

Investigations and actions taken during 2011 due to the first finding of *Echinococcus multilocularis* in Sweden

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Echinococcus multilocularis is a parasite that can cause alveolar echinococcosis disease. After the first positive finding of *E. multilocularis* in Sweden in 2011, a consulting group with representatives from relevant authorities was summoned. In this group, all relevant information was shared, strategies for information dissemination and any actions to be taken due to the finding of *E. multilocularis* were discussed and decided. The present paper describes the actions taken during 2011 and the results thereof, including surveillance in animals, risk assessment for humans to become infected and recommendations given to the public. Further discussion about whether the parasite was introduced, and if so, how, as well as possible future development of the infection in animals and humans in Sweden and future actions are included.

Introduction

Alveolar echinococcosis (AE) is a disease in humans caused by the larval stage of the tapeworm *Echinococcus multilocularis* (EM). It is considered to be the most serious parasitic disease in humans in Europe [1]. The parasite develops with a tumour-like growth almost exclusively in the liver and the disease is characterised by a long incubation period, between five and 15 years, followed by a subsequent chronic course [2]. Although a serious disease, in Europe, the reported prevalence in humans is low, up to 1.4 per 100,000 population [2]. During the last decades, the known range of the parasite in Europe has extended and, although data is not comprehensive, it is assumed that the parasite is present over most of Europe with the exception of the British Isles and the Mediterranean region [1]. It is however unclear whether this extension corresponds to its true range or whether it reflects previous absence of surveillance [1]. In Sweden, Norway and Finland, surveillance in animals from 2000 to 2009 had shown that in 2009, using a design prevalence of 1%, these

countries were most probably free from the parasite [3]. However, in February 2011, EM was identified in a red fox (*Vulpes vulpes*) in Lanneröd, Sweden for the first time [4]. The fox was shot within the routine surveillance programme in 2010. After this finding, a consulting group, lead by the National Board of Health and Welfare (SoS), was summoned. The group consisted of representatives of the Swedish Board of Agriculture (JV), the Swedish Institute for Communicable Disease Control (SMI), the National Food Agency (NFA), National Veterinary Institute (SVA), the Swedish Work Environment Authority and the relevant county medical- and county veterinary officers. Regular teleconferences were usually held every 1–2 weeks, during which information concerning EM and the situation in the country was shared, and strategies for information dissemination and actions to be taken were discussed and decided.

The aim of the present paper is to describe the actions taken due to this finding and the results thereof, i.e. surveillance in animals, risk assessment for humans to become infected and recommendations given to the public. Further discussion about whether the parasite was introduced, and if so, how, as well as possible future development of the infection and future actions are included.

Methods

Surveillance in animals

Immediately after the finding of EM, increased surveillance in foxes was started [4]. Hunters were requested to submit foxes primarily from southern Sweden because it was considered that EM was most probably introduced in this area. The aim was to analyse 3,000 foxes with segmental sedimentation and counting technique (SSCT) [5], thereby detecting a prevalence

of 0.1% on country basis. Furthermore, faecal samples from hunting dogs (n=119) in the four municipalities around Lanneröd were examined at SVA by egg flotation [6] and an in-house real-time polymerase chain reaction (PCR). A non-random sampling of potential intermediate hosts was also started in an area within a 50-km radius surrounding Lanneröd. During March–April, 2011, a total of 236 rodents were collected, mainly *Arvicola amphibius* followed by *Myodes glareolus*, *Microtus agrestis*, *Apodemus sylvaticus*, and *Apodemus flavicollis*. The rodents were autopsied and liver or other organs with lesions (n=72) were tested by an in-house PCR. As extensive sampling of rodents is probably needed to identify the intermediate host species in an area with very low prevalence of EM, sampling of rodents continues.

Risk assessment

By 3 March 2011, the Swedish government gave a mandate to JV and SoS to, in cooperation with relevant authorities and organisations, clarify necessary actions to protect public health as a consequence of the finding of EM. Within the government mandate, a qualitative risk assessment about the probability of humans becoming infected with EM was performed in the spring of 2011 by SMI and NFA.

