19

EUCESTODA

Echinoccocus (Genus)

Akira Ito and Scott. L. Gardner

Phylum Platyhelminthes
  Class Cestoda
    Subclass Eucestoda
      Order Cyclophyllidea
        Family Taeniidae
          Genus *Echinococcus*

doi:10.32873/unl.dc.ciap019
2024. *In* S. L. Gardner and S. A. Gardner, eds. Concepts in Animal Parasitology. Zea Books, Lincoln, Nebraska, United States.

Chapter 19

Echinococcus (Genus)

Akira Ito
Department of Parasitology, Asahikawa Medical University, Asahikawa, Hokkaido, Japan

Scott L. Gardner
Harold W. Manter Laboratory of Parasitology, University of Nebraska State Museum, Lincoln, Nebraska, United States; and School of Biological Sciences, University of Nebraska–Lincoln, Lincoln, Nebraska, United States
slg@unl.edu

Introduction

Species of *Echinococcus* have captured human interest from antiquity. The hydatid, which is the metacestode stage of *E. granulosus*, has been known since the time of Hippocrates (~ 460–377 BCE) (Eckert and Thompson, 2017) and Pallas (1776) first recognized the metacestode cyst as the living larval stage of taeniids (and this was confirmed by Goeze in 1782).

In this section, the taxonomy as well as the life cycles and pathogenicity of *Echinococcus* spp. are the focus since this dynamic parasite infects livestock and wild animals, as well as humans at times.

Beyond this basic introduction, 2 issues of Advances in Parasitology (Thompson et al., 2017a; 2017b) focusing on *Echinococcus* and echinococcosis are among the best resources to consult for understanding the species and their pathogenicty.

Morphology

Adult species of tapeworms in the genus *Echinococcus* are characterized by some clear synapomorphies, including: 1) Small bodies consisting of only a **scolex** and 3 (or at the most 4) **proglottids**; 2) characteristically shaped **hooks** on the **rostellum** (Figures 1 and 2); 3) mature proglottids with many **testes** arranged medially, generally not crossing the lateral **excretory ducts**; and 4) testes extending anteriad of the **cirrus sac** almost to the edge of the segment and posteriad, distal to the **vitelline gland** (Rausch, 1993; Rausch and Bernstein, 1972; Gardner et al., 1988; 2013).

The whole animal reaches a maximum length of less than about 7 mm, and usually shorter, depending on the species.

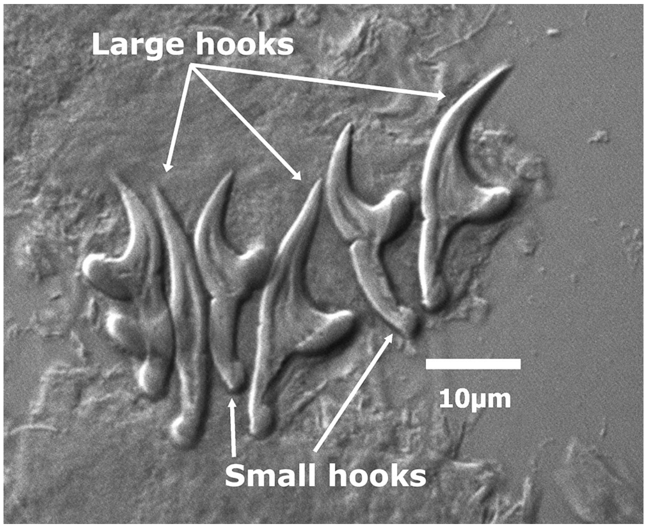

Figure 1. Hooks of *Echinococcus multilocularis* collected from the area near Har Us Lake, Hovd, Mongolia. Specimen number NK223782. Taeniids typically have 2 rows of hooks on the rostellum with 1 row consisting of smaller hooks and another row with larger hooks. Source: S. L. Gardner, HWML. License: CC BY.

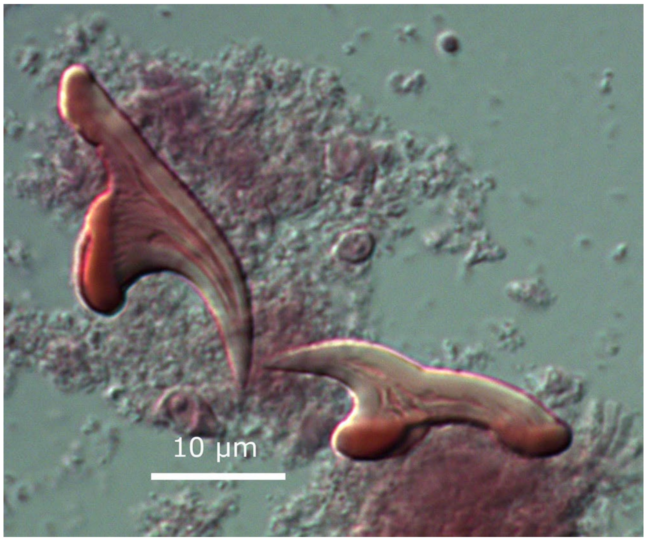

Figure 2. Two hooks (large and small) from a protoscolex of *Echinococcus multilocularis* from near Taos, New Mexico, United States from a deer mouse *Peromyscus maniculatus*. The specimen was cleared in lactophenol on a microscope slide under a number 1 coverslip. Using a small amount of pressure with a pencil eraser on the coverslip, the protoscolex was squashed gently enabling the hooks to be separated from the protoscolex for viewing and imaging. Images were made with Normarsky optics using a Zeiss Axiophot TM microscope. Source: A. T. Dursahinhan and S. L. Gardner, HWML. License: CC BY.

As with most cyclophyllidean cestodes, the anterior end (as noted) includes a scolex with 4 muscular **suckers**, lacking hooks or spines on the suckers, and a rostellum on the apical

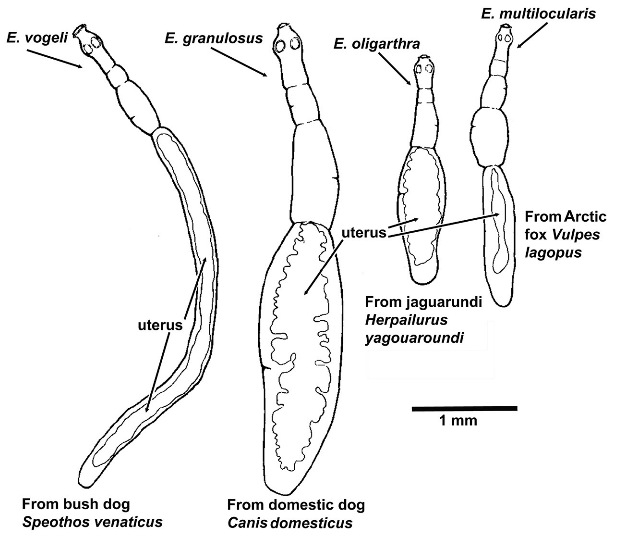

Figure 3. Comparisons among *Echinococcus vogeli*, *E. granulosus*, *E. oligarthra*, and *E. multilocularis*. Note the longer, thinner gravid proglottid in *E. vogeli* compared to the other species in the figure. The eggs are not shown in the uteri in this figure. Source: S. L. Gardner, HWML. License: CC BY.

