



Assessment of risk of introduction of *Echinococcus multilocularis* to mainland Norway

Opinion of the Panel on biological hazards of the Norwegian Scientific Committee for Food Safety

Date: 15.01.12.

Doc. no.: 11-106-final

ISBN: 978-82-8259-043-3

VKM Report 2012: 06



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Acknowledgements

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Summary

In the light of the recent findings of the tapeworm *Echinococcus multilocularis* (EM) in four red foxes from three different locations in Sweden, the Norwegian Scientific Committee for Food Safety (Vitenskapskomiteen; VKM), Panel of Biological Hazards (Faggruppe hygiene og smittestoffer) took the initiative to undertake a risk assessment regarding the probability of this parasite being introduced to mainland Norway and thus becoming a threat to public health in the country.

EM is a small tapeworm that resides in the intestine of carnivores (e.g. foxes, dogs) that function as final hosts for the adult tapeworm. The infection here gives few or no symptoms. Adult tapeworms produce eggs that are released in the faeces of the carnivores and may be ingested by mammals, usually rodents or lagomorphs¹, which act as intermediate hosts. In the intermediate hosts, the larval form of the tapeworm produces cysts, predominantly in the liver, where they proliferate and may invade the surrounding tissues. If the infected intermediate host is eaten by a susceptible final host, the adult tapeworm develops in the intestine and the lifecycle is completed.

EM is of public health significance as humans may act as accidental intermediate hosts if they ingest eggs, either through contaminated foods or water, or from contact with infected final hosts (dogs, foxes) or their faeces. In untreated patients the disease is often fatal (10 year survival rate of 29 %), and in treated patients the 10 year survival rate is 80 %. The anthelmintic treatment is long-term (for several years, possibly life-long) and expensive. Liver transplantation may be required.

Conclusions

Based on the fact that EM is endemic in many European countries, that the incidence in endemic countries is increasing, and that the areas of endemicity are expanding it seems likely that EM will be imported into Norway at some point, perhaps within the next 10 years.

Given the high numbers of pets crossing the border between Sweden and Norway and the paucity of checks regarding compliance with treatment legislation, this seems to be a likely route of entry of EM to Norway, should this occur. Introduction of checks may reduce this likelihood.

Under the current monitoring conditions, VKM find it less likely that EM will be detected upon the first introduction to Norway. EM will probably only be detected once the prevalence in foxes is greater than 1%. The red fox population size is estimated to be between 70 000 to 120 000 animals. This means between 700 to 1200 red foxes would need to be infected before EM infection is likely to be detected under the current monitoring program. If EM is identified early enough after introduction, then it might be possible to avoid the establishment of EM in Norway and/or to limit the region of endemicity. This is dependent on optimal detection techniques and sufficient monitoring.

VKM considers that it is unlikely that EM will be imported to Norway via contaminated produce (berries, fruits and mushrooms).

Norway's strong 'outdoor' culture, in which hunting, camping, berry-picking and other outdoor activities play a significant role, may place the Norwegian population at greater

¹ The lagomorphs are mammals, members of the taxonomic order Lagomorpha, of which there are two living families, the Leporidae (hares and rabbits), and the Ochotonidae (pikas).

likelihood of contracting EM than populations in other European countries. However, it should be noted that even in countries with endemic EM, human echinococcosis is, apparently, relatively rare.

Sammendrag

Med bakgrunn i funnet av bendelorm *Echinococcus multilocularis* (EM) i fire rødvrev fra tre forskjellige steder i Sverige, har VKM ved Faggruppe hygiene og smittestoffer tatt initiativ til å foreta en vurdering av sannsynligheten for at EM kan bli introdusert til fastlands Norge og sannsynligheten for at mennesker i så fall også kan bli smittet.

EM er en liten bendelmark som parasitterer i tarmen hos rovdyr (for eksempel rev, hunder) som fungerer som *hovedverter* for den voksne bendelmarken. Infeksjonen gir her få eller ingen symptomer. Bendelmarken produserer imidlertid egg som skilles ut med vertens avføring og som kan inntas av gnagere eller haredyr som på sin side fungerer som *mellomverter*. I mellomverter produserer bendelmarkens larvestadium cyster, hovedsakelig i leveren hvor de oppformerer seg og eventuelt kan invadere omkringliggende vev og gi opphav til svært alvorlige infeksjoner. Hvis den infiserte mellomverten blir spist av en mottakelig hovedvert, utvikler den voksne bendelormen seg i tarmen hos denne og livssyklus er fullført.

EM er av folkehelsebetydning fordi mennesker kan opptre som tilfeldige mellomverter hvis de infiseres med egg, enten via forurenset mat eller vann, eller via kontakt med infiserte hovedverter (hunder, rever) eller deres avføring. Uten behandling er sykdommen ofte dødelig (10 års overlevelse på 29%), mens hos pasienter som får behandling er 10 års overlevelse 80%. Behandlingen med antihelmintika er langvarig (flere år, i noen tilfeller livslang) og kostbar. Levertransplantasjon kan være nødvendig.

Konklusjoner

Basert på det faktum at EM er endemisk i mange europeiske land, at insidensen i endemiske land generelt er økende og at de endemiske områdene i tillegg blir stadig større, virker det sannsynlig at EM vil bli importert til Norge på et eller annet tidspunkt, kanskje i løpet av de neste 10 årene.

Gitt det høye antallet kjæledyr som krysser grensen mellom Sverige og Norge og at den lovpålagte profylaktiske parasittbehandlingen sjelden og bare sporadisk blir kontrollert, kan dette synes som en sannsynlig vei for en eventuell introduksjon av EM til Norge. Innføring av strengere kontroll ved landets grenser kan redusere denne sannsynligheten.

Under dagens overvåkingsforhold finner VKM det lite sannsynlig at EM vil bli oppdaget ved første introduksjon til Norge. Det er beregnet at EM trolig først vil bli oppdaget når prevalensen i revene er større enn 1%. Den norske bestanden av rødvrev er anslått å være mellom 70 000 - 120 000 dyr. Dette betyr at man antar at mellom 700-1200 rødvrev må være smittet før EM infeksjon kan bli oppdaget under det nåværende overvåkingsprogrammet. Dersom EM blir identifisert tidlig nok etter introduksjonen, kan det være mulig å hindre etablering og/eller begrense utbredelsen av endemiske områder i Norge. Dette er avhengig av optimale deteksjonsteknikker og tilstrekkelig overvåking.

VKM anser det som usannsynlig at EM vil bli importert til Norge via forurensede produkter (bær, frukt og sopp).

Norges sterke friluftskultur, hvor jakt, camping, bærplukking og andre utendørs aktiviteter spiller en viktig rolle, kan muligens bidra til en noe større sannsynlighet for human smitte med EM enn hva tilfelle er i andre europeiske land. Det skal imidlertid bemerkes at selv i land hvor EM er endemisk, er humane EM-infeksjoner forholdsvis sjeldne.

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Background

Echinococcus multilocularis (EM) is a small parasitic tapeworm that resides in the intestines of carnivores (e.g. foxes, dogs) that eat rodents and lagomorphs. Adult tapeworms produce eggs that are released in the faeces of the carnivores and may be ingested by rodents or lagomorphs that act as intermediate hosts. In the intermediate hosts the larval form of the tapeworm produces cysts, predominantly in the liver, but the cysts proliferate and may invade the surrounding tissues. If the infected intermediate host is eaten by a susceptible final host, the adult tapeworm develops in the intestine and the lifecycle is completed.

EM is of public health significance as humans may act as accidental intermediate hosts if they ingest eggs, either through contaminated foods or water, or from contact with infected final hosts (dogs, foxes) or their faeces. In untreated patients the disease is often fatal (10 year survival rate of 29 %), and in treated patients the 10 year survival rate is 80 %. The anthelmintic treatment is long-term (for several years, in some cases life-long) and expensive. Liver transplantation may be required.