Recommendations and public health measures

To ensure that relevant and harmonised information concerning what was known as well as what was not known was given to the public, this issue was continuously discussed in the consulting group. Furthermore, optimal ways of dissemination of this information was also investigated.

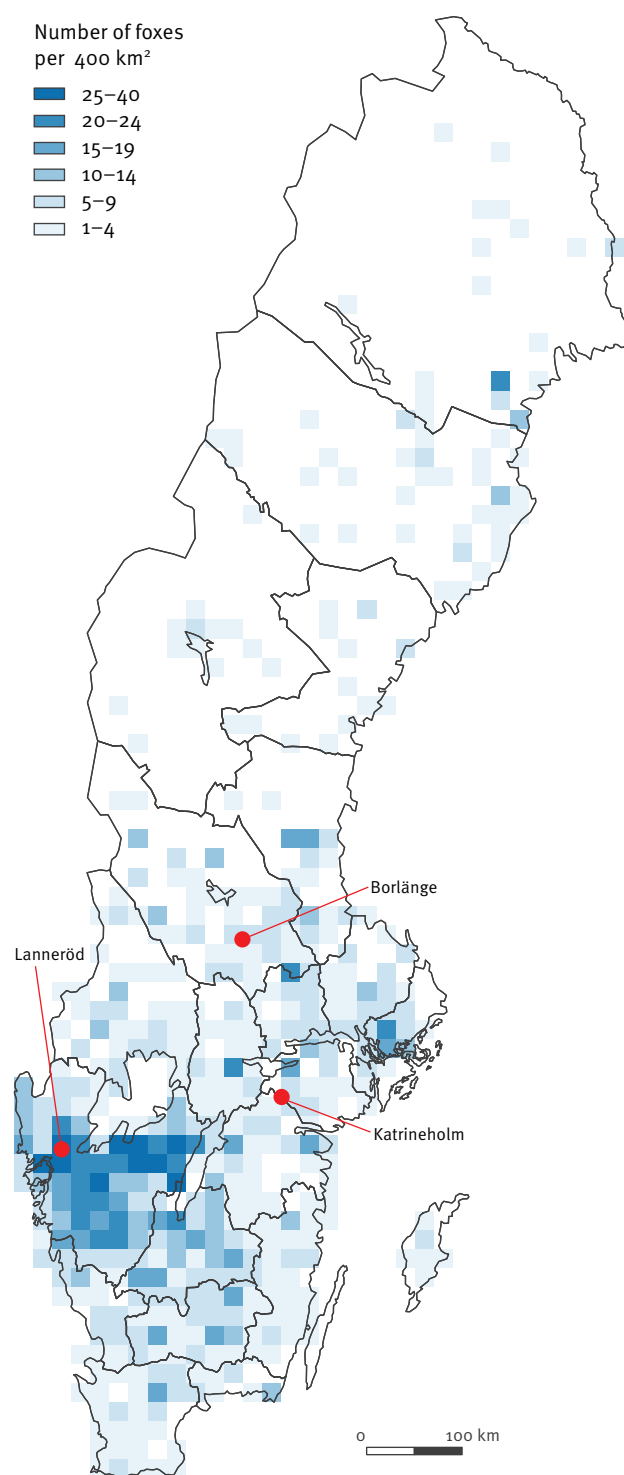
Results

Surveillance in animals

Shortly after the first fox testing positive for EM was found, the prevalence of EM in foxes seemed to be very low in Sweden, probably well below 1%. Surveillance of red foxes during 2000–2009 (n=2,962) had yielded negative results [3] and after the first positive finding, several hundred foxes, shot within the increased surveillance, were analysed with no further animals testing positive. Analysis of all faecal samples from hunting dogs in the four municipalities around Lanneröd did not yield any positive results and none of the rodents tested within the 50 km radius surrounding Lanneröd were found positive. The question was raised whether it could be possible to control and even eradicate EM. It was considered most probable that EM had been introduced to Sweden in recent years by infected dogs [4] and therefore the spread of EM could be geographically restricted. Besides Rebus Island, Japan, where EM was eradicated [7], the parasite had previously only been successfully controlled in geographically limited areas. However, based on advice from international experts and literature research, it was concluded that it might be possible to eradicate EM. A preliminary cost–benefit