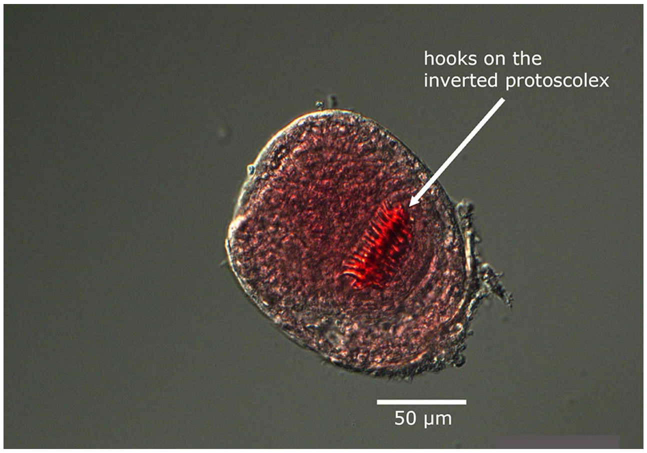

Figure 4. Protoscolex from the cyst of *Echinococcus multilocularis* obtained from a deer mouse *Peromyscus maniculatus* collected from near Taos, New Mexico, United States. The specimen was stained using Semichon's acetic carmine (which is the usual method). Source: A. T. Dursahinhan and S. L. Gardner, HWML. License: CC BY.

Figure 5. Adult *Echinococcus granulosus* from the intestine of a dog. Eggs can be seen in the last gravid segment. Source: S. L. Gardner, HWML. License: CC BY.

Figure 6. Posterior gravid segment of *Echinococcus multilocularis* from an experimental infection in a dog in Alaska, United States. Source: R. L. Rausch. License: CC BY.

end of the **scolex** that is supplied with 2 rows of hooks that alternate surrounding the rostellum and are of characteristic shapes and sizes, depending on the species (see Figure 3) (Rausch, 1993; Rausch and Bernstein, 1972; Gardner et al., 1988; 2013).

Each adult cestode in its carnivore host is derived from a single **protoscolex** (Figure 4) that is produced by asexual budding in a hydatid cyst of its intermediate host. Each fully developed protoscolex can transform into an adult tapeworm in the small intestine of the carnivore that consumes it while feeding on the infected intermediate host. The adult

Table 1. *Echinococcus* taxonomy.

Species	Genotypes and strains, genotype denoted as G1–G10
Echinococcus granulosus Batsch 1796	G1, G2, G3, sheep/buffalo strains
E. equinus Williams and Sweatman 1963	G4, horse strain
E. ortleppi Lopez-Neyra and Soler Planas, 1943	G5, cattle strain
E. canadensis Webster and Cameron, 1961	G6, G7, camel and pig strains; G8, American cervid strain; G10, Nordic cervid strain
E. felidis Ortlepp, 1937	Lion species, warthog intermediate hosts
E. multilocularis Leuckart, 1863	Canid final hosts, rodent intermediate hosts
E. shiquicus Xiao et al., 2005	Canid final hosts, lagomorph intermediate hosts
E. oligarthra Diesing, 1863	Felid final hosts, hystricognath/echimyid intermediate hosts
E. vogeli Rausch and Bernstein, 1972	Canid final hosts, hystricognath intermediate hosts

tapeworms then live in the intestine of carnivores and embed the anterior end (scolex) deep in the base of the **villi** (also called the **crypt of Lieberkühn**) in the mucosal layer of the host's duodenum. When observed after cutting the host's intestine open longitudinally, severe infections (numbering in the hundreds of thousands of cestodes) make the intestine appear to be covered with felt. Each worm can produce a few hundred **eggs** per day and, along with the thousands of other adults in an infected dog, together can produce hundreds of thousands of eggs each day (see Figures 5 and 6) (Rausch, 1993; Rausch and Bernstein, 1972; Gardner et al., 1988; 2013).

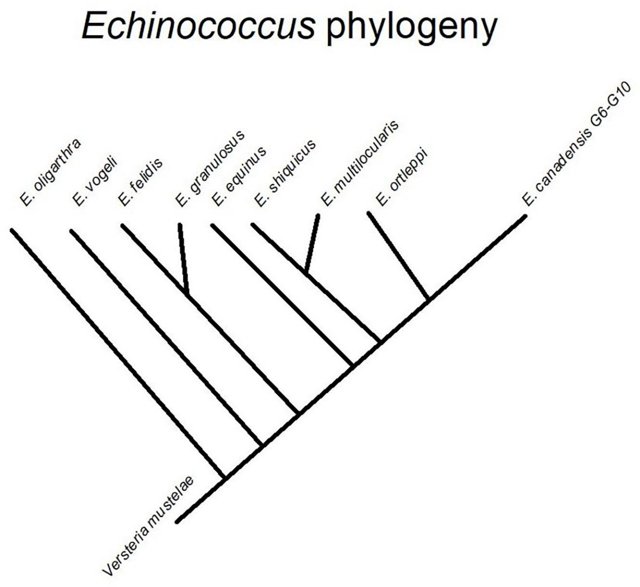

Figure 7. *Echinococcus* phylogeny. Estimated evolutionary relationships among all known species of *Echinococcus*. *Echinococcus canadensis* genotypes G6–G10 are shown as a single branch/species in this tree. The tree was based on a maximum likelihood analysis of mitochondrial genomes and nuclear protein-coding genes. Source: Adapted from Nakao et al., 2013b. License: CC BY-NC-SA 4.0.

