. Emerging Risk: *Echinococcus multilocularis* in Ontario [Internet]. 2016 [cited 14 March 2017]. Available from: http://oahn.ca/resources/companion-animals/emerging-risk-echinococcus-multilocularis-in-ontario-infographic/

21. Davidson R, Romig T, Jenkins E, Tryland M, Robertson L. The impact of globalisation on the distribution of *Echinococcus multilocularis*. Trends in Parasitology. 2012;28(6):239-247.

Appendix A

Literature search strategy

The following electronic databases were used:

- Primo, University of Guelph**:** http://www.lib.uoguelph.ca.subzero.lib.uoguelph.ca/
- Google Scholar: https://scholar.google.ca/

Keywords and date ranges:

Databases were searched using a different combinations of the following keywords: "*Echinococcus multilocularis*", "Echinococcus", "Canada", "Ontario", "endemic", "canine import", "public health", "distribution". Titles of articles were scanned for relevance to the topic of *E. multilocularis* in Canada, and abstracts of articles with relevant titles were reviewed to determine the level of appropriateness for this evidence review.

The main literature search was restricted to those articles published in English between 2004-2017. Articles published prior to this date range were included if originally published data on the natural history of the parasite occurred at that time.

Inclusion and exclusion criteria:

Only articles discussing or researching the *E. multilocularis* species were included in this evidence review. Articles pertaining more to other species of the tapeworm, such as *Echinococcus granulosus*, were not included. Articles related to domestic animal and human infections in Canada were included. Articles discussing *E. multilocularis* in other countries were included only if they contributed to the discussion of Canadian geographic range expansion of *E. multilocularis* (ex: spread of parasite range via canine import) or provided further evidence supporting a public health risk.

Appendix B

Article summaries

Reference	Study Type	Article Summary
Masolo et al., 2014 [1]	Review of present data	• Review of *E. multilocularis* infections reported in wild and domestic animals and humans is presented • Information available regarding the geographic distribution of *E. multilocularis* is reviewed • New case reports and also knowledge gaps in transmission, distribution, and host interactions in North America are highlighted in the context of the parasite as a public health concern
Eckert & Deplazes, 2004 [3]	Review article	Only the section "*E. multilocularis* and Alveolar Echinococcosis" was utilized. • *E. multilocularis*, its life cycle, and its survival in the environment is described • The pathophysiology of AE in humans is outlined, as well as diagnostic methods and treatment options • Risk areas and modes of spread are explored • Control and prevention methods in both definitive hosts and humans are suggested
Skelding et al., 2014 [4]	Case report	• First case of endemic *E. multilocularis* is identified in a dog in Ontario
Brower et al., 2015 [5]	Informative update in laboratory newsletter	• Four cases of *E. multilocularis* in dogs have been identified in Ontario since March of 2013 • Alveolar echinococcosis should be considered a differential diagnosis for any dog presenting with one or more intra-abdominal masses • One third of dogs with the visceral form of echinococcosis also have enteric infections making them potentially infectious to humans via fecal shedding • Evaluation of *E. multilocularis* infestations in foxes and

		coyotes throughout southern Ontario is expected to commence in September 2015
Oscos-Snowball *et al*., 2014 [6]	Case report	• Second case of endemic *E. multilocularis* is identified in a dog in Ontario
Jenkins et al., 2010 [7]	Case report	• Case description of a domestic dog with confirmed European strain of *E. multilocularis* not known to be established in Canadian wildlife
Liccioli et al., 2012 [8]	Cross sectional study	• Gastrointestinal parasites in urban coyotes in Calgary, Alberta were collected via carcass necropsy and analyzed • Coyote feces were collected within urban Calgary to evaluate for evidence of parasites • Evidence of *E. multilocularis* inside city limits; tapeworm may have ability to complete its lifecycle in urban Calgary
Torgerson et al., 2008 [10]	Retrospective cohort study	• Survival analysis of humans with AE in Switzerland • Prognosis of patients with AE has improved significantly in recent years • Cost-effectiveness of modern treatment is analyzed
Peregrine et al., 2012 [12]	Case report	• First case reported in the literature of AE in a domestic dog in North America • The case was discovered in British Columbia, and the dog had never travelled outside of the province
Torgerson & Craig, 2009 [13]	Risk assessment	• Evaluated the likelihood of *E. multilocularis* to be imported into the UK if pre-import treatment requirements for dogs become more lenient • Based on current data at the time and mathematical models, the authors predicted import of the tapeworm into the UK would be extremely likely and recommend continuing mandatory praziquantel treatment prior to importing dogs
Peregrine, 2015 [14]	Editorial	• General background on the parasite, its lifecycle, and distribution are given • Clinical signs in dogs, cytological hallmarks, and importance of histopathology are summarized

		• Lack of canine import regulations in Canada possibly led to parasite introduction
Trotz-Williams et al., 2016 [15]	Descriptive article of local public health investigation	• The public health investigation that followed four confirmed cases of *E. multilocularis* in Ontario dogs is described • Should additional human exposures be identified in Ontario going forward, a step-wise guide is provided for public health decision-making • Highlights potential for human cases in Canada in the future
Catalano et al., 2012 [16]	Cross-sectional study	• Necropsies of hunted or road-kill coyotes were performed to determine prevalence of *E. multilocularis* in the urban coyote populations in Calgary and Edmonton, Alberta • Adult worms found were confirmed as *E. multilocularis* via morphology and PCR • 25.3% of total coyotes sampled were positive for *E. multilocularis*
Liccioli et al., 2014 [17]	Cross-sectional study	• Spatial and temporal patterns within the coyote-rodent *E. multilocularis* lifecycle in Calgary, Alberta are examined • Small mammal intermediate hosts and coyote feces were collected; findings supported a sylvatic lifecycle in an urban setting
Stieger et al., 2002 [18]	Cross-sectional study	• The fox population in Zurich, Switzerland was assessed in order to characterize the spatial and temporal patterns of *E. multilocularis* between urban, border, and periurban zones • Domestic animals and people frequenting the periphery of urban areas (zones of highest contamination) may be at risk
Davidson et al., 2012 [21]	Review article	• Human influences on range expansion and tapeworm spread are explored in multiple regions of the world • Public health prevention options are discussed, including education campaigns, hand hygiene, and effectiveness of previous wildlife deworming programs