FIGURE 1

Geographical distribution of all georeferenced foxes shot and analysed for *Echinococcus multilocularis*, Sweden, January–June 2011 (n=2,900)



The three locations where the three *Echinococcus multilocularis* positive foxes were respectively shot are indicated on the map. Foxes were georeferenced with the coordinate system RT90.

analysis showed that if eradication was possible, benefits would exceed the costs [8].

By 31 March 2011, when a total of 1,140 foxes (shot in 2011) had been analysed for EM, a second infected fox was found. This fox was shot in the Lanneröd region at the same location and by the same hunter as the first infected fox (shot in 2010). This finding confirmed the presence of the infection in this region but did not change the interpretation of the situation. By 27 April, when 1,758 foxes had been analysed, a third case was found nearby Katrineholm, more than 200 km north-east of Lanneröd. Although the probability that EM was spread to other parts of Sweden increased, investigation into ways to eradicate EM continued and the deworming recommendation was extended to include dogs at risk in this area as well. However, by the end of May, when 2,525 foxes had been analysed, a fourth infected fox was found outside Borlänge about 200 and 300 km respectively north of the previous findings (Figure 1). Thus it was concluded that EM was probably not restricted to only the few known infected areas in Sweden and that eradication was not feasible. By the end of June, the increased surveillance of foxes was completed and had resulted in the finding of a total of three positives of 2,985 analysed foxes (0.1%). The geographical distribution of foxes with georeferences (n=2,900) is illustrated in Figure 1.

Risk assessment

Humans become infected by ingesting eggs from the parasite and several modes of transmission are plausible, such as consuming contaminated food or water, inhaling eggs from contaminated environments or by letting contaminated hands or objects come in contact with the mouth. However, due to the long incubation period and the low incidence of AE there is little evidence in the literature to help discriminate the relevance of the different modes.

Evidence for direct food transmission is the observation that monkeys and pigs became infected by consumption of grass probably contaminated with fox faeces [9]. One epidemiological study identified consumption of unwashed strawberries as well as chewing on grass as risk factors, but not picking berries, eating unwashed herbs or vegetables [10]. In another study, consumption of strawberries, mushrooms, blueberries, herbs, parsley or cranberries were not identified as risk factors [11]. In contrast, using well water rather than tap water [12] or using water from certain lakes [2], was identified as a risk factor.

The results of the literature search were similarly inconsistent for risk factors regarding farming, gardening and hunting [11-13]. Many risk factors regarding environmental exposure are hard to separate from the consumption of food. One of the studies related two-thirds of the cases to farming or similar activities, probably reflecting contact with a contaminated environment [10]. The only garden activity more common among

cases than controls was growing (not consuming) leaf or root vegetables, supposedly due to the amount and intensity of care required for annual compared to perennial plants [10].

Interaction with animals, regarding the risk of humans getting infected, has been investigated and inconsistent results have been presented. Two of five case-control studies identified dog ownership as a risk factor for acquiring AE [10,14], especially if the dog was left unattended in the garden or if it was killing game, whereas in the three remaining studies dog ownership was not found to be a significant risk factor [11-13]. The two studies on cat ownership as a potential risk factor, both found an association between being an AE case and owning a cat [10,11]. However, in one study the risk was small and much smaller compared to owning a dog [10].

A correlation between the prevalence in foxes and in humans has been found. However, although the prevalence in fox populations in some countries is high, the reported number of cases in humans is relatively low [15,16]. This may indicate that the actual risk of becoming infected is not only linked to exposure to the pathogen, but also to individual susceptibility, perhaps because of immunological differences [17].

In conclusion, risk factors most often identified in epidemiological studies are associated with living, working or other activities in rural environments, which makes it difficult to distinguish between environmental, food, soil, and other routes of transmission. With the evidence available, contact with contaminated environment, is considered to be an important risk factor and farmers, hunters and dog owners, whose dogs eat rodents were considered to be the group at highest risk.

Due to the current low prevalence in foxes and since no cases of AE have been reported in Sweden, the competent authorities concluded that the risk to humans in Sweden of developing AE was considered to be small. It was estimated that about one person among the nine million Swedes would be infected and develop AE every fifth year. Moreover, if the probability of infection in humans were to become similar to Switzerland this figure could increase to 20-30 cases yearly. As the prevalence of EM in the fox population could change over time, it was considered important to repeatedly monitor the fox population to be able to assess a possible increase of EM prevalence, and the risk that this may pose to humans

Recommendations and public health measures

Initially, recommendations to prevent human infection were kept general, but emphasised the importance of proper hand hygiene after contact with free running pets in risk areas. After finalisation of the risk assessment, it was concluded that the importance of food and drinking water for the transmission of AE to

humans could not be assessed and that there were no documented risk-reducing effects of washing vegetables and berries. Based on these knowledge gaps and the low number of reported AE cases even in areas in mainland Europe where the prevalence of EM in foxes is high, and taking the benefits of outdoor activities including harvesting and consuming berries and vegetables into consideration, the NFA and SMI concluded that it was not appropriate to issue any specific recommendations about EM and food. However, consumers were informed that good hygienic practices when handling food apply also with regard to EM. To consumers who do not accept any risk, information was given that boiling food is the only effective way to inactivate EM. Recommendations were communicated by authorities via the internet and also by a common information site (www.krisinformation.se).

After the first positive finding of EM in a Swedish fox in Lanneröd, JV issued recommendations that dogs at risk, i.e. dogs that could catch rodents, in the four surrounding municipalities should be dewormed monthly. Later, when another fox tested positive near Katrineholm, the deworming recommendation was extended to also include dogs at risk in this area. However when results of the surveillance indicated that EM was endemic at a very low prevalence in Sweden, recommendations to dog owners in the country were withdrawn. For worried dog owners, whose dogs eat rodents, deworming the dogs monthly was nevertheless suggested to prevent infection.

For the particular case of pet dogs entering the country from abroad, it was decided that dog owners should be informed, that dogs coming from endemic regions of mainland Europe need be dewormed before entry in Sweden. It is important to highlight that the risk of dogs becoming infected is greater in many European countries where the prevalence of EM is much higher compared to Sweden. In Sweden the prevalence in foxes appears so far to be very low, about 0.1%, but in certain areas in Europe 50% of foxes or more may be infected [2]. Deworming will reduce the risk not only for the individual dog owners, but also prevent introduction to areas where EM may not yet be present.

It was concluded that should the prevalence of the EM within the Swedish fox population remain very low, no further recommendations to the public would be given. Monitoring the fox population, however, was considered important to be able to reassess information campaigns to the public if an increase of EM would be observed. In addition, increased monitoring was considered necessary as the geographical spread of EM as well as the prevalence in different areas is not well known. There is also a need for more information on the fox population density in different areas of Sweden and how the population changes over time. Of special interest are urban foxes as they, due to closer contact with people, are considered to pose a greater risk. It was therefore concluded that increased and repeated

monitoring of EM in foxes as well as monitoring of the fox population is needed.

If high population densities of urban foxes with a high prevalence of EM were found in Sweden, this would increase the risk to humans. Because control strategies applied locally, such as deworming dogs and baiting strategies for foxes can reduce this risk [16,18] it was concluded that an action plan should be prepared in case such high risk areas were found in Sweden. The action plan should also clarify how relevant information is provided to the public and groups most at risk.

Finally it was concluded that there is a need for research. More knowledge about the epidemiology of EM in Sweden is also needed, such as which intermediate hosts are involved in the life cycle of EM and what the present and expected future distribution and prevalence of EM in the country may be. More knowledge is needed on risk factors for developing AE as well as what can be done to prevent infection.

Discussion

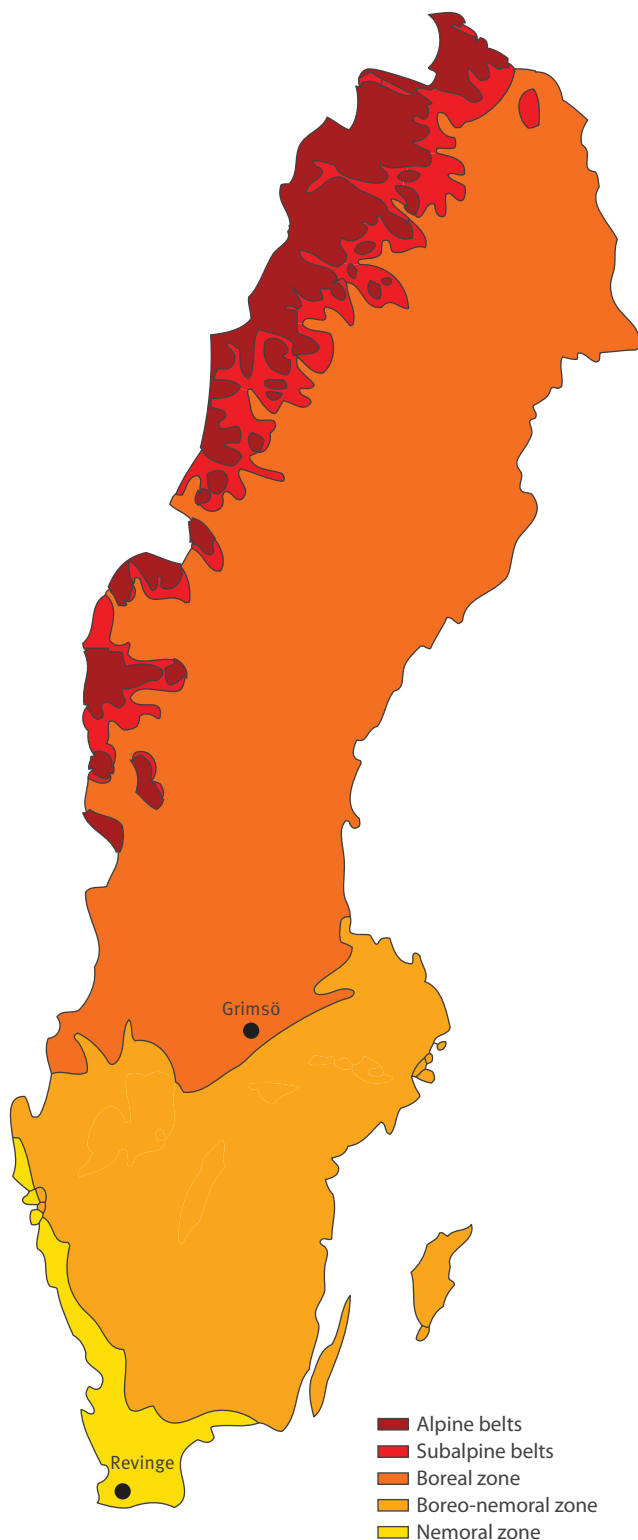
It is not known when EM was introduced to the Scandinavian Peninsula. However, if introduction was recent, unlawful admission of dogs from mainland Europe is the most probable explanation. Risk assessments have shown that without a very high compliance with import requirements, introduction of dogs from endemic areas constitutes a risk of introduction of EM [19,20]. Compliance with import requirements has decreased and the number of imported dogs has increased substantially in Sweden since 1994 (personal communication, Maria Cedersmyg, January 2012). Prior to 1994, all dogs were dewormed in quarantine prior to entry to Sweden. In 1994, for dogs from certain European countries, this was replaced by a requirement that a veterinary deworming certificate should be shown at the border. Furthermore, in 1995, border control was restricted as Sweden joined the European Union (EU), thereby prohibiting routine control of deworming certificates of dogs.