Taxonomy: From Morphological to Molecular

Echinococcus is one of the major groups in the family Taeniidae (Knapp et al., 2011; Nakao et al., 2010a; 2013a; 2013b; Romig et al., 2015; Thompson and McManus, 2002) (see Figure 7). In the past, 4 morphospecies had generally been accepted as valid taxa, namely, *E. granulosus*, *E. multilocularis*, *E. vogeli*, and *E. oligarthrus* (see Rausch and Bernstein, 1972). *Echinococcus granulosus* is the most common species and it is distributed worldwide. Early systematists, such as Robert L. Rausch (1921–2012) and others, did not have reliable tools for differentiation of *E. granulosus* so they proposed several intraspecies variations or strains rather than name distinct species (Rausch, 1967; 1995; 2003; Moro and Schantz, 2009); these are referred to as G1–G10 (although the G9 genotype is unresolved; see Table 1) (McManus, 2013; Thompson and McManus, 2002; Rostami et al., 2015). Studies using molecular approaches have revealed that the broad umbrella of *E. granulosus* is properly differentiated into at least 5 independent species, namely: *E. granulosus* sensu stricto (s. s.; dog and sheep species, G1, G2, G3), *E. equinus* (horse species, G4), *E. ortleppi* (cattle species, G5), *E. canadensis* (G6, G7, G8, G10), and *E. felidis* (see Hüttner et al., 2008; Nakao et al., 2007; 2010b; 2013b).

Subsequent to and including the pioneering work on *Echinoccocus granulosus* using mitochondrial DNA analyses by Bowles and colleagues (1992; 1995), there have been many molecular studies published on *Echinococcus* (see Bretagne et al., 1996). Among them, Nakao and colleagues (2007) reconstructed the phylogenetic relationships of *E. oligarthra* (= *E. oligarthrus*, see the change recommended by Nakao et al., 2013b), *E. vogeli*, *E. multilocularis*, *E. shiquicus*, *E. equinus*, *E. ortleppi*, *E. granulosus* sensu stricto (G1), and 3 genotypes of *E. granulosus* sensu lato (s. l.; G6, G7, G8) inferred from complete mitochondrial genomes. Nakao and colleagues (2007) suggested that:

1) The 3 *E. granulosus* genotypes corresponding to the camel, pig, and cervid strains are monophyletic and their high level of genetic similarity supports taxonomic species unification of these genotypes into *E. canadensis*;

2) Sister species relationships are confirmed between *E. ortleppi* and *E. canadensis*, and between *E. multilocularis* and *E. shiquicus*;

3) The basal positions on the phylogenetic tree are occupied by the Neotropical endemic species *E. oligarthra* and *E. vogeli* whose definitive hosts are derived from carnivores that migrated from North America around the time of the formation of the Panamanian land bridge;

4) Host-parasite biogeographic comparisons suggest that the ancestors of *E. oligarthra* and *E. vogeli* originated in South America and at the same time there was a speciation event that gave rise to all other species of *Echinococcus*. An alternate explanation is that the ancestors of *Echinococcus* originated in North America or Asia depending on whether the ancestral definitive hosts were canids or felids (Nakao, 2013b).

Echinococcus shiquicus is a species from the Tibetan plateau, China (Xiao et al., 2005; 2006) that was discovered in part thanks to conversations that took place during a small international meeting on echinococcosis and cysticercosis organized by Akira Ito held in Chengdu, China in July 2000 (Ito et al., 2003a; 2003b). One of the coauthors of a study presented there, J. M. Qiu, the head of Echinococcosis Research at the Sichuan Center for Disease Control and Prevention at that time, mentioned a unique species of *Echinococcus* during his conference session. Qiu thought *E. shiquicus* might just be an aberrant form of *E. multilocularis* since the adult stage looks like a stunted *E. multilocularis*, but the larval stage of *E. shiquicus* appears to be unicystic, whereas the larval stage of *E. multilocularis* is multilocular or alveolar.

The year 2000 was important for the study of echinococcosis since several groups working independently in China from around 1990 finally met at the conference in Chengdu (Ito et al., 2003a; 2003b) and in another, bigger meeting in Poznań, Poland in September that same year (Craig and Pawłowski, 2002). The United States National Institutes of Health (US NIH) R01 Project on Parasitic Zoonosis (echinococcosis) transmission in China (principal investigator: P. S. Craig) also commenced in October 2000 and continued for 8 years. Ning Xiao also conducted a molecular analysis of *Echinococcus shiquicus* under the direction of Minoru Nakao and published the work as his PhD thesis (Xiao et al., 2005; 2006).

Other studies on the taxonomy of *Echinococcus* include a reevaluation by molecular approaches using fresh eggs from lion feces in Uganda to support revision of *E. felidis*, which was initially described in 1934 from African lions (Ortlepp, 1934) but later included as a subspecies or strain of *E. granulosus*. Adult worms in a lion intestine fixed in formalin were also reevaluated later by Anna Verster in South Africa (Hüttner et al., 2008; 2009; Hüttner and Romig, 2009). From this work, *E. felidis* and *E. granulosus* sensu stricto (G1) are now considered to be sister species (Nakao et al., 2013b).

Further molecular studies on *Echinococcus canadensis* revealed that *E. canadensis* (G6/G7) and *E. canadensis* (G8/G10) are sister species but are still different species (Nakao et al., 2013c; Laurimäe et al., 2018). It was also confirmed in later studies that the G1 and G3 strains of *E. granulosus* s. s. differ from each other (Kinkar et al., 2018b).

Based on molecular analyses of *Echinococcus granulosus* sensu stricto, the genetic bottleneck effect was discovered when samples from the Middle East, China, and Peru were studied (Casulli et al., 2012; Moro et al., 2009; Nakao et al., 2013b; Yanagida et al., 2012). It was initially suggested that *E. granulosus* s. s. (G1) emerged in western Asia and expanded anthropogenically worldwide. However, further studies in Africa strongly suggest that the origin might be in Africa (Wasserman et al., 2016; Ito and Budke, 2017; Ito et al., 2017).

Molecular analyses of *Echinococcus* specimens offer great numbers of new findings. For example, see Álvarez Rojas et al. (2014), Hüttner and Romig (2009), Ito et al. (2017), and Romig et al. (2015) for good, updated reviews on *E. granulosus* sensu lato.

Life Cycle: Complicated through Global Transport of Livestock, Wild Animals, and Humans

The *Echinococcus* life cycle is completed through predator (carnivore) and prey (omnivore and herbivore) interactions; meaning that an infected intermediate host is eaten by a definitive host where the larvae mature into adults in the small intestine. The definitive hosts for *Echinococcus* are carnivores, either canids or felids (Figure 8). As there are many updated reviews on this topic (Nakao et al., 2013b; Romig et al., 2015), new findings may be discovered about the host animals of *E. shiquicus* and *E. felidis*, as well as other aspects of the life cycle involving all other affected species.