EM is widely distributed over the northern hemisphere, including in Europe, with many areas considered endemic. However, in Norway, the only known occurrence has been in Svalbard, in which introduction of the intermediate host (sibling vole; *Microtus levis*) resulted in the lifecycle establishing between arctic foxes and this vole species. This was first identified in 1999, although it cannot be determined when the lifecycle originally established in Svalbard. As recently as 2010, mainland Fennoscandia (Finland, Sweden, and Norway) were considered free of this parasite. However, under the current monitoring conditions it might have established, but remained undetected.

However, EM was found in four red foxes shot in south-east Sweden (two in Uddevalla in February 2011, one in Katrineholm and one in Borlänge in June 2011). One of these locations (Uddevalla) is approximately 60 km from the Norwegian border.

In the light of these recent findings in Sweden, the Norwegian Scientific Committee for Food Safety (Vitenskapskomiteen; VKM), Panel of Biological Hazards (Faggruppe hygiene og smittestoffer) took the initiative to undertake a risk assessment regarding the probability of introduction and establishment of EM to mainland Norway and its significance to human health.

Terms of reference

The Panel has decided on the following terms of reference:

1. To assess the probability of introduction of EM to mainland Norway via movement of dogs (and cats) from:
 - a. Sweden (pets, that have/have not undergone the anthelmintic treatment prior to entry)
 - b. Other countries
 - c. Svalbard
2. To assess the probability of introduction of EM to mainland Norway via movement of infected wildlife:

- a. Intermediate hosts, predominantly rodents, from Sweden
 - b. Foxes and other wild canids from Sweden
 - c. Intermediate hosts, predominantly rodents, from Denmark or other European countries where EM is endemic
 - d. Foxes from Denmark or other European countries where EM is endemic
3. To assess the probability of detection under current monitoring conditions if EM is introduced into mainland Norway
4. To assess:
- a. The risk of EM becoming endemic in mainland Norway
 - b. The risk for human health
 - c. The effectiveness and efficiency of applicable disease control options

Hazard identification

EM, also known as the dwarf fox tapeworm (in Norwegian: “revensdvergbandelmark”), is a small tapeworm measuring between two to four millimetres in length (Figure 1). It is made up of three to five segments (proglottids), of which the terminal gravid proglottid measures half the length of the parasite and contains 200-300 eggs. The scolex has four suckers and is armed with a double row of hooks (Taylor *et al.*, 2007).

The life cycle of EM involves two mammalian hosts; a *definitive host*² harbouring the adult worm and an *intermediate host*³ harbouring a larval stage (metacestode) (Figure 2). The main definitive hosts for this parasite in Europe are canidae such as dogs, red foxes (*Vulpes vulpes*), wolves (*Canis lupus*) and raccoon dogs (*Nyctereutes procyonoides*). Felids may also be involved but they are regarded as less suitable hosts than canids (Kapel *et al.*, 2006a). Infection in the definitive host occurs in the small intestine, most commonly found in the proximal part, where the parasite develops into sexually mature tapeworms and produces eggs which are passed out into the environment with the faeces. The time taken from point of infection to the production of eggs (the prepatent period) can be as short as 26 days (Matsumoto & Yagi 2008). Experimental infections have shown that eggs can be produced for up to three months after infection in foxes and up to five months in dogs (Matsumoto & Yagi 2008). The parasitic burden in definitive hosts can vary considerably, from one to many thousands of worms. Intestinal EM infections are generally asymptomatic in the definitive hosts (Taylor *et al.*, 2007).

Faeces containing the eggs contaminate the environment and intermediate hosts are infected when they ingest these eggs. The eggs measure 30-40 µm in diameter and have a dark striated outer keratinised embryophore (Figure 3). This keratinised layer is extremely environmentally resistant (WHO/OIE 2001). Microtine rodents such as water voles (*Arvicola amphibious*) and the common vole (*Microtus arvalis*) are the most commonly infected intermediate hosts. All mammals, including humans, can potentially act as intermediate hosts. Dogs and cats can act as both definitive hosts, when infected by metacestodes, and as intermediate hosts, when infected by eggs. The parasite develops in a gelatinous matrix in the internal organs of the intermediate host as a proliferative mass, the hydatid cyst. Infection develops in the liver and may spread to other organs such as the lungs and central nervous system. The hydatid cyst can take up to 6 weeks to mature in the intermediate hosts and thereafter grows slowly. Matsumoto and Yagi (2008) found that such cysts did not lead to death in the rodent intermediate host in experimental infections. However, any reduced fitness due to the cyst may leave the intermediate host more vulnerable to predation.

Surveillance programmes to detect EM focus on the most common definitive hosts, such as the red fox and racoon dog, and this is the approach currently recommended by EFSA (2011). Screening of intermediate rodent hosts in endemic countries has also been attempted. This has been successful in muskrats (*Ondatra zibethicus*), as in some countries, such as Belgium, the prevalence of EM in muskrats is high (Mathy *et al.*, 2009). However, even in highly endemic areas, high numbers of voles (in the thousands or more) need to be screened to detect a few positive animals (Thomas Romig, personal communication).

² A definitive host or primary host is a host in which the parasite reaches maturity and, if applicable, reproduces sexually.

³ An intermediate host is a host that is essential in the lifecycle, and in which development must occur, but there is no sexual reproduction.

During the last decade, Sweden, Finland, and Norway have established national surveillance programmes for wild canids, and, in some cases, rodents, to monitor for the presence of this parasite. Surveillance in wild canids was implemented in Sweden and Finland as of 2000, whilst an official surveillance programme was not in place in Norway until 2006, although a biobank containing suitable fox faecal samples was made available for the period 2002-2005 (Table 1). Each country chose slightly different methods for their surveillance programmes (Wahlstrom *et al.*, 2011). Finland initially opted for copro-ELISA and confirmatory SCT⁴ before switching to copro-ELISA with confirmatory PCR in 2008. Sweden has based their surveillance program on copro-ELISA and confirmatory SCT, whilst Norway screened the biobank material with copro-ELISA and confirmatory PCR. Since 2006 Norway has based the surveillance program on egg-isolation and PCR. The conclusion of the screening programs was that until 2009 there was a high probability (0.98-0.99) that the three countries were free from EM. Norway, Sweden and Finland are currently working towards harmonizing the EM surveillance methods used in each country (Øivind Øines, Norwegian Veterinary Institute, personal communication).

Since the first EM infected red fox was detected in Sweden, monitoring was increased to include sampling of ten foxes per municipality in the affected county of Västra Götaland and Halland, and Skåne that was deemed as the counties where there was a higher probability of introduction of EM. Four foxes per municipality were sampled in the other counties. As of 13th June 2011, National Veterinary Institute (SVA, Sweden) had investigated a total of 2984 foxes during the 2010 -2011 red fox hunting season for EM (Jordbruksverket/Socialstyrelsen 2011).

Monitoring in Norway is based upon the annual investigation of between 400-500 red fox faecal samples using egg isolation and molecular identification methods (Davidson *et al.*, 2009). The program was cancelled during the 2009-2010 hunting season due to budgetary cuts at the Norwegian Food Safety Authority (Mattilsynet), but it was revived for the 2010-2011 hunting season. The sensitivity of the method is estimated to be just 50% and a current research project addressing the question of diagnostic test sensitivity (Øivind Øines, personal communication). A total of 2166 red fox samples have tested negative since monitoring began (Madslie *et al.*, 2011), of these 1838 red fox samples were analysed between 2006 and 2011. This gives a cumulative estimated prevalence of 0.0% for the last five years and a 95% confidence interval of 0-0.33%. Fox samples have been collected from throughout the country although the distribution, at the municipality level, is somewhat patchy (Madslie *et al.*, 2011).

Potential introduction of EM to UK as a consequence of adopting harmonised EU rules regarding the non-commercial movements of pet animals, including no requirement of treatment against EM for animals coming from an EU Member State or from a listed 3rd country, has been considered in a qualitative risk assessment (DEFRA 2011). In this risk assessment, which considers only introduction via pet animals (i.e., movement of wildlife is not included), it is concluded that there is a high risk of EM becoming established in UK (on moving to harmonised rules) within the next ten years or so, as based upon; i) the continuing increase in geographic distribution of EM in the northern hemisphere; ii) the volume of pet movements from endemic EU member states; iii) the increase in pet movements expected with harmonisation; iv) the immunological naïvety of the UK fox and vole population; v) the current lack of requirement for an approved surveillance programme in UK red foxes; vi)

⁴Sedimentation counting technique.

comparable situations in other islands, such as Japan. Some of these factors are also relevant for the Norwegian situation. Norway is probably more at risk for initial introduction than UK, as it is part of mainland Europe, and since EM has been detected in neighbouring Sweden.

Hazard characterisation

Human alveolar echinococcosis (AE), caused by EM, is a serious public health problem in some countries where it is regarded as an emerging or re-emerging disease.

Epidemiology – humans

Humans acquire the infection by ingesting viable parasite eggs. The environment is contaminated with parasite eggs from the faeces of definitive hosts that harbour the adult parasite in their intestine. Eggs are environmentally resistant and can remain viable for months or years. It is generally assumed that humans can become exposed to the eggs of EM by handling infected definitive hosts or by ingesting food or water contaminated with eggs. However, studies of the epidemiological significance of the various potential methods of transmission are few (Eckert & Deplazes 2004).

Conclusions about possible risk factors can be difficult to prove due to the long incubation period and the possible lack of data due to undetected confounding factors (Eckert & Deplazes 2004). Exposure of humans to eggs may be influenced by occupational and behavioural factors. Data from central Europe have indicated that persons working in agriculture are at increased risk of infection due to proximity to infected foxes, dogs or cats (Eckert 2001).

The high prevalence of EM in wild carnivores, compared with the low incidence of AE in the same areas, suggests that the risk of being infected for humans is limited. It has therefore been suggested that humans have a relatively high degree of innate resistance to the infection (Eckert & Deplazes 2004). However, prevalence trends of AE in humans appear to follow parasite abundance in wildlife (Kern *et al.*, 2004).

The gender ratio among infected persons is often close to 1:1. The most frequent age at diagnosis is usually between 35 and 65 years (Eckert & Deplazes 2004).

The great majority (> 90 %) of human AE seems to occur in China (Torgerson *et al.*, 2010). The core endemic areas of human AE in Europe are centred on Turkey, Switzerland, southern Germany and eastern France, but human infections in these regions are relatively rare. The incidence in endemic areas varies from 0.03 to 1.2 per 100.000 population. The incidence seems, however, to be increasing. In European endemic areas the annual incidence of AE per 100.000 population increased from 0.10-0.15 prior to year 2000 to 0.26 during 2001-2005 (Moro & Schantz 2009; Schweiger *et al.*, 2007). Human AE may therefore be considered as an emerging disease in Europe.

This means that wherever the parasite is endemic, human exposure to infectious eggs is possible, either by accidental hand-to-mouth ingestion or by consumption of food items contaminated with EM eggs.

Infectious dose

The infectious dose for EM in humans is not known. In experimental studies in rodents, typically 200-500 eggs of EM obtained from faeces of infected carnivores have been inoculated orally to ensure the establishment of the parasite in the recipients (Hildreth & Granholm 2003; Matsumoto *et al.*, 2010). Different species and strains of rodents have been

used in such experimental studies, and it is evident that their susceptibility to infection varies significantly, even between strains of mice (Hildreth & Granholm 2003).

Clinical significance – humans

Humans can act as an incidental or aberrant intermediate host when infected with viable parasite eggs. The eventual infection has the potential to cause one of the most lethal helminthic diseases in humans. However, the indications that humans have a relatively high degree of innate resistance to the infection suggest that the risk of being infected for humans may be limited (Eckert & Deplazes 2004).

Incubation period: AE is characterised by a long incubation time and is therefore difficult to detect in early stages. The incubation time, from ingestion of eggs to onset of clinical symptoms, can be months to years, and even decades (Kemp & Roberts 2001). This period depends on the location of the cysts and how fast they grow.

Symptoms: In humans, several main phases of the infection and several pathological entities can be distinguished. The initial phase is always asymptomatic and the patient may be cured spontaneously. In addition, depending on how and which organ is affected, the patient may remain asymptomatic although continuing to harbour the parasite.

Symptoms usually develop gradually, in association with the development of EM-cysts. The initial clinical symptoms can be vague, and the infection might not be discovered before the patient suffers from insufficiency of the liver or other affected organs.

Metacestodes of EM initially develop almost exclusively in the liver (approximately 99% of cases) (Eckert 1998), usually in the right lobe, with foci from a few millimetres up to 15-20 cm or more in diameter. These cysts have the ability to reproduce aggressively by asexual lateral budding. From the liver, metacestodes may spread to other organs, such as the lungs, spleen, heart and kidney, by infiltration or metastasis formation (Kern *et al.*, 2004). The gradual invasion of adjacent tissue is tumour-like and the initial symptoms are therefore often highly similar to those of a malignant tumour. This proliferative and invasive characteristic of the parasite invading surrounding tissues (Moro & Schantz 2009) is the basis for the severity of this zoonosis. Sections of the parasite may also later “metastasize” to other parts of the body, such as bones or brain. The advanced stage is characterized by severe hepatic dysfunction, often associated with portal hypertension. In earlier cohorts, fatalities exceeded 90 % within 10 years, but the introduction of treatment with benzimidazoles in 1976 has considerably improved the prognosis (Kemp & Roberts 2001).

Diagnosis: A combination of methods is needed to diagnose AE in a patient, such as imaging techniques, histopathology and/or nucleic acid detection, and serology.

Treatment: The condition is difficult to treat because of its proliferative and invasive characteristics. Radical resection is the primary goal, and, when possible, excision of the entire parasitic lesion should follow the rules of tumour surgery (Brunetti *et al.*, 2010). Long-term (and possibly life-long) anthelmintic drug (benzimidazoles) treatment is necessary in inoperable patients, as well as following surgical resection of parasitic lesions (Reuter *et al.*, 2003).

Epidemiology in animals

EM is widely distributed in the northern hemisphere and is found mainly in the central and northern areas of Europe, Asia (including northern parts of Japan) and North America, and in the Arctic regions.

In Europe, EM exists predominantly in a sylvatic cycle that includes red foxes as main definitive host and rodents of the family *Arvicolidae* (voles and lemmings) and *Cricetidae* (muskrats and related rodents) as intermediate hosts. In North America, the coyote (*Canis latrans*) is also a suitable definitive host for this parasite. In Arctic regions, the arctic fox (*Vulpes lagopus*) is the principal definitive host. Wolves or wild felidae may perhaps also serve as definitive hosts. The same may be true for domestic dogs and cats which in some areas, such as Alaska or China, play an additional or even a dominant role as an infection source for humans.

It has been suggested that there is now no longer a geographic gap in distribution between the European and Asian foci of EM. During the 1990s and 2000s a number of additional countries reported this parasite in both wildlife and in human populations. Prior to 1990 it was thought to have a distribution restricted to the mountainous regions of central southern Europe (Germany, France, Switzerland and Austria) (WHO/OIE 2001). However, by 2011 reports of this parasite occur westwards into central parts of France, Belgium and the Netherlands, northwards to Denmark, through the Baltic countries and, most recently, Sweden (Figure 4) and eastwards in Slovakia, Slovenia and towards the Balkans. In Norway, EM has never been identified – except from on Svalbard where it was identified in foxes and rodents in 1999 (and later also in 2002) (Fuglei *et al.*, 2008; Henttonen *et al.*, 2001). A degree of uncertainty exists as to whether some of these places represent new distribution areas or just improved surveillance in many of the countries, since baseline data prior to the first reports is often incomplete. It may be that the prevalence has been so low previously as to be below the threshold of detection. Indications in endemic areas are that the prevalence of the parasite has increased significantly in intermediate hosts from less than 1 % (in 1980-1989) up to a recorded 20 % within a decade (1995-2000) (Berke *et al.*, 2008) and in the definitive hosts as well (Romig 2002). Genetic characterisation of EM from the different regions (Knapp *et al.*, 2009) supports a core area (mainland) with high genetic diversity and newly colonised areas (islands) with more limited genetic diversity. These data lend support to the hypothesis of increased prevalence and distribution range.