Another possible explanation for the present findings of EM in foxes is that the parasite has been endemic for a long time but escaped detection due to limited surveillance. According to the negative binomial distribution and assuming a test with 100% sensitivity, 3,000 foxes have to be analysed to have a 95% probability of detecting EM given a prevalence of 0.1%. In the routine surveillance in Sweden, started in the year 2000, more than 2,900 samples were analysed before the first case was detected. This highlights that extensive surveillance is needed to detect a low prevalence of EM. Introduction by foxes from Finland was considered unlikely as, despite intensive surveillance [3], the parasite has not been found in this country.

The present and future spread of EM in Sweden is unknown. The epidemiology of EM depends on the fox population density as well as the interaction with

FIGURE 2

Vegetational zonation in Sweden, 1999



Locations where fox population densities have been estimated, Grimsö and Revinge, are shown. Vegetation data is reproduced with permission from Acta Phytogeographica Suecica [35].

intermediate hosts. For non-urban mainland Europe fox population densities have been reported to be 0.5–3 foxes/km² [21–25]. In Sweden, the corresponding figures (during the 1970s) were 0.8 (Revinge, nemoral zone) and 0.2–0.4 foxes/km² (Grimsö, southern boreal zone) [26,27] (Figure 2). During the 1980s an epizootic of sarcoptic mange struck the Swedish fox population and the density of foxes declined considerably especially in southern Sweden [28]. However, the population recovered to the levels of the 1970s in the early 1990s, and monitoring has not revealed any dramatic change after this recovery [29,30]. The fox population density varies, from relatively high and stable in the nemoral and boreonemoral zones (south) to a lower density with a much higher degree of fluctuation in the boreal zone (north) [26,27,31,32] and the fluctuations in the north follow those of vole populations [33]. The three areas where EM has been found have suitable fox habitat characterised by a mixture of forest and agricultural land. It is concluded that although the fox population density in Sweden is lower compared to mainland Europe, it is sufficient to maintain the lifecycle of EM. Perhaps besides northern Sweden, where the decreased fox density during the lowest phase of the population fluctuation may be too low for EM to prevail, there is no reason to believe that EM could not be established in the rest of Sweden. In urban areas, the fox populations in mainland Europe have been reported to be high and may exceed 10 foxes/km² [34] and these fox populations play an important role in the transmission of human AE [18]. However, although foxes are present in cities also in Sweden, information on the urban fox population densities are lacking.

Furthermore, it is not known which intermediate host species are involved in the life cycle of EM in Sweden. Based on previous knowledge on EM prevalence among intermediate host species [36–38], known and expected food preference by the red fox in Sweden and Norway [39], and the occurrence of different small rodents in the identified EM-infected areas in Sweden, the most likely intermediate host candidates should be *Arvicola amphibius*, *Microtus agrestis* and *Myodes glareolus*; all common and distributed throughout Sweden [40]. *Microtus arvalis*, one of the principal intermediate hosts in mainland Europe does not occur in Sweden.

It was concluded that the risk of developing AE in Sweden is low. However, it might be argued that the risk of being infected by EM could be higher in Sweden than in other countries with similar prevalence. One reason is the unique legislation on Right of Public Access to land, which gives the public right to roam freely in the countryside. Outdoor activities such as hiking, camping and berry- and mushroom picking are long standing traditions in Sweden. Hunting is a widespread activity that adds to the number of people in close contact with nature. Still, there is a lack of scientific studies comparing behaviour in different countries, making it not possible to assess whether the risk is higher in Sweden due to particular behaviours, such

as outdoor activities. Another reason for the risk being hypothetically higher in Sweden is that EM was only recently detected, so there is no tradition of how to minimise risk of exposure. It has not been shown that information will reduce the risk, but there are studies reporting differences between countries in Europe in terms of knowledge and perception of the risk of AE [41]. In some other countries in Europe, where EM is endemic, there are recommendations to rinse and/or cook berries and vegetables before eating them and to wash the hands thoroughly after contact with soil or vegetation, to avoid being infected with EM. For dog and cat owners there are recommendations to regularly deworm the pets in case they roam outdoors and eat wild rodents.

After concluding that eradication was not possible, the only preventive action taken by the authorities was issuing recommendations. However, due to lack of knowledge, the recommendations given were quite general. In this situation, there was a requirement from the general public and especially from hunters to at least try to prevent further spread of EM. The question was raised whether increased fox hunting could be beneficial. However, because hunting may increase the immigration rate and lower the age distribution of the fox population [26], hunting may increase the spread of EM especially if the prevalence of EM is higher in adjacent areas. Hunting may also increase the EM biomass if the proportion of young foxes increases as, apart from one recent study in Lithuania [42], the worm burden has been reported to be higher in younger foxes [43,44]. A hunting pressure high enough to influence spring density of reproducing animals is probably seldom attained. It was concluded that intensified hunting in infected areas and especially in hot-spots may be beneficial however, increased fox hunting in areas where EM has not been found is not recommended.

According to the authorities, more knowledge about the prevalence of EM in different areas is needed. Although an extensive surveillance was performed after the first finding, there is a need for additional sampling especially in areas where the sampling intensity was lower. Furthermore, there is a need for long term monitoring to follow any future changes in prevalence. It is also important to extend the current monitoring of the population density of small rodents [45,46] and to also involve the south of Sweden. At present there is no suitable method for large scale surveillance of EM. Until now surveillance in Sweden has been based on foxes shot by hunters. The latter foxes were analysed with coproantigen enzyme-linked immunosorbent assay (ELISA) [47] or in-house PCR, and after the first positive finding with SSCT [5]. However, collection of foxes shot by hunters is cumbersome, costly and associated with a risk of exposure to EM. Sampling of fox faeces is expected to lower the costs and also the risk of exposure but none of these are considered suitable for large scale surveillance. However, earlier modeling results have indicated that, depending on the

expected prevalence of EM infections in wild boars and the sensitivity of the test, surveillance of EM-lesions or antibodies in wild boars could be used to monitor EM in areas with a dense wild boar population [3]. Investigations are ongoing to evaluate whether surveillance in wild boars could be appropriate for the southern half of Sweden where 57,300 wild boars were shot during the hunting season 2010/11 [48].

Finally, the need for more research was identified by the authorities. Most important, more knowledge about risk factors for becoming infected with EM is needed so that relevant recommendations can be given to minimise risk of infection. Risk factor studies using diagnostic tools such as serology may have the potential to improve knowledge about risk for exposure to EM. The most important knowledge gaps identified in the risk assessment of transmission of EM via food were the importance of the risk of consumption of berries, fruits and other vegetables and how much the risk can be reduced by careful washing/rinsing of berries and vegetables. There is also a need for a cost effective surveillance that could be implemented on a large scale to estimate the level of contamination in different geographical regions and also assess future trends. Furthermore, from a Swedish point of view, there is a need for scientific studies comparing human behaviour in different countries, so it can be investigated whether the Swedish Right of Public Access to land (allowing people to roam freely in the country side and for example pick berries and mushrooms) and the present use of it, affects the risk of becoming infected by EM. Finally, there is a need to increase our understanding of the epidemiology of the disease in Sweden by efforts such as increased surveillance to identify the intermediate host species for EM.

Conclusions

The present risk to humans of becoming infected with EM and developing AE is considered to be small. It is most probable that EM is already spread within Sweden. Increased surveillance is needed to enhance knowledge about present and future prevalence of EM. An action plan will be developed to handle a potential future increased risk for humans, if the prevalence of EM increases. There is a need for more research about the epidemiology and surveillance of EM.

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