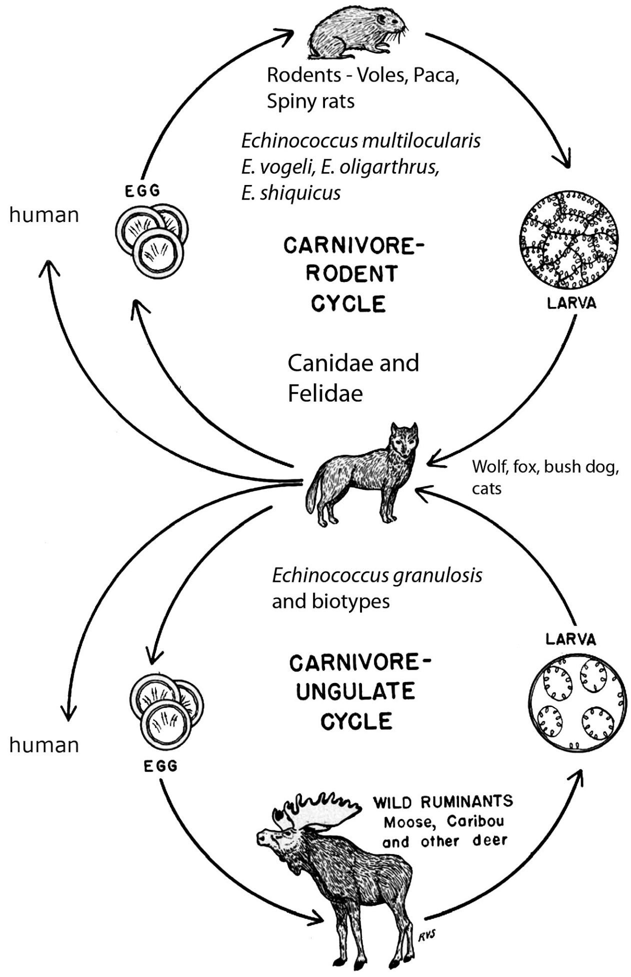

Figure 8. The general life cycle or life history of species of the genus *Echinococcus* showing the carnivore-rodent cycle and showing the carnivore-ungulate cycle. All *Echinococcus* species are not listed here. Source: S. L. Gardner, HWML. License: CC BY.

Both *Echinoccocus shiquicus* and *E. multilocularis* are co-endemic in their areas of overlap in the Qinghai Tibet plateau, China.

Echinococcus shiquicus

The main intermediate hosts for *Echinococcus shiquicus* are rodents (and not the plateau pika *Ochotona cruzoniae*) (Ma et al., 2012; Wang et al., 2018) and the definitive hosts are the red fox (Jiang et al., 2012) and domesticated dogs (Boufana et al., 2013). There are no known human cases of *Echinococcus shiquicus*, although this may be because the human population in the endemic area is relatively small and because the local foxes generally keep away from people. But it is possible that *Echinococcus shiquicus* may be able to infect humans since it is the sister species of *E. multilocularis*.

Echinococcus multilocularis (Figure 9)

Of all known species of cestodes, and among the Taeniidae and *Echinococcus* in particular, *E. multilocularis* is the most serious for human health since it causes alveolar echinococcosis (AE), also called alveolar hydatid disease. AE occurs in humans when the egg of *E. multiolocularis* is ingested and the larvae lodge in various organs, but usually the liver, and grow over time. The growth of the cysts in both humans and rodent intermediate hosts is via **exogenous budding** (growth of the cyst from the surface of the original cyst). This growth is slow in humans and very rapid in rodents. For the adults, the main definitive host is the red fox *Vulpes vulpes*, but all other carnivores may be suitable definitive hosts and almost all species of wild carnivores, both canids and felids, and domesticated dogs and cats, are presumed to be suitable definitive hosts. This hypothesis has been tested and demonstrated in many laboratory studies where the parasite life cycle has been maintained.

A similar broad intermediate host-range has been shown through experimental infections for these cestodes in the case of intermediate hosts, which are mainly rodents, particularly *Microtus* voles, but many other herbivores may also serve as intermediate hosts. *Ochotona* (see Li et al., 2018; Wang et al., 2018) and *Lepus* (see Xiao et al., 2004) species live in the definitive hosts' territories and, so, are expected to be suitable intermediate hosts. It is possible that *Echinoccocus multilocularis* has been shown to be widely distributed in all countries in Eurasia other than the tropical areas. Even if there are no data, with no records showing positive infections of animals in a geographic area, it does not mean that the areas are free of this parasite, but rather that there is simply a lack of surveillance (Botero-Cañola et al., 2019; Gardner et

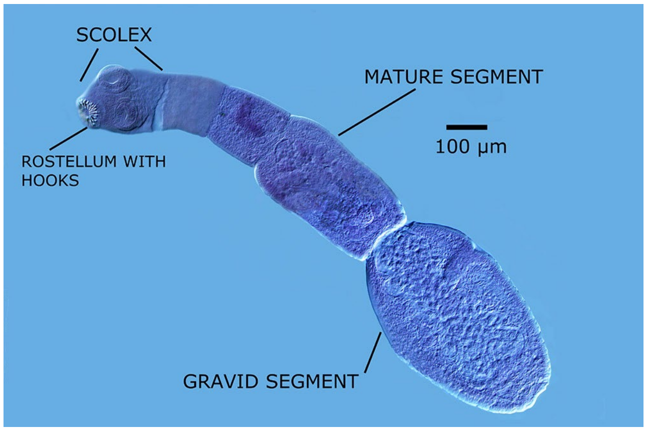

Figure 9. Mature specimen of *Echinococcus multilocularis* from Alaska, United States. Note that the posterior segment that would be full of eggs is missing in this specimen. Source: R. L. Rausch. License: CC BY.

al., 2013; Bagrade et al., 2016; Beck et al., 2018; Lass et al., 2016; Massolo et al., 2014; Umhang et al., 2015).

Human living-environments are often invaded by wildlife (Gottstein et al., 2015; Liccioli et al., 2015; Mackenstedt et al., 2015; Robartdet et al., 2011). There are countless examples of the borderless world with wildlife and domesticated animals and humans in urbanized cities in Europe (Switzerland, Germany, France, Italy, and others), Japan (Ito et al., 2003a; 2003b), and Canada. The best method for avoiding accidental alveolar echinococcosis (AE) in city life is to keep wildlife far from cities. Vaccination of foxes or domesticated dogs, or deworming with praziquantel, will not be successful since *Echinococcus multilocularis* is a wildlife parasite! As this parasite is very pathogenic and without treatment kills humans at a rate of about 97%, surveillance for the presence of the cestode in geographic regions should be completed with the direct evidence of the parasite itself, not simply with molecular evidence (Morishima et al., 2006; 2016). Without any direct evidence of adult worms from dogs, all laboratory work might be in error due to the contamination of the tools used to collect specimens or analyze data in a laboratory. What this means is that sequencing of environmental DNA is not an appropriate method to identify and diagnose this species (because of potential DNA contamination from other sources in the laboratory, in the process of collection, or in the process of transportation and sample preparation). Therefore, direct sequencing of a single egg, or recovered strobilae, using several genes should be employed to avoid introducing accidental artifacts. Another global concern is the migration of *E. multilocularis* through anthropogenically mediated transfer of foxes, and perhaps also rodents, from Europe to North America (Nakao et al., 2013b).

The extent of the genetic diversity inherent in *Echinococcus multilocularis* was first reported by Bretagne and colleagues (1996). They described 3 different geographic genotypes, named: North American, Asian, and European. Tang et al. (2004; 2006) reported *E. multilocularis*-like species with some different biological characteristics and expected it to be an independent species with a previous name, *E. sibiricensis*. This was later proved to be an intraspecies variant and called the Inner Mongolian genotype (Nakao et al., 2009; 2010b). Later, Ito and colleagues (2010; 2013) and Gardner and colleagues (2013) confirmed that this genotype is widely distributed in Mongolia and even in Russia (Konyaev et al., 2013) and have called it the Mongolian genotype (instead of the Inner Mongolian genotype).

The North American genotype is well known to be distributed widely in wildlife (Rausch, 1995; Rausch and Schiller, 1951; Schantz et al., 1995; Storandt and Kazacos, 1993; Storandt et al., 2002), but has been known to occur only very rarely in humans (Yamasaki et al., 2008). However, there have been quite a few cases of AE confirmed in Canada (Catalano et al., 2012; Gesy and Jenkins, 2015; Gesy et al., 2013; 2014; Jenkins et al., 2012; Santa et al., 2018a; 2018b; Shurer et al., 2018). Molecular analysis has revealed that all these AE cases and parasites from wildlife, including wild voles, do not have the North American genotype, but instead have the European genotype. So, it may be concluded that European *Echinococcus multilocularis* appeared only recently in North America (Nakao et al., 2013b). Recent ecological niche-modeling work by Botero-Cañola and colleagues (2019) has shown a possible expansion of the range of *E. multilocularis* in North America. However, the previous purported absence of this parasite in New Mexico (United States) may have been due to nobody having looked for it before, rather than representing an actual geographic range expansion (Botero-Cañola et al., 2019).

Echinococcus felidis

Although the intermediate hosts for *Echinococcus felidis* have been presumed to be several herbivore species living in African lion territory, based on molecular data, only hippopotamuses, warthogs, and pet dogs have been included definitively (Halajian et al., 2017; Mulinge et al., 2018). Several other carnivores, including leopards, lions, and hyenas, are presumed to be additional definitive hosts. These new findings indicate that the environment for wildlife has been complicated by increased pet dog ownership. Although humans are aberrant hosts for the *Echinococcus* life cycle, Macpherson (1983), in work done in Africa, revealed humans as a suitable intermediate host. Macpherson's work leads to the question about whether humans may be involved in the life cycle of *E. granulosus* s. s. or *E. felidis*, in addition to wildlife.

Echinococcus granulosus sensu lato (s. l.)

As described above, human cystic echinococcosis (CE) cases are mainly caused by *Echinococcus granulosus* s. s. (G1), with its cosmopolitan distribution (88.44%), followed by *E. canadensis* (11.07%) and *E. ortleppi* (Álvarez Rojas et al., 2014; Romig et al., 2015; Ito and Budke, 2017; Ito et al., 2017). Recent studies on mitochondrial genes of *E. granulosus* s. s. (G1) or *E. granulosus* s. l. worldwide more strongly reveal a dynamic genetic polymorphism (Álvarez Rojas et al., 2013; 2017; Carmena and Cardona, 2013; 2014; Hassan et al., 2017; Kinker et al., 2018b; Laurimäe et al., 2016).

Echinococcus vogeli and *E. oligarthra*

Recent molecular studies contributed data from these two species in the Americas. Since *Echinococcus granulosus* s.

s. was introduced into the Americas long ago, *E. vogeli* and *E. oligarthra* may be co-distributed with *E. granulosus* in the Americas (Ávila et al., 2017; das Neves et al., 2017).

Therefore, through the acceleration of globalization in the 21st century, the distribution of *Echinococcus* spp. has a much more complicated and chaotic trajectory in the 20th century. More studies from molecular approaches are essential to clarify the origin and spread of the parasite on a global scale (Kinkar et al., 2018a).

Implications of Dual Infections in Intermediate and Definitive Hosts

Recent studies on *Taenia solium* (Yanagida et al., 2014) and *T. asiatica* (Okamoto et al., 2010; Yamane et al., 2013) and those reviewed by Ito and colleagues (2016), have revealed that outcrossing may occur when infections with multiple tapeworms takes place in the definitive host, which is humans. The most recent data in China, where 3 human types of taeniasis occur, show that taeniasis may be caused by *T. solium*, *T. asiatica*, and *T. saginata*. These species are highly co-endemic, indicating that all *T. asiatica* and *T. saginata* are hybrids and dual infection with these 2 species, or even a triple infection with 3 including *T. solium*, is not rare (Li et al., 2018). These molecular studies on inter-species or intra-species hybridization in other species of Taeniidae strongly suggest that intra- and inter-species genetic diversity of *Echinococcus* spp. is a possibility. Indeed, there are several reports revealing that 2 species are confirmed from the same definitive and intermediate host animals. Although there is a report that individuals of *E. multilocularis* and *E. granulosus* may occupy a different part of the small intestine (Thompson and Eckert, 1983), that may not always be true.

How can coinfection with *Echinococcus granulosus* s. s. and *E. canadensis* be tested? These 2 species may occupy the same part of the small intestine, and dual infection may cause outcrossing and hybridizations. As the definitive host slowly acquires immunity to reinfection, meaning that the new infections from separate incidents of carnivory of intermediate hosts can occur for at least several weeks after the first establishment of the cestodes in a canid (Kouguchi et al., 2016), it is easy to imagine dual infections with adult *Echinococcus*, especially with different species of predators when they have different chances for catching infected intermediate host prey. If the immunity to the intestinal tapeworm is species-specific, dual infection with different species is easily established. However, there have been very few reports showing 2 or 3 different-aged tapeworm infections among any cestode infections except those caused by *Vampyrolepis nana* (synonymous with *Hymenolepis nana*). Even in *V. nana*, dual infection happens only when the definitive host gets a primary infection with cysticercoids which follows autoinfection by a large number of second-generation tapeworms (Ito, 2015; 2016). As far as is known, there is no answer explaining why there are no reports of multiple different-aged tapeworm infections even though premunition versus the crowding effect has often been implicated. More experimental infection studies are necessary to understand this issue in tapeworms and especially in the Taeniidae.

An easier explanation is that the definitive hosts get a dual infection from the intermediate host which is coinfected with different species. Then, how do the intermediate hosts get coinfected with different species? As reinfection immunity in the intermediate mammalian host has been shown to be very rapid, usually only 1 population with 1 chance of infection can be established. It is the basic background for production of vaccines against echinococcosis and cysticercosis in livestock (Ito and Smyth, 1987; Lightowlers, 1996; 2006; Lightowlers et al., 1996; 2003). If oncospheres of different species cause reinfection immunity that are species-specific, eggs of different species may cause infection in the same individuals (Álvarez Rojas et al., 2013; Gauci et al., 2018; Oudini-M'rad et al., 2016). Ecological competition for strobilization in the definitive host's intestine between the established tapeworms and newcomers may be one reason the newcomers cannot be established other than affecting intestinal immunity. *Echinococcus* species may be much easier to establish if they occupy different parts of the same host's intestine. If dual infection in the same part of the intestine happens, it may be much easier to speculate that dual infection happens through only a single incidence of eating intermediate hosts which are coinfected with different species. Cross-fertilization in 1 population (Lymbery et al., 1989) or mixed populations may happen. Hybrids in *Echinococcus* spp. in wildlife may be more common than two genotypes of *Taenia solium* (Yanagida et al., 2014) crossed with *T. asiatica*, and crossed with *T. saginata* in humans (Okamoto et al., 2010; Yamane et al., 2013).

Host Range

The predator-prey interaction is the essential factor maintaining the *Echinococcus* life cycle. So, herbivores and omnivores are the intermediate hosts, and carnivores are the definitive hosts. However, cannibalism not only in carnivores but also in omnivores or even in herbivores is not rare but rather common, especially in a stressful environment. There are no data on what happens with echinococcosis due to cannibalism.

There are reports indicating that carnivores including foxes and dogs may be coinfected with 2 different stages. One manifestation is metacestodes in the liver and simultaneously adult *Echinococcus multilocularis* in the intestine in red fox

(Ishino, 1941), metacestodes in dogs (Antolová et al., 2018; Losson and Coignoul, 1997; Meyer et al., 2013; Skelding et al., 2014), and metacestodes of *E. granulosus* s. s. in cats (Armúa-Fernández et al., 2014; Burgu et al., 2004; Konyaev et al., 2012). When eggs of *Echinococcus* or other helminths are ingested by the suitable intermediate hosts, oncospheres hatch and invade the intestinal tissue and migrate to the suitable organs and tissues to differentiate into the metacestode stage, a hydatid. However, there are not sufficient data on the fate of eggs ingested by non-suitable mammalian hosts, including definitive hosts. There is evidence that metacestodes cannot develop into adults in the intermediate host, but carnivores as the definitive hosts for *Echinococcus* spp. may become the intermediate hosts, as well. The mechanism remains unresolved. See the section on *Taenia* for additional information on alternative rodent definitive hosts.

Pathology in Echinococcosis

The larval stage of *Echinococcus* spp. is implicated in human pathologies that may be differentiated into 2 main types: Cystic and cerebral. Cycstic echinococcosis (CE) involves endogenous budding, versus exogenous budding, which occurs in cases of alveolar echinococcosis (AE). In CE, approximately 70% of the cysts are established in the liver, whereas, in AE, over 97% are established in the liver. Differences in tropism, or preference for establishment and growth in various organs in humans by different species of these cestodes, is not clearly established for the various species, perhaps due to confusion relative to identification of the species that cause echinococcosis (Nguyen and Duyet, 2017; Ito et al., 2017). CE is relatively rare, but most recent molecular studies on human cerebral CE cases in children show that they are caused mainly by *E. canadensis* (Shirmen et al., 2018). In contrast, since almost all AE cases are established in the liver, AE cases in the brain, lung, or any other organ are thought to derive from a metastasis of hepatic AE. However, there is no evidence that only 1 oncosphere invades the host tissue. Rather, after multiple eggs are ingested, it may be common that multiple oncospheres simultaneously hatch and invade the intestinal tissue, penetrating and traveling to the liver via the hepatic-portal system where they may lodge and begin to grow via exogenous proliferation (Rausch, 1954; Rausch and Schiller, 1954; Rausch and Jentoft, 1957; Aoki et al., 2015). When advanced hepatic AE cases are confirmed, the big hepatic lesion may be not from a single lesion, but instead from multiple primary lesions fused together. It is possible that non-hepatic AE cases may be caused by both metastasis of the original infection as well as primary infection with the oncosphere larvae disseminating to any area of the body after passing through the liver to the heart.

Although mice show a difference in fertile and sterile AE cysts (Nakaya et al., 1997) and species of *Peromyscus* appear to manifest a larval form in the liver substantially different in structure from those that develop in arvicoline voles (Rausch and Richards, 1971), such host differences need additional investigation, such as those conducted using newer techniques by Islam and colleagues (2018).

Echinococcus granulosus s. l., *E. felidis*, and *E. oligarthra* develop into typical cystic lesions, whereas *E. multilocularis* develops into an alveolar lesion, and often mutlifocal lesions which are likely to have been established by metastasis (see Figure 1.6 in Thompson, 1986). However, multi-organ AE cases may be due to a primary multi-organ infection with multiple oncospheral invasions. *Echinococcus shiquicus* and *E. vogeli* are polycystic and are intermediate in pathogenicity between the CE and AE forms.

Literature Cited

Álvarez Rojas, C. A., D. Ebi, R. Paredes, G. Acosta-Jamett, et al. 2017. High intraspecific variability of *Echinococcus granulosus* sensu stricto in Chile. Parasitology International 66: 112–115. doi: 10.1016/j.parint.2016.12.001

Álvarez Rojas, C. A., C. G. Gauci, and M. W. Lightowlers. 2013. Antigenic differences between the EG95-related proteins from *Echinococcus granulosus* G1 and G6 genotypes: Implications for vaccination. Parasite Immunology 35: 99–102. doi: 10.1111/pim.12009

Álvarez Rojas, C. A., T. Romig, and M. W. Lightowlers. 2014. *Echinococcus granulosus* sensu lato genotypes infecting humans: Review of current knowledge. International Journal for Parasitology 44: 9–18. doi: 10.1016/j.ijpara.2013.08.008

Antolová, D., B. Vichová, J. Jarošová, V., Gál, et al. 2018. Alveolar echinococcosis in a dog: Analysis of clinical and histological findings and molecular identification of *Echinococcus multilocularis*. Acta Parasitologica 63: 486–494. doi: 10.1515/ap-2018-0058

Aoki, T., M. Hagiwara, H. Yabuki, and A. Ito. 2015. Unique MRI findings for differentiation of an early stage of hepatic alveolar echinococcosis. British Medical Journal Case Reports 2015: bcr2014208123. doi: 10.1136/bcr-2014-208123

Armúa-Fernández, M. T., O. F. Castro, A. Crampet, Á. Bartzabal, et al. 2014. First case of peritoneal cystic echinococcosis in a domestic cat caused by *Echinococcus granulosus* sensu stricto (genotype 1) associated to feline immunodeficiency virus infection. Parasitology International 63: 300–302. doi: 10.1016/j.parint.2013.11.005

Ávila, H. G., G. B. Santos, M. A. Cucher, N. Macchiaroli, et al. 2017. Implementation of new tools in molecular epidemiology studies of *Echinococcus granulosus* sensu lato in South America. Parasitology International 66: 250–257. doi: 10.1016/j.parint.2017.02.001

Bagrade, G., G. Densne, Z. Ozolina, S. J. Howlett, et al. 2016. *Echinococcus multilocularis* in foxes and raccoon dogs: An increasing concern for Baltic countries. Parasites and Vectors 9: 615. doi: 10.1186/s13071-016-1891-9

Beck, R., Ž. Mihaljević, R. Brezak, S. Bosnić, et al. 2018. First detection of *Echinococcus multilocularis* in Croatia. Parasitology Research 117: 617–621. doi: 10.1007/s00436-017-5732-3

Botero-Cañola, S., A. T. Dursahinhan, S. E. Rácz, P. V. Lowe, et al. 2019. The ecological niche of *Echinococcus multilocularis* in North America: Understanding biotic and abiotic determinants of parasite distribution with new records in New Mexico and Maryland, United States. Therya 10: 91–102. doi: 10.12933/therya-19-749 http://132.248.10.25/therya/index.php/THERYA/article/view/749

Boufana, B., J. Qiu, X. Chen, C. M. Budke, et al. 2013. First report of *Echinococcus shiquicus* in dogs from eastern Qinghai-Tibet region, China. Acta Tropica 127: 21–24. doi: 10.1016/j.actatropica.2013.02.019

Bowles, J., D. Blair, and D. P. McManus. 1992. Genetic variations within the genus *Echinococcus* identified by mitochondrial DNA sequencing. Molecular and Biochemical Parasitology 54: 165–173. doi: 10.1016/0166-6851(92)90109-w

Bowles, J., D. Blair, and D. P. McManus. 1995. A molecular phylogeny of the genus *Echinococcus*. Parasitology 110: 317–328. doi: 10.1017/s0031182000080902

Bretagne, S., B. Assouline, D. Vidaud, R. Houin, et al. 1996. *Echinococcus multilocularis*: Microsatellite polymorphism in U1 snRNA genes. Experimental Parasitology 82: 324–328. doi: 10.1006/expr.1996.0040

Burgu, A., S. A. Vural, and O. Sarimehmetoglu. 2004. Cystic echinococcosis in a stray cat. Veterinary Records 155: 711–712. doi: 10.1136/vr.155.22.711

Carmena, D., and G. A. Cardona. 2013. Canine echinococcosis: Global epidemiology and genotypic diversity. Acta Tropica 128: 441–460. doi: 10.1016/j.actatropica.2013.08.002

Carmena, D., and G. A. Cardona. 2014. Echinococcosis in wild carnivorous species: Epidemiology, genotypic diversity, and implications for veterinary public health. Veterinary Parasitology 202: 69–94. doi: 10.1016/j.vetpar.2014.03.009

Casulli, A., M. Interisano, T. Sreter, L. Chitimia, et al. 2012. Genetic variability of *Echinococcus granulosus* sensu stricto in Europe inferred by mitochondrial DNA sequences. Infection, Genetics and Evolution 12: 377–383. doi: 10.1016/j.meegid.2011.12.014

Catalano, S., M. Lejeune, S. Liccioli, G. G. Verocai, et al. 2012. *Echinococcus multilocularis* in urban coyotes, Alberta, Canada. Emerging Infectious Diseases 18: 1,625–1,628. doi: 10.3201/eid.1810.120119

Craig, P. S., and Z. Pawłowski. 2002. Cestode zoonoses: Echinococcosis and cysticercosis. NATO Science Series I: Life and Behavioural Sciences 341. IOS Press, Amsterdam, Netherlands, 395 p.

das Neves, L. B., P. E. Teixeira, S. Silva, F. B. de Oliveira, et al. 2017. First molecular identification of *Echinococcus vogeli* and *Echinococcus granulosus* (sensu stricto) G1 revealed in feces of domestic dogs (*Canis familiaris*) from Acre, Brazil. Parasites and Vectors 10: 28. doi: 10.1.186/s13071-016-1952-0

Eckert, J., and R. C. A. Thompson. 2017. Historical aspects of echinococcosis. Advances in Parasitology 95: 1–64. doi: 10.1016/bs.apar.2016.07.003

Gardner, S. L., A. T. Dursahinhan, G. R. Rácz, N. Batsaikhan, et al. 2013. Sylvatic species of *Echinococcus* from rodent intermediate hosts in Asia and South America. Occasional Papers, Museum of Texas Tech University 318: 1–13.

Gardner, S. L., R. L. Rausch, and O. C. J. Camacho. 1988. *Echinococcus vogeli* Rausch and Bernstein, 1972 from the paca, *Cuniculus paca* L. (Rodentia: Dasyproctidae) in the Departamento de Santa Cruz, Bolivia. Journal of Parasitology 74: 399–402. doi: 10.2307/3282045

Gauci, C. G., C. A. Álvarez Rojas, C. Chow, and M. W. Lightowlers. 2018. Limitations of the *Echinococcus granulosus* genome sequence assemblies for analysis of the gene family encoding the EG95 vaccine antigen. Parasitology 145: 807–813. doi: 10.1017/S0031182017001767

Gesy, K., J. E. Hill, H. Schwantje, S. Liccioli, et al. 2013. Establishment of a European-type strain of *Echinococcus multilocularis* in Canadian wildlife. Parasitology 140: 1,133–1,137. doi: 10.1017/S0031182013000607

Gesy, K. M., and E. J. Jenkins. 2015. Introduced and native haplotypes of *Echinococcus multilocularis* in wildlife in Saskatchewan, Canada. Journal of Wildlife Diseases 51: 743–748. doi: 10.7589/2014-08-214

Gesy, K. M., J. M. Schurer, A. Massolo, S. Liccioli, et al. 2014. Unexpected diversity of the cestode *Echinococcus multilocularis* in wildlife in Canada. International Journal for Parasitology: Parasites and Wildlife. 3: 81–87. doi: 10.1016/j.ijppaw.2014.03.002

Goeze, J. A. E. 1782. Versuch einer Naturgeschichte der Eingeweidewűrmer thierischer Kӧrper. Pape, Blankenburg, Germany, 471 p.

Gottstein, B., M. Stojković, D. A. Vuitton, L. Millon, et al. 2015. Threat of alveolar echinococcosis to public health: A challenge for Europe. Trends in Parasitology 31: 407–412. doi: 10.1016/j.pt.2015.06.001

Halajian, A., W. J. Luus-Powell, F. Roux, M. Nakao, et al. 2017. *Echinococcus felidis* in hippopotamus, South Africa. Veterinary Parasitology 243: 24–28. doi: 10.1016/j.vetpar.2017.06.001

Hassan, Z. I., A. A. Meerkhan, B. Boufana, A. A. Hama, et al. 2017. Two haplotype clusters of *Echinococcus granulosus* sensu stricto in northern Iraq (Kurdistan region) support the hypothesis of a parasite cradle in the Middle East. Acta Tropica 172: 201–207. doi: 10.1016/j.actatropica.2017.04.028

Hüttner, M., and T. Romig. 2009. *Echinococcus* species in African wildlife. Parasitology 136: 1,089–1,095. doi: 10.1017/S0031182009990461

Hüttner, M., M. Nakao, T. Wassermann, L. Siefert, et al. 2008. Genetic characterization and phylogenetic position of *Echinococcus felidis* (Cestoda: Taeniidae) from the African lion. International Journal for Parasitology 38: 861–868. doi: 10.1016/j.ijpara.2007.10.013

Hüttner, M., L. Siefert, U. Mackenstedt, and T. Romig. 2009. A survey of *Echinococcus* species in wild carnivores and livestock in East Africa. International Journal for Parasitology 39: 1,269–1,276. doi: 10.1016/j.ijpara.2009.02.015

Ishino, H. 1941. Alveolar echinococcosis in an Arctic fox in Simushir Island, Kuril Islands. Kachiku Eisei Kyoukaihou 9: 115. [In Japanese.]

Islam, M. A., D. Torigoe, Y. Kameda, T. Irie, et al. 2018. Analysis for genetic loci controlling protoscolex development in the *Echinococcus multilocularis* infection using congenic mice. Infection, Genetics and Evolution 65: 65–71. doi: 10.1016/j.meegid.2018.07.017

Ito, A. 2015. Basic and applied problems in developmental biology and immunobiology of cestode infections: *Hymenolepis*, *Taenia*, and *Echinococcus*. Parasite Immunology 37: 53–69. doi: 10.1111/pim.12167

Ito, A. 2016. Immunology in cestode infections. *In* M. J. H. Ratcliffe, ed. Encyclopedia of Immunobiology, Volume 4. Academic Press, Oxford, United Kingdom, p. 159–165.

Ito, A., and C. M. Budke. 2017. The echinococcoses in Asia: The present situation. Acta Tropica 176: 11–21. doi: 10.1016/j.actatropica.2017.07.013

Ito, A., G. Agvaandaram, O. E. Bat-Ochier, B. Chuluunbaatar, et al. 2010. Histopathological, serological, and molecular confirmation of indigenous alveolar echinococcosis cases in Mongolia. American Journal of Tropical Medicine and Hygiene 82: 266–269. doi: 10.4269/ajtmh.2010.09-0520

Ito, A., G. Chuluunbaatar, T. Yanagida, A. Davaasuren, et al. 2013. *Echinococcus* species from red foxes, corsac foxes, and wolves in Mongolia. Parasitology 140: 1,648–1,654. doi: 10.1017/S0031182013001030

Ito, A., M. Nakao, A. Lavikainen, and E. Hoberg. 2017. Cystic echinococcosis: Future perspectives of molecular epidemiology. Acta Tropica 165: 3–9. doi: 10.1016/j.actatropica.2016.05.013

Ito, A., T. Romig, and K. Takahashi. 2003a. Perspective on control options for *Echinococcus multilocularis* with particular reference to Japan. Parasitology 127 (Supplement): S159–S172.

Ito, A., and J. D. Smyth. 1987. Adult cestodes: Immunology of the lumen-dwelling cestode infections. *In* E. J. L. Soulsby, ed. Immune Response in Parasitic Infections: Immunology, Immunopathology, and Immunoprophylaxis, Volume 2. CRC Press, Boca Raton, Florida, United States, p. 115–163.

Ito, A., C. Urbani, J. Qiu, D. A. Vuitton, et al. 2003b. Control of echinococcosis and cysticercosis: A public health challenge to international cooperation in China. Acta Tropica 86: 3–17. doi: 10.1016/s0001-706x(02)00269-3

Jenkins, E. J., A. S. Peregrine, J. E. Hill, C. Somers, et al. 2012. Detection of European strain of *Echinococcus multilocularis* in North America. Emerging Infectious Diseases 18: 1,010–1,012. doi: 10.3201/eid1806.111420

Jiang, W., N. Lin, G. Zhang, P. Renqing, et al. 2012. Specific detection of *Echinococcus* spp. from the Tibetan fox (*Vulpes ferrilata*) and the red fox (*V. vulpes*) using copro-DNA PCR analysis. Parasitology Research 111: 1,531–1,539. doi: 10.1007/s00436-012-2993-8

Kinkar, L., T. Laurimäe, G. Acosta-Jamett, V. Andresiuk, et al. 2018a. Global phylogeography and genetic diversity of the zoonotic tapeworm *Echinococcus granulosus* sensu stricto genotype G1. International Journal for Parasitology 48: 729–742. doi: 10.1016/j.ijpara.2018.03.006

Kinkar, L., T. Laurimäe, I. Balkaya, A. Casulli, et al. 2018b. Genetic diversity and phylogeography of the elusive, but epidemiologically important *Echinococcus granulosus* sensu stricto genotype G3. Parasitology 145: 1,613–1,622. doi: 10.1017/S0031182018000549

Knapp, J., M. Nakao, T. Yanagida, M. Okamoto, et al. 2011. Phylogenetic relationships within *Echinococcus* and *Taenia* tapeