PUBLIC HEALTH FOLLOW-UP OF SUSPECTED EXPOSURE TO ECHINOCOCCUS MULTILOCULARIS IN SOUTHWESTERN ONTARIO

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Impacts

• Echinococcus multilocularis is a parasite capable of causing serious and potentially fatal illness (alveolar echinococcosis) in humans.
• The parasite is an emerging zoonosis in Ontario.
• This article describes a local public health department’s investigation of the potential exposure of several people who had had contact with a case of alveolar echinococcosis in a dog, and summarizes a comprehensive decision process that can be used by public health departments to assist in the follow-up of such exposures.

Keywords:
Echinococcus multilocularis; alveolar echinococcosis; dogs; public health

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INTRODUCTION AND BACKGROUND

The occurrence, in 2012, of a case of hepatic alveolar echinococcosis (AE) in a 2-year-old Boxer dog that had spent all its life in southern Ontario (Brooks et al., 2013; Skelding et al., 2014), was the first indication that the area of North America considered to be endemic for Echinococcus multilocularis might have expanded into the province of Ontario. This parasitic cestode, originally considered endemic only in the Arctic and in north-central areas of North America (Massolo et al., 2014), is now recognized to have gradually increased its geographic distribution over the past few decades, possibly because of the increasing range of wild canids (e.g. foxes and coyotes) that serve as its definitive hosts. The importation of dogs from endemic areas in North America or Europe without any requirement for anthelmintic (specifically cestocide) treatment is equally likely to have been a contributing factor. Wild canids, such as foxes and coyotes, are the primary definitive hosts of this parasite. Domestic dogs, and to a lesser extent cats (which are of relatively minor importance in the epidemiology of the parasite), can also serve as definitive hosts (Deplazes et al.,...
ingestion of species, including non-human primates and humans, after Alveolar hydatid cysts can also occur in certain other animal infected rodent by a definitive host completes the life cycle. As AE, which most often affects the liver. Ingestion of the tapeworm in the abdominal organs, a condition known lesions (alveolar hydatid cysts) containing the larval form of species, such as small rodents, results in the development of and the consumption of those eggs by intermediate host worms in the intestines of these species are shed in the faeces, of large numbers of E. multilocularis eggs from the environment (Haller et al., 1998; Brouwer et al., 2015), which would most likely have been shed in the faeces of infected wild canid hosts such as foxes and coyotes. Cases of canine AE have to date been considered a rare finding in North America (Massolo et al., 2014); with this in mind, the diagnosis of four cases in southern Ontario within a 3-year period is worthy of note, especially because until recently, this region has not been considered an area endemic for the parasite.

If the recent cases of canine AE diagnosed in Ontario are indeed an indication of heavy environmental contamination with E. multilocularis eggs in some areas of the province, there is the potential for a public health risk in those areas. In this article, we describe a local public health department’s follow-up of a number of individuals who had potentially been exposed to the eggs of the parasite by contact with a case of canine AE diagnosed in summer 2015, and summarize a comprehensive decision process that can be used to assist in the follow-up of such exposures.

Methods

Description of canine case and human exposures
Details of the canine case of AE are described elsewhere (Brouwer et al., 2015). In brief, a 4-year-old male Boxer dog was presented at the Ontario Veterinary College Health Sciences Centre in June 2015 for exploratory laparotomy, following a history of lethargy, vomiting and abdominal pain, and radiographic detection of an abdominal mass. During surgery, two large, fluid-filled hepatic masses measuring 10–25 cm in diameter were excised and submitted for histopathology. The masses contained multilocular cysts with cross-sections of larval tapeworm protoscolices and evidence of inflammatory changes. Alveolar echinococcosis was suspected, and polymerase chain reaction (PCR) and sequencing on tissue samples sent to the Institut für Parasitologie, University of Bern, Switzerland, confirmed the diagnosis (Trachsel et al., 2007). No faecal testing of the dog for intestinal infection was performed at the time, so whether or not an intestinal infection existed was unknown. Therefore, the animal was treated with praziquantel at 10 mg/kg bodyweight as soon as the presumptive diagnosis was made (2 days after admission to the referral facility for surgery), and instructions were given for retreatment 2 weeks later. The local public health department (WDGPH) was notified of the presumptive diagnosis and was again notified after AE had been confirmed by
PCR. The department was also informed that some of the veterinary staff who had attended to the dog during its stay at the referral facility might have been exposed to the parasite if the dog had been shedding eggs in its faeces at the time of contact. Human AE is not a reportable disease in Ontario. However, the incident was reported to WDGPH because of the risk of human exposures and the potentially serious consequences of AE in humans, and the health department considered it important to investigate further in order to assess and ameliorate any risk to human health.

The dog was owned by a local family who also owned cats as well as other dogs, and it had spent most of its life in Southwestern Ontario. However, about two and a half years before being diagnosed with AE, it had also lived for approximately 7 months in Alberta, a region known to be endemic for *E. multilocularis* (Massolo et al., 2014). In both provinces, the dog had reportedly spent a considerable amount of time outdoors and had interacted with wildlife, including having more than one encounter with coyotes. According to veterinary records, the dog had not been treated with any cestocide effective against *E. multilocularis* (either praziquantel or epsiprantel) in the 4 years of its life before diagnosis.

**Risk assessment and follow-up**

The following steps were taken by public health to follow-up on the report of the possible exposures, with some chronological overlap between the various steps as the investigation unfolded:

1. **Documentation of time, nature and setting(s) of exposure, and of individuals possibly exposed.** The clinical incubation period of canine AE is unknown, but is thought to vary widely from case to case, with the age at diagnosis ranging from 1 to over 10 years in one study of 23 dogs living in a highly endemic area (Corsini et al., 2015). To make the public health follow-up of contacts feasible, the immediate investigation focused on those considered to be at highest risk: household members of the animal, and people who had come into physical contact with the animal during its stay at the veterinary referral facility where the presumptive diagnosis had been made.

2. **Interview of individuals who had handled the animal at each known setting of exposure.**

3. **Documentation of information on specimens collected from the animal before the case was reported to public health.** Collection and testing of additional samples from in-contact animals and humans was also performed where deemed necessary.

4. **Assessment of human risk of exposure to *E. multilocularis*, based on information received from the aforementioned steps, and on current knowledge of the life cycle and epidemiology of the parasite.**

5. **Education and testing of any individuals thought to be at significant risk of exposure to infection.**

**Documentation of exposure(s) and individuals**

In this investigation, the possible exposures had occurred within the circle of family and friends in the household of the family that owned the dog, and at one veterinary clinic and one veterinary referral centre at which the animal had been examined and/or stayed overnight and received the surgical procedure. Notes were made of the time periods during which clinic staff could have been directly or indirectly exposed to any eggs shed by the animal in faeces, as well as the nature and settings of potential exposures (e.g. general care during hospitalization of the animal or exposure during the surgical procedure).

Information about the home environment of the animal (i.e. number of household human and animal members) was also collected and documented at this time.

**Interviews of those potentially exposed**

At the time of the interviews, the status of the animal with regard to intestinal infection with *E. multilocularis* was unknown; however, a laboratory confirmed diagnosis of AE had been made, and on that basis, it was recognized that there was a possibility that an intestinal infection existed in addition to the AE. As a result, interviews were carried out with all individuals who were thought to have had close contact with the animal, at its home or at either of the two veterinary facilities where it had been treated. For the interviews, two standardized questionnaires (available from the authors on request) were developed: one for staff and the other for members of the animal’s household. These included questions on the nature of interaction with the animal, designed to assess whether or not that interaction might have involved direct or indirect contact with its faeces, especially during the period before the diagnosis of AE had been made and contact precautions put in place. Responses that indicated that direct or indirect contact with faeces had occurred were considered to indicate a higher level of risk.

**Documentation of samples collected and tested, and recommendation of additional testing**

As described, shortly after the initial notification of public health of the presumptive diagnosis made on the case, the diagnosis of *E. multilocularis* had been confirmed in the canine case by PCR and sequencing of specimens from the hepatic lesions. No faecal testing of the animal had been performed. To better assess the public health risk posed by the case, WDGPH, with the assistance of the Department
of Pathobiology, Ontario Veterinary College, University of Guelph, requested that arrangements be made for the collection of faecal samples from the case as well as all other animals (two dogs and two cats) living in the same household, as well as blood samples for serology from the case and three of the other four animals; at the request of the owners, the older of the two cats was excluded from blood sample collection due to its advanced age. All blood samples were sent to the Institut für Parasitologie in Bern, Switzerland, for serological evaluation against *E. multilocularis* antigen by enzyme-linked immunosorbent assay (ELISA), using the technique described by Corsini et al. (2015) – with substitution of the anti-dog conjugate with an anti-cat conjugate for feline serology. Faecal samples were sent to the National Veterinary Institute, SVA (Sweden), for real-time PCR using the protocol described by Isaksson et al. (2014).

**Assessment of risk of human infections**

At the time of the reported possible exposures to the canine case of AE, it was unknown whether or not the animal was currently hosting or had hosted in the past, an intestinal *E. multilocularis* infection. As previously mentioned, the presence of an AE lesion could possibly have indicated a previous or existing intestinal infection or could have resulted from ingestion of eggs directly from the environment in either of the provinces in which it had lived. Either of these scenarios could have posed a risk to people in direct contact with, and/or frequenting the same environment as, the canine case. Because of this, and in the absence of the ability to rule out this possibility at the beginning of the public health investigation, the assumption was made at that time that the dog could be harbouring an intestinal infection. Therefore, the investigation included an assessment of risk of human exposures among people who had had contact with the animal.

Information obtained from interviews with the owners of the canine AE case and with the staff at the two veterinary facilities at which the animal had been treated, along with the results of the faecal and serological testing of the animals in the household as these became available, was used to estimate the level of risk posed by any contact that had occurred. This was an evolving process as the various streams of information were gathered. Based on this assessment, decisions were made about next steps in the process of following-up the reported exposure incident.

**Education and testing of individuals at risk**

During initial interviews carried out with individuals who had had significant contact with the infected animal, there was the opportunity to provide some education in response to questions asked. In addition, all individuals thought to be most at risk among the contacts of the case were offered serological testing via the Tropical Disease Unit at the Toronto General Hospital, Toronto, Ontario; blood samples taken from these individuals were sent to the Institut für Parasitologie, University of Bern, Switzerland, via the Public Health Ontario Laboratory for testing against *E. multilocularis* antigen by two specific ELISAs (Em2-ELISA and recEm18-ELISA), supplemented by a Western blot (Müller et al., 2007).

**Results**

**Results of interviews**

In total, 36 staff at the two veterinary facilities where the dog had been treated, in addition to all household members of the case, were interviewed by Public Health using the questionnaires developed for this purpose. Where necessary, interviews included education about the parasite and its risks to humans.

Because of information gathered from interviews and veterinary staff, the household members of the animal were considered to be at highest risk of exposure if the animal had hosted an intestinal infection at any point of its life, due to their closer and more prolonged contact with the case. Therefore, household contacts were advised to be tested for exposure to *E. multilocularis* infection as described above, even before the results of the additional tests carried out on the household pets had been received. Because of their relatively brief contact with the case, the risk of exposure to the veterinary staff was very likely much lower than any risk to the owners of the case and their

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**Fig. 1.** Decision flow chart for assessment of risk of human exposure following a diagnosis of *Echinococcus multilocularis* infection in an animal.

*Some dogs with AE may also harbour intestinal infections of *E. multilocularis* (Deplazes and Eckert, 2001). **Other household dogs and cats may have been exposed and/or infected by the same source of infection as the reported case. †Recommended PCR protocol for faecal testing is as described by Isaksson et al., 2014; results of other protocols may be less reliable. Ideally, coprological examination for taeniid eggs should accompany a positive PCR finding to ensure that result is due to a patent intestinal infection, which would indicate a higher risk to humans. ‡It is important to note that faecal testing may not sensitive enough to definitively rule out intestinal infection based on a negative result. Therefore, treatment of the animal with praziquantel is recommended regardless of the result of faecal testing. ††Note that treatment for intestinal infections in dogs should begin as soon as possible after a presumptive diagnosis is made. If possible, faecal specimen(s) for testing should be collected before treatment has begun. §§Information gathered via interviews of contacts to be used to help assess risk of exposure.
other pets. Therefore, it was decided to await the results of the tests on the household animals and people before encouraging or recommending serological tests of the staff.

Results of tests
As mentioned previously, the canine AE case had tested positive for *E. multilocularis* by PCR on samples from the liver lesion shortly after the surgical procedure was performed at the referral facility. The blood sample from the dog, which was submitted for ELISA along with samples from the other household animals approximately a month after the surgery, tested positive for antibodies to *E. multilocularis*.

Results of serological and faecal PCR tests performed on the three blood samples and four faecal samples from the other animals in the household (two dogs and two cats) were all negative; the canine AE case also tested negative by faecal PCR.

Members of the animal’s household, as those who had been in closest contact with the animal, provided baseline and follow-up blood samples for serological testing, with the follow-up tests carried out 6–12 months following baseline tests. As of the time of publication of this report, all serological test results were negative; that is, there was no detection of antibodies to *E. multilocularis* antigen Em2 and Em18 and no seroreactivity by *E. multilocularis*-specific immunoblotting.

Results of risk assessment
Because of the negative test results of the household human and animal contacts of the case, and because of the negative faecal PCR results of the case itself, the risk of human infection posed by the case of canine AE was assessed as very low, if not non-existent. Household and clinic contacts of the animal were informed of the test results, and of Public Health’s assessment of the risk as being very low. In light of the assessment, no additional serological testing of human contacts was recommended by Public Health beyond that described here.

Discussion and Recommendations
The case of canine AE that prompted this investigation by WDGPH had a history of travel to an area known to be endemic for *E. multilocularis*. However, the three dogs previously diagnosed with AE in southern Ontario had had no known out-of-province travel history. The occurrence of AE in Ontario dogs with no travel history, and the fact that canine AE is thought to result from either the ingestion of eggs from the environment, or from concurrent or previous intestinal carriage of *E. multilocularis* infection, indicated that the likelihood of intestinal infection in this AE case as well as in other animals of the same household could not be ignored (Deplazes et al., 1997; Haller et al., 1998; Deplazes and Eckert, 2001; Massolo et al., 2014; Corsini et al., 2015); however, neither could intestinal carriage be assumed. Therefore, the follow-up investigation by public health included testing of the household animals and humans in addition to interviewing and educating contacts of the case, to determine whether intestinal infections were present in any of the household animals and thus to better assess the risk to people who had had contact with the animal.

Fortunately, the results of faecal PCR tests of the canine case and its closest animal contacts indicated that there was no evidence of intestinal infection in any of the animals. Likewise, serological tests on its closest canine, feline and human contacts showed no evidence of exposure to the parasite. As previously mentioned, the faecal sample from the case was collected approximately 1 month after the dog had been given the first dose of praziquantel. It was important to treat the animal as soon as the presumptive diagnosis of AE had been made; however, the delayed sample collection may have adversely affected the ability of the testing to determine whether there may have been an intestinal infection before treatment. Even so, no evidence of either exposure or intestinal infections was found in any of the closest animal contacts of the case, and there was also no serological evidence of exposure of any of its closest human contacts, in spite of the fact that those people and animals had lived in the same home as the canine case for several years. Therefore, even though there could have been historical intestinal infection and shedding of eggs, the risk to human contacts in both the household and clinic environments was concluded to be very low to non-existent. Had there been any evidence of intestinal infection or serological reactivity in any of the household animals, the next step would likely have been repeated serological testing of all human contacts considered to be at significant risk, namely, those directly or indirectly exposed to parasite eggs shed by the infected animal. In Europe, individuals thought to have been exposed to *E. multilocularis* eggs are serologically investigated 3, 6 and 12 months after the known or estimated exposure time-point. Where all three tests are negative, the case is closed, whereas in the event of a seropositive finding, the individual is referred for specialized imaging and other clinical investigations (Gottstein, B., personal communication, 2016).

With the recent occurrence of cases of canine AE in Ontario, most of which have had no known out-of-province travel history, it cannot be ruled out that human exposure to *E. multilocularis*, by contact with eggs shed by infected wild or domesticated canids, will eventually
present a public health risk in the province. It is important that local public health departments be prepared for this and have a comprehensive process in place for identifying and interviewing contacts, testing humans and animals, and assessing risk using information from interviews as well as results from appropriate diagnostic tests. To aid in the investigation of future reports of exposure to cases of AE and/or cases of intestinal *E. multilocularis* infection, WDGPH developed a guidance document for internal use and (Fig. 1) a decision flow chart; these will be used when following up such incidents.

Human AE is not on the list of diseases reportable to public health in Ontario, nor is it reportable at the federal level. Throughout North America, there have been very few cases of human AE reported in the literature to date (Massolo et al., 2014). One possible explanation is that, until recently, the strains of *E. multilocularis* known to be endemic in North America have been the North American strains and, to a lesser degree, the Asian strain, which has been reported in one area of Alaska (Massolo et al., 2014). However, since 2012, at least one strain of AE has been reported in dogs in British Columbia, Alberta and southern Ontario that appeared to be European in origin (Jenkins et al., 2012; Massolo et al., 2014; Peregrine, A. S. and colleagues, unpublished data). European strains are typically associated with more human infections (Jenkins et al., 2012). As one or more European strains may now be established in some areas of Canada, there may be some likelihood that cases of human AE will occur in the months and years to come. To promote increased physician awareness of this rare but serious and potentially life-threatening disease, human AE should perhaps be made reportable in all provinces and territories in Canada. In addition, at some point in the future, if sufficient cases of either AE in people or dogs, or canine intestinal infections with *E. multilocularis* occur to make the financial investment worthwhile, ensuring the availability of serological and molecular tests for *E. multilocularis* exposure and infection in humans and animals in Canadian laboratories would facilitate the investigation of suspected exposures in Canada, in terms of accessibility of the necessary tests as well as reduced costs of shipping and processing of specimens. Further, it is hoped that the assessment of risk of exposure will soon also be made easier by studies on the prevalence of *E. multilocularis* in wild canids in southern Ontario; in recent studies carried out in northern and western areas of Canada, the prevalence in wild canids was found to be as high as 30%, and higher in some instances (Massolo et al., 2014).

In conclusion, there is now increasing evidence that *E. multilocularis* is becoming, or has already become, established in southern Ontario, possibly by expansion of the geographic distribution of the North American strain from previously endemic areas within the continent, and/or by introduction of one or more European strains – both of which could have occurred via importation of dogs from endemic areas. In the light of these developments, it is important that local and provincial public health authorities in Ontario be prepared for this emerging and potentially serious public health threat. In addition, physicians in the province need to be aware of the potential risk of locally acquired human AE, to increase the likelihood of this disease being considered among the differential diagnoses of patients presenting with symptoms and infiltrative hepatic lesions consistent with human AE.

**References**