Many countries do not have systematic surveillance programmes in place, making comparison between countries and estimation of prevalence challenging. The prevalence in the definitive host can vary considerably even within endemic regions, with hot-spots with high prevalence and the absence of the parasite from neighbouring areas (Tanner *et al.*, 2006).

The varying ecosystems, from urban, village and fragmented farming, to small forests and wide uninterrupted grasslands will all impact on the population densities of both intermediate and definitive hosts. These, in turn, will influence EM prevalence.

In urban areas, the distribution of intermediate hosts is often limited to the peripheries or to larger parks, which have the highest risk of EM transmission in conurbations (Deplazes *et al.*, 2004). EM prevalence reports in red foxes in the EU in 2007-2009 varied from 0 % in Italy, Austria, Belgium and the Nordic countries and from 4-29.1 % in the other lands that reported to EFSA (in ascending order of prevalence: Poland, Netherlands, Hungary, Luxembourg, France, Germany, Slovakia, Switzerland, The Czech Republic) (EFSA 2011). However, individual regions in Germany, France and Switzerland report higher local prevalence levels, sometimes up to 50 % in red foxes (Denzin *et al.*, 2009; Guislain *et al.*, 2008; Reperant *et al.*, 2007). In the general dog population, infection is uncommon. However, hunting dogs or dogs that live outside can have higher infection levels (Kern *et al.*, 2004).

Survival of EM eggs in the environment

Eggs of EM (the infectious stage of the parasite for intermediate hosts, including humans) are dispersed in the environment via the faeces of carnivores. Eggs may contaminate various types of food plants, including fruits and vegetables from gardens or fields and orchards, as well as drinking water. The eggs are extremely tolerant of environmental conditions, as the oncosphere membrane surrounds and protects the infective part of the egg from the environment. EM eggs are also extremely freeze-tolerant (Table 2). Freezing the eggs at minus 20°C does not affect their infectivity (Vuitton 2010). Freezing to minus 80°C for a minimum of 48 hours is necessary to inactivate the eggs making them safe for investigative purposes (Eckert & Thompson 1991; Frank 1989; Veit *et al.*, 1995). Normal household freezers do not reach this temperature and the eggs can survive and remain infective at standard domestic freezer temperatures (WHO/OIE 2001). Infective eggs have been recorded after 18 months' storage in water at 4°C (Veit *et al.*, 1995). However, the eggs are sensitive to desiccation and heat. Four days at room temperature (21°C) and a low relative humidity are sufficient to kill the eggs. Heating the eggs to 60°C-80°C for five minutes, or boiling them (heating to 100°C) is thought to kill *Echinococcus* eggs (WHO/OIE 2001). EM eggs may therefore remain infectious at temperatures ranging from -50°C to +60°C

The eggs of EM are also particularly resistant to chemical disinfectants. Ten commercially available disinfectants containing active ingredients such as aldehydes, phenol derivatives or ethanol phosphoric acid did not inactivate EM eggs at the dilution doses that were recommended (Veit *et al.*, 1995). Currently only sodium hypochlorite (NaOCl) at a minimum concentration of 3.75 % is recommended for use against EM. Many commercially available bleaches contain this chemical with levels of <5 %. However, the chlorine component evaporates quickly so many solutions, unless fresh, are not of sufficient strength to penetrate the egg and damage the oncosphere. NaOCl can be used to wipe down surfaces and instruments can be soaked in it for three to five minutes to inactivate any EM eggs. It should be noted that this chemical is very corrosive and environmentally hazardous (WHO/OIE 2001).

Control measures

Mandatory

Dogs/cats coming to Norway from countries other than Sweden, or directly from Finland, must be treated against EM with approved medication (e.g. praziquantel or epsiprantel) within the last 10 days prior to import, and this treatment must be repeated in the first 7 days after arrival in Norway. Harmonization of treatment within the EU is planned for introduction from 2012. It is unclear how compliance with these treatment regulations is ensured, particularly regarding for animals arriving by road, and with particular regard to the second treatment. Since the detection of EM in foxes in Sweden, further regulations have been introduced for cats and dogs entering from there. All dogs and cats entering Norway from Sweden must be treated against EM during the 48 hours prior to entry, and with regular treatment, at least every 28 days, for dogs and cats that are regularly crossing the border. It is unclear how adherence to these requirements is ensured, although occasional checks at the border control stations may be conducted (Mattilsynet, personal communication 2nd Sept 2011). However, anecdotal evidence indicates that most dogs and cats crossing the border from Sweden do not have their documentation checked. Additionally, a limited survey of dogs and cats entering Norway from Sweden at one border crossing point, demonstrated that of 97 animals checked, 13 did not have appropriate, legislated treatment against EM (Mattilsynet, 2011). Additionally, of a further 8 animals that were surveyed at campsites during the survey period, a further 3 had not received the legislated EM treatment. Thus, in total, 19 of 105 animals (18 %) were not appropriately treated against EM (Mattilsynet, 2011). Dogs and cats that are

imported via plane or ferry will almost certainly have their documentation checked at landing, and those animals which require prolonged quarantine will have repeat medication ensured. However, for other animals, there seems to be no clear system for ensuring that the post-arrival treatment is fulfilled, nor that the treatment requirements prior to import have been carried out. According to the Norwegian Food Safety Authority, “reliance is placed on the willingness and sense of justice of the pet owners” (Mattilsynet, personal communication 2nd Sept 2011).

Other possible measures

A number of trials using praziquantel-laced baits for wildlife have been tried in different endemic countries (Romig *et al.*, 2007; Tackmann *et al.*, 2001; Tsukada *et al.*, 2002). The most successful trial to date reduced EM prevalence in a red fox population in Germany from 35 % to 1 % (Konig *et al.*, 2008). Individual baits containing 50mg of praziquantel were placed out using airplane-drops and/or strategic placing of baits at a density of 20-50 baits/km². Baits were distributed at monthly intervals for 18 months. Continued treatment is required in order to maintain low prevalence levels (Hegglin & Deplazes 2008). The high cost of treatment may be prohibitive and eradication of this parasite from endemic areas is probably not feasible.

Other options for EM control can be aimed at education of the general public regarding risk behaviour. Avoidance of infection is not clear cut, since living in rural areas, farming and owning dogs that live outside all increase the risk (Kern *et al.*, 2004). Beyond taking normal hygiene precautions, the general public is not able to influence the risk factors to any great extent. Treatment of domestic dogs can be useful if those dogs exhibit risk behaviour, i.e. eating rodents, thus reducing the potential risk to owners. Blanket treatment of dogs in an endemic area would probably not disrupt the EM lifecycle to any great degree. A third option would be the reduction of the density of potential definitive and intermediate (animal) hosts. Hunting pressure is not thought to be a good way at controlling the spread of the parasite (Franck Boué, French Agency for Food, Environmental and Occupational Health and Safety, Malzéville, France, personal communication): firstly, the reproductive index in the remaining red foxes increases, and secondly, removal of foxes from one area opens niches for migrating animals from other areas. This means that despite increasing hunting pressure significantly, fox population numbers in a region would not be reduced and new cases of EM could spread into the region.

Exposure assessment

Introduction to Norway

EM has the potential to be introduced to mainland Norway either via the definitive hosts (dogs and wild canids, and cats) or intermediate hosts (e.g. rodents, particularly voles and lemmings). If EM is introduced via an intermediate host, then this must be ingested by a definitive host for the lifecycle to be completed and thus provide the potential for environmental contamination.

It is also theoretically possible that the infection may be introduced via contaminated produce (e.g. berries, particularly those harvested from the wild, fruits and mushrooms). Carrion birds, filth flies, and other arthropods have also been postulated as potential vectors or carriers of *Echinococcus* eggs (Public Health Agency Canada 2001).

In determining the risk of introduction of EM to Norway, the necessary information is the number of potentially infected hosts entering Norway. Thus, the relevant data are: numbers of potential definitive hosts entering Norway (dogs, cats, wild canids) and the likelihood of them

being infected, and the extent of potential intermediate hosts (particularly rodents) entering Norway, and the likelihood of them being infected. These are considered individually below. In both scenarios, for EM to establish in Norway, merely introduction is insufficient; the lifecycle must be completed. That is, should an infected intermediate host enter Norway, then it must be consumed by a susceptible definitive host, or if an infected definitive host should enter Norway, then the EM eggs excreted must be ingested by a susceptible intermediate host.

Introduction via dogs and cats

Transport of dogs and cats into Norway is one possible route of introduction of EM into Norway. In order to estimate the likelihood of introduction, it is important to have an estimate of the prevalence of EM in dogs and cats entering from endemic areas, and the numbers of animals that travel into Norway from endemic areas.

Despite the potential importance of pet dogs and cats as a means of transporting EM, there is surprisingly little surveillance data on EM in Europe. A survey from a German veterinary clinic, found 43 of 21588 canine faecal samples (0.2 %), from various European countries, positive for EM (by PCR) (Dyachenko *et al.*, 2008). All the positive samples were amongst the sub-sample from Germany (17,894 samples examined), with a significantly higher prevalence amongst dogs from southern Germany compared with northern Germany. Of 10,650 samples from cats that were examined, 25 were found to be positive for EM (0.23 %), with positive samples being detected in cats from Denmark (1 out of 169 examined), Germany (23 out of 9064 examined), and the Netherlands (1 out of 361 examined). An older survey from Switzerland demonstrated similar results for both dogs and cats (Deplazes *et al.*, 1999). Cats have been considered to be poorly susceptible to EM (Kapel *et al.*, 2006b), but it appears that susceptibility may range from refractory to highly susceptible (Jenkins & Romig 2000). Additionally, cats may be more likely to consume intermediate hosts, and therefore have greater exposure to potential infection.

Data obtained from the Norwegian Food Safety Authority by VKM in 2005 (Rabies risikovurdering) indicated that approximately 25000 pets, mostly dogs, came to Norway annually from countries other than Sweden. Increasing travel activity in the last 6 years may have increased this number, but no data are available (Mattilsynet, personal communication 2nd Sept 2011). These include Norwegian pets that are returning to Norway, as well as foreign pets coming into Norway, temporarily or permanently. A questionnaire-based survey from Sweden in 2010 suggested that about 18 % of dog owners travel with their pets, usually for vacation (Hirvonen 2010), and more than 50 % of these planned to visit countries where EM was endemic in wildlife. However, knowledge of EM was rather poor among dog owners prior to EM being reported in foxes in Sweden. Based on the responses to the questionnaire, only around 40 % of owners were estimated to comply with treatment recommendations. It could be expected that similar proportions probably apply in Norway, and a limited survey from Mattilsynet suggests that around 18 % of dogs and cats entering Norway from Sweden by road may not have been treated against EM (Mattilsynet, 2011).

In addition to legal transport of dogs and cats, some owners may import cats and dogs without following the regulations. Also, tourists on boats may allow their dogs onshore without considering the treatment regulations. No data are available on this (Mattilsynet, personal communication 2nd Sept 2011).

Introduction by wildlife

Movement of wild animals cannot be controlled by border regulations, and therefore available data are even more liable to uncertainty. Wild animals in neighbouring countries may cross the border into Norway themselves, or wild animals from further afield (not necessarily

neighbouring countries) may reach Norway in cargo or similar, freighted from more distant countries. Unintended transport of rodents is a reality of globalisation that cannot be ignored. Although the introduction of EM to Svalbard is considered to have occurred via an arctic fox, the introduction of the sibling vole (presumably with forage for Russian cattle from the St. Petersburg area sometime between 1920 and 1960; (Henttonen *et al.*, 2001)) is the reason that the lifecycle has been able to establish there.

As both definitive hosts and intermediate hosts have the potential to introduce EM to Norway, these are considered separately in the risk characterisation section.

Human exposure

Due to a very strong increase of the distribution and density of the red fox (*Vulpes vulpes*) in European countries, as a result of reduced mortality due to rabies vaccination campaigns and reduced hunting (Deplazes *et al.*, 2004; Vervaeke *et al.*, 2003), the distribution and prevalence of EM is increasing. The establishment of fox populations in cities during recent years and the development of urban cycles of the parasite have also increased the risk for human exposure to the parasite (Siko *et al.*, 2011). In a survey of public knowledge about EM in Europe, it was concluded that the growing fox population in Europe has led to increasing concern about human AE, and that more public information is needed on how people can minimize their infection risk and how public anxiety could be avoided (Hegglin *et al.*, 2008).

Occupational risks

In Bavaria, southern Germany, a study among 58 patients with AE identified farmers as the occupational group with highest risk of acquiring the disease, and the distribution of prevalence in man was closely correlated with the infection rates in foxes (Nothdurft *et al.*, 1995). Other studies have also found farmers to be at risk, due to handling contaminated soil or inhaling dust containing eggs (Romig *et al.*, 1999). It is also reasonable to believe that veterinarians working with dogs and cats in regions where EM is endemic may have an occupational risk of being exposed to the parasite. People such as biologists working in the field may also be infected through contact with contaminated substrates during their professional work.

Recreational exposure

Recreational exposure may occur via contact with wildlife, drinking water from open sources in the field, and through eggs in the fur of dogs (and cats). In a study in Austria, both owning a cat and hunting were identified as important risk factors for being exposed to EM, whereas eating berries that grow close to the ground was not (Kreidl *et al.*, 1998). Dogs tend to "scent roll" in foreign material, such as faeces from wild animals, and the fur may become contaminated and function as a vehicle from wildlife to man. Thus, people can become infected by petting and handling infected household dogs or cats. Regarding Svalbard, where the presence of the parasite is restricted to the area where the vole population exists, it has been argued that the risk of exposure of humans to the parasite could be reduced by restricting the recreational and touristic use of the regions where the parasite is endemic (Fuglei *et al.*, 2008). However, infected arctic foxes may be found away from the vole habitat, and it is the fox that is the source of human infection, not the vole (Stien *et al.*, 2010).

Other possible exposure routes

A third possible way of being exposed to the parasite is via fruits, other produce and other food items. One fatal case of AE in UK was considered to have been transmitted to the patient via contaminated cheese that was imported from Switzerland and was made of non-pasteurised milk (Cook 1991). Previous reports have claimed that eating mushrooms and wild

berries that grow near the ground are the main risk factors for human infection in endemic regions (Eckert & Ammann 1990; Kimmig & Muhling 1985). In a study conducted in Germany, chewing grass and eating unwashed strawberries were the only food consumption that could be associated to AE, probably through ingestion of eggs from contaminated plants or from soil-contaminated hands (Kern *et al.*, 2004). However, some publications indicate that this may not be an important risk factor for AE (Kreidl *et al.*, 1998). A study from Alaska also indicated no association between the disease and picking and eating raw products from the garden or berries or mushrooms from the field or forest (Stehr-Green *et al.*, 1988). These case-control studies all indicated that owning a dog is a much higher risk than eating berries and mushrooms, and it has been suggested that the risk of transmission of EM infection via ingestion of contaminated wild berries and mushrooms has been over-emphasised (Daniel Hegglin, University of Zurich, Zurich, Switzerland, personal communication).

Risk characterization

Definition of probability/risk levels

For the purposes of this document the following definitions are used, as based upon the Biosafety Resource Book published by FAO in 2011 (Sensi *et al.*, 2011).

Descriptors of likelihood:

- Highly likely - is expected to occur in most circumstances
- Likely - could occur in many circumstances
- Unlikely - could occur in some circumstances
- Highly unlikely (negligible or effectively zero) - may occur only in very rare circumstances

Descriptors of risk estimate:

- Negligible - risk is insubstantial and there is no present need to invoke actions for mitigation
- Low - risk is minimal, but may invoke actions for mitigation beyond normal practices
- Moderate - risk is of marked concern that will necessitate actions for mitigation that need to be demonstrated as effective
- High - risk is unacceptable unless actions for mitigation are highly feasible and effective

Introduction to mainland Norway

Via definitive wildlife hosts (canids/felids)

Although various species of wildlife (wolves, foxes, wolverines, raccoon dogs, etc.) have the potential to act as definitive hosts of EM, in terms of population size, red foxes are undoubtedly the most important, and therefore are the main focus of this section.

Norway is bordered by Sweden, Finland and Russia. The Russian-Norwegian border (Murmansk Oblast-Finnmark) is rather short (196 km), whilst the Finnish-Norwegian (Lappland-Finnmark) border is 736 km, and the Swedish-Norwegian border is rather long

(1619 km). As Finland is considered free from EM, and has been relatively extensively surveyed, it seems to be the least probable route of entry of EM to Norway.

Wild canids may range relatively long distances. For example, the home range size of red foxes in Norway varies, depending on food availability, from 2-10 km² (Odden *et al.*, 2004; Overskaug *et al.*, 1995). Although an adult fox rarely travels more than 10 km in a day, dispersing foxes may roam 100 km or more in search of new territory. Thus, it is perfectly possible for a fox to migrate from one side of the Swedish-Norwegian border to the other. Many foxes most probably also have a hunting territory that straddles the border. The population of red foxes in Norway is estimated to be approximately 70000 (winter population) – 120000 (summer population) based on hunter statistics, with between 18000-21000 foxes shot annually (Statistics Norway). The population of red foxes in Sweden is assumed to be higher, based on habitat availability. Red and arctic foxes also occur in Russia, but population sizes are uncertain. Available data on the prevalence of EM in wild canids are presented in the Hazard Identification section. In Hokkaido, Japan, where 5 to 20 new patients with AE were diagnosed annually towards the end of the 20th century (1989 onwards), EM is considered endemic, with 0.4 % prevalence in domestic dogs and 40 % prevalence in foxes (Nonaka *et al.*, 2009). EM is considered to have been originally introduced to Hokkaido via a single infected red fox from Russia in 1924 (Furth *et al.*, 2000). This indicates that infection may become endemic in a locality due to a single introduction event. However, for infection to establish, susceptible intermediate hosts and further definitive hosts need to be already present. Similarly, the introduction of EM to Svalbard is considered to be via migrating arctic foxes (Henttonen *et al.*, 2001), although whether this introduction was simultaneous with the anthropogenic introduction of the sibling vole to Svalbard, or beforehand (with the eggs surviving in the environment until the arrival of a susceptible intermediate host), or subsequent, is impossible to determine.

It is possible that infected wild canids/felids may reach Norway with freight transport such as lorries or boats. Such transport is occasionally reported in local press, but is probably much more relevant for small rodents.

Via intermediate hosts (particularly small rodents)

In Norway, the populations of small rodents that may act as intermediate hosts of EM are high, and this is also true of the neighbouring countries of Sweden, Finland, and Russia. Although some intermediate hosts (e.g. voles) tend to travel only very short distances, some, such as muskrats, may travel somewhat greater distances in association with breeding patterns. Others, such as lemmings, may have short seasonal movements, interspersed with long-distance movements (migrations) occurring with a periodicity of several years, the reasons for which have not properly been established. Thus, although some potential intermediate hosts may not travel far across a national boundary, others may journey quite some distance. It should be noted that Norwegian lemmings (*Lemmus lemmus*) are particularly interesting in this context, as this species is considered to escape helminth parasitism (of any species of helminth) almost completely, perhaps because of their specialized food consumption (Laakkonen *et al.*, 2001). However, EM has been found in other species of lemming elsewhere in the world (e.g. the brown lemming, USA) (Holt *et al.*, 2005), and it may be considered that Norwegian lemmings has evaded infection with EM in Fennoscandia previously, merely due to lack of exposure. The fact that lemmings have been reported in very high numbers during 2011, suggests that this potential intermediate host should be considered seriously as a potential importer of EM to Norway. However, data regarding prevalence of EM in intermediate hosts in the countries bordering Norway is either negative (Sweden and Finland; Table 1) or lacking (Russia), and therefore the potential for

import with of EM via such animals should currently be considered as unlikely or unknown, respectively. Although humans can be infected it is highly unlikely that they would be consumed by a potential definitive host, and therefore infected humans present a negligible risk for the infection establishing in Norway.

Via contaminated produce

Exposure of humans to contaminated produce is discussed under exposure assessment. Whilst Norway remains free of EM, infection of humans via contaminated produce could only occur via import of such produce. Such an event is considered to be unlikely, and would not result in the establishment of the lifecycle in Norway (unless the contaminated imported produce was consumed by other intermediate hosts, which were subsequently consumed by definitive hosts).

Potential intermediate hosts other than humans may also be exposed to infection via import of other goods. For example, hay is often imported to northern areas of Norway as animal fodder, especially for horses, and thus import of contaminated hay is another potential route for bringing EM eggs in contact with local rodents. Research regarding the survival times of EM eggs in hay bales is lacking, but the eggs are known to be robust. Another possibility of contamination is the presence of rodents as stowaways in imported hay bales, which has been suggested as the way rodents were imported to Svalbard (Henttonen *et al.*, 2001).

Answer to the questions

1. What is the probability of introduction of EM to mainland Norway via movement of dogs (and cats)

Due to the paucity of quantitative data, only qualitative opinions are possible.

- a. From Sweden (pets, that have/have not undergone the anthelmintic treatment prior to entry)

Due to the apparently low prevalence of EM in foxes in Sweden (no further positive findings Sweden since June 2011) and that EM has not, to date, been identified in dogs/pets in Sweden, introduction of EM to Norway directly from Sweden currently appears unlikely. However, given the high numbers of pets crossing the border between Sweden and Norway and the paucity of checks regarding compliance with treatment legislation, this seems to be a likely route of entry of EM to Norway. Should EM become endemic in Sweden, with increased prevalence in final and intermediate hosts, then the likelihood of introduction to Norway will increase.

- b. Other countries

As pets reaching mainland Norway by plane will be subject to control, this seems an unlikely route of entry of EM to Norway. However, the likelihood is increased if the pets travel by boat or road, as described in 1 a. above.

- c. Svalbard

Since EM is not reported as endemic in the dog population at Svalbard and since the rodent population seldom expand to the settlements in Longyearbyen, the chance of pets in Longyearbyen being exposed to EM is low. Further, as pets reaching mainland Norway from Svalbard must, by necessity, travel by boat or plane, this seems an unlikely route of entry of EM to Norway, provided that regulations are followed and controlled.

2. What is the probability of introduction of EM to mainland Norway via movement of wildlife?

- a. Intermediate hosts, predominantly rodents, from Sweden
- b. Infected foxes and other wild canids from Sweden
- c. Intermediate hosts, predominantly rodents, from Denmark or other European countries where EM is established
- d. Infected foxes from Denmark or other European countries where EM is established

Except for a few individuals tagged with radio-collars (wolves, lynx and brown bears), representing shared populations between Norway and Sweden, there are no data available on movements of wildlife in general. It is thus impossible to estimate the probability of introducing EM to Norway via infected rodents and foxes and other wild canids from Sweden or other European countries where EM is endemic.

Between February 2011 and June 2011, 2984 foxes have been investigated for EM in Sweden and only four have been positive. Thus it seems unlikely, but not impossible, that an infected fox from Sweden will migrate to Norway under the current conditions.

3. What is the probability of detection under current monitoring conditions if EM is introduced into mainland Norway?

Unless regular and extensive monitoring for EM is established and maintained, then it is unlikely that the entry of EM to Norway will be detected until the disease has become sufficiently established that it can be considered endemic. Currently the monitoring program is reviewed on an annual basis and is vulnerable to changes in budgeting priorities. The program was cancelled during the 2009-2010 hunting season due to budgetary cuts at the Food Health Safety Authority (Mattilsynet). It was revived in the 2010-2011 hunting season.

4. Assessment of:

a. The risk of EM becoming endemic

Given the high occurrence and wide geographic distribution of suitable definitive and intermediate hosts throughout Norway, along with limitations within monitoring, it is likely that if EM is introduced to Norway then it will become endemic in Norway. However, it is unclear whether EM has become established (endemic) in Sweden, despite the detection of 4 infected foxes.

b. The risk for human health

Even in countries with endemic EM, human disease is, apparently, relatively rare. Norway has a strong 'outdoor' culture, in which hunting, camping, berry-picking and other outdoor activities play a significant role. This may place the Norwegian population at greater risk than populations in other European countries. However, in contrast with older studies that have suggested that consumption of wild berries is a major risk factor in endemic regions, more recent studies have listed owning a dog and also other risk factors as far more relevant. Nevertheless, this may be a population-specific finding. Owning a dog may thus remain as the most important risk factor.

c. The effectiveness and efficiency of applicable disease control options

Current disease control is based on non-enforced regulations regarding dogs travelling into Norway from endemic countries. In order to assess the effectiveness and efficiency of this control, a monitoring regime, based on statistically-determined number and distribution of samples, should be established. Additionally, investigation of whether dog owners follow these regulations would be pertinent. It should be noted that lack of clear information at border-crossings (with the exception of airports) means that many people travelling with pets are probably unaware of the requirement to declare their pet upon crossing into the country. Veterinary and public knowledge regarding the import regulations varies. In some countries the travel advice given for Norway, is incomplete and sometimes even incorrect. The border authorities have no register for dogs and cats entering the country so there is no way to enforce the second treatment requirement post-entry.

Positioning of signs at border-crossings with instructions for those travelling with dogs and cats to report to customs to have their paperwork checked would increase the likelihood of

appropriate treatment of pets. This would, in turn, reduce the likelihood of people entering Norway with infected animals.

Wildlife cannot be controlled, but regular monitoring of definitive hosts, with focus on the red fox along the border to Sweden, and taking prompt action (such as treatment baits) if positive animals are identified, may reduce the speed of establishment or spread.

Data gaps

In the course of writing this assessment several data gaps have become apparent. These include:

- An absence of information on the movement of dogs and cats in and out of Norway by road or by boat. This implies that it is difficult to estimate the risk such animal movements represent in terms of introducing EM to Norway.
- An absence of information on the proportion of dogs entering Norway that are treated according to the regulations. This means that it is impossible to assess whether the current regulations and control measures work as intended. However, the limited data that are available suggests that around 20 % of pets entering Norway by road may not be treated against EM.
- An absence of information on movement of wildlife (both definitive and intermediate hosts) across Norwegian borders. Norway and Sweden have shared populations of many definitive and intermediate wildlife host species, but information on border crossing exists only from a restricted number of radio-collared wolves, lynx and brown bears, which may not represent species that are most likely to import the parasite into Norway. For most wildlife species, it will be difficult to obtain such information, but in certain regions and with focus on the red fox, it should be possible to obtain range and migration data that could be useful for establishing epidemiological models in which movements of the red fox is included as a variable.
- An absence of information on the import of berries and other potentially contaminated produce from endemic areas.
- An absence of data on the extent of contamination of berries and other fresh produce in areas of known endemicity.

Conclusion

Although it seems unlikely that EM will be imported into Norway under the current conditions, it seems likely that this will happen at some future point. This conclusion is based on the fact that EM is endemic in many European countries, that the incidence in endemic countries is increasing, that the areas of endemicity are expanding, and that the Norwegian fox and vole population are immunologically naive. In addition, EM has now been found in Sweden.

A UK risk assessment concludes that the risk of EM being imported to UK within the next 10 years is high, should all the harmonised rules regarding pet movements be implemented, and which include a lack of requirement for treatment against EM for animals coming from an EU member state or listed 3rd country (Defra, 2010). It should be noted that UK continues to require treatment against EM for dogs (apart from those coming directly from Finland, Ireland, or Malta) even after harmonisation (see: <http://www.defra.gov.uk/wildlife-pets/pets/travel/pets/pet-owners/parasites/>); due to the geography of UK, treatment compliance can be relatively easily checked at pet entry.

Although we do not have exact numbers, we know that many dogs and cats are imported to Norway on a regular basis. It is also evident that the mandatory drug treatment regime upon import of dogs and cats is poorly controlled, leaving uncertainty whether these control measures have significant prophylactic effect on introducing EM to the country. Therefore, this seems to be a likely route of entry of EM to Norway, should this occur.

Implementation of routines that ensure that travellers with dogs and cats are aware of the pet treatment requirements, and also that they follow them, may be one method to reduce the likelihood of import of EM to Norway.

Further, the situation in Sweden and its long border with Norway, provides the opportunity for red foxes (and other definitive, as well as intermediate, hosts), to cross the border, with the potential to import EM to Norwegian ecosystems. Migration of wildlife from Russia should also be considered as a possible route of introduction of EM to Norway.

Import of EM to Norway via produce (berries, fruits and mushrooms) seems to be unlikely.

Under the current monitoring conditions, VKM considers it unlikely that EM will be detected upon the first introduction to Norway. EM will only be detected once the prevalence in foxes exceeds a minimum of 1.0 % (that is, between 700 and 1200 foxes would be infected).

If EM should be introduced into Norway, it may be possible to avoid the establishment of the parasite or to limit the extent of its endemicity if it is identified early enough. This is dependent on sufficient monitoring with optimal detection techniques, and possibly resources to conduct local anthelmintic treatment of wildlife over a period of time.

Norway, Sweden and Finland are currently working towards harmonizing the EM surveillance methods used in each country. An on-going research project is evaluating and optimizing the laboratory detection methods used in Norway and Sweden and once an optimal method is determined, the plan is to implement it in all three countries.

Monitoring with focus on imported dogs and cats would reveal whether the current regulations are effective. Further, it is important to establish a systematic monitoring of the red fox, through collection of samples in cooperation with hunters.

Even in regions where EM is endemic in wildlife, cases of human AE do not occur often. Based on recent systematic surveys from other countries the most important risk factor for human health seems to be associated to owning a dog. It is possible that Norway's strong 'outdoor' culture, in which hunting, camping, berry-picking and other outdoor activities play a significant role, may place the Norwegian population at greater risk of contracting EM than populations in other European countries.

The likelihood of being infected with EM via consumption of wild berries, fruits and mushrooms, including imported produce from endemic regions, may be lower than previously considered.

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Tables, figures and pictures

Table 1. The number of red foxes, racoon dogs and rodents screened in Finland, mainland Norway and Sweden as part of the *Echinococcus multilocularis* surveillance programs in 2000-2009 and all found to be negative for *E. multilocularis* (Wahlström et al 2011).

| Country | Red foxes | Racoon dogs | Rodents |
|-----------------|-----------|-------------|---------|
| Finland | 1999 | 1306 | 19700 |
| Mainland Norway | 1619 | 1 | 1 |
| Sweden | 2962 | 49 | 3000 |

Table 2. Survival and inactivation of *Echinococcus multilocularis* eggs at different temperature regimes and timeframes (adapted from WHO/OIE 2001).

| Temperature | Timeframe | Infective(+)/Inactivated (-) | Reference |
|----------------|-----------|------------------------------|--|
| -18°C | 240 days | + | Veit <i>et al.</i> 1995 |
| -27°C | 54 days | + | Schiller 1955 |
| -30°C | 24 hours | + | Colli and Williams 1972 |
| -50°C | 24 hours | + | Colli and Williams 1972 |
| -70°C | 96 hours | - | Blunt et al. 1991 |
| -80°C to -83°C | 48 hours | - | Frank 1989; Eckert <i>et al.</i> 1991; Veit <i>et al.</i> 1995 |

Figure 1. Photograph of an adult *Echinococcus multilocularis* (Øivind Øines, Norwegian Veterinary Institute).

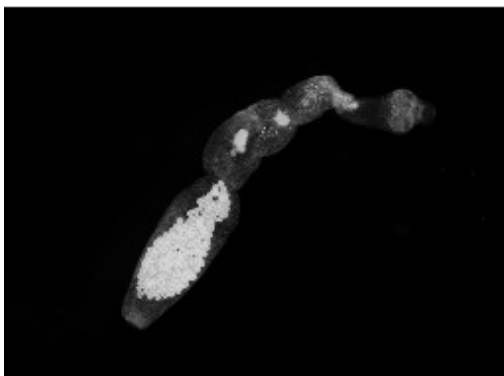


Figure 2. *Echinococcus multilocularis* lifecycle (Inger Hamnes, Norwegian Veterinary Institute).

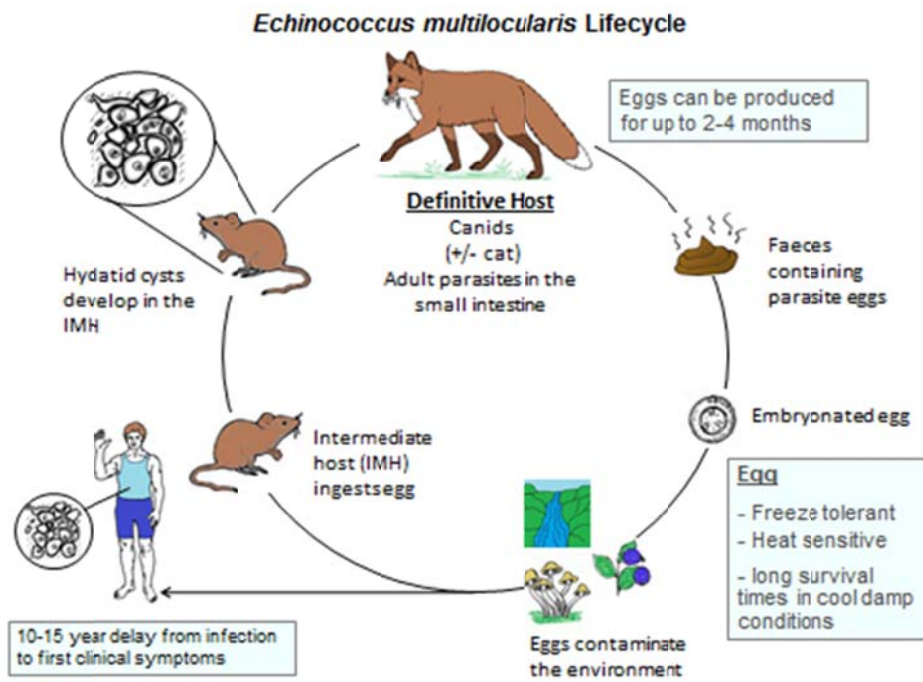


Figure 3. Photograph of an *Echinococcus* sp. egg (Øivind Øines, Norwegian Veterinary Institute)

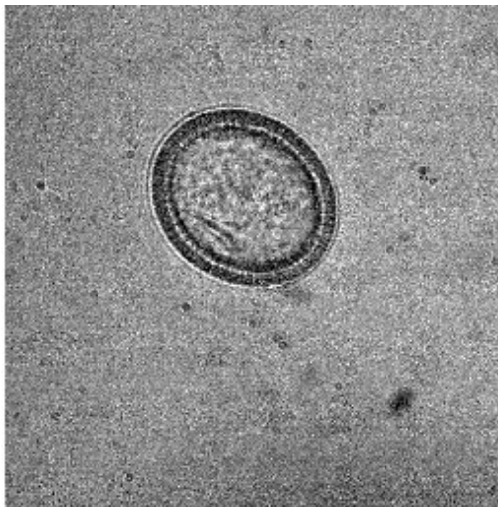


Figure 4. Map of Sweden showing three areas from which *Echinococcus multilocularis* was identified in four red foxes (*Vulpes vulpes*) in 2011 (Chiek Er, Norwegian Veterinary Institute). Uddevalla in Sweden is approximately 60 km from the Norwegian border



Annex 1

Diagnostics in definitive hosts

Diagnosis in definitive hosts is achieved by the demonstration of the adult parasite in the digestive tract, either at post-mortem or through purging, or via the species determination of taeniid eggs in the faeces. The gold standard for the identification of the parasite is the sedimentation counting technique (SCT) although other methods such as sequential SCT (SSCT) and intestinal scraping technique (IST) are also suitable for the detection of this small parasite in the gastrointestinal tract. SCT involves dividing the small intestine into five sections and allowing them to soak in physiological saline prior to longitudinal bisection and stripping the mucosal membrane between thumb and forefinger. The sediment is then examined using a stereomicroscope for adult tapeworms. SSCT has been proposed as more suitable for screening large numbers of animals given that only a proportion of the intestinal sediment fluid is examined (up to two of five segments) (Umhang *et al.*, 2011). The examination of segment 4 together with either segment two or three gave a 98% sensitivity compared to standard SCT examination of all five segments. ICT requires multiple scrapes to be made of the mucosal surface and these examined microscopically. All three methods remain relatively time consuming and therefore their use in surveillance programmes would be prohibitively expensive. Purging of live animals is carried out by administration of the drug arecoline hydrobromide and examining the faeces for the adult tapeworm (OIE 2008). Another alternative is the use of copro-ELISA, an immunological assay to detect the presence of EM antigen in the faeces. Commercial tests were initially available but proved unreliable and currently this examination is only available as an in-house test at the University of Zürich. The idea behind copro-ELISA is that it allows a large number of animals to be screened rapidly for EM antigen in their faeces and then only those that are antigen positive require further confirmatory testing such as SCT or species identification of taeniid eggs in the faeces (PCR). Current copro-ELISA tests are not considered sufficiently sensitive and specific to replace SCT as the gold standard (Edoardo Pozio, personal communication).

An alternative method is to examine the faeces directly for taeniid eggs rather than carrying out copro-ELISA first. A number of various flotation methods are capable of isolating taeniid eggs from the faecal sample. A modified version was described by Davidson *et al.* (2009), in which faecal samples were pooled from three animals prior to egg-isolation and molecular methods. A two-step sieving stage removed the largest particles at the first sieve and trapped the eggs at the second. The material captured by the second sieve could then be collected and any eggs identified to species level using molecular methods. Alternatively traditional McMaster's techniques can be used to screen samples to see if taeniid eggs are present – this method can have sensitivity as low as 10 EPG (eggs per gram). A number of molecular methods have been published regarding the species identification of EM eggs. A multiplex-PCR capable of distinguishing between EM, *E. granulosus* and *Taenia* spp. (Mathis *et al.*, 1996; Stefanic *et al.*, 2004) is currently used at the Norwegian Veterinary Institute (Davidson *et al.* 2009). Real-time PCR methods capable of identifying EM have also been developed, and one such method is currently used at the Swedish Veterinary Institute (SVA) (Osterman *et al.*, 2011).

Diagnosis in the intermediate rodents host is dependent upon the identification of lesions at necropsy and then the morphological and/or molecular identification of EM hydatid cysts. Some aberrant intermediate hosts do not have the classic alveolar hydatidosis that is associated with EM. In pigs and wild boar liver lesions may just appear as white spots making it challenging to detect reliably at meat inspection unless experienced. In Japan, meat inspection is considered to be of use in detecting EM in swine (Ito *et al.*, 2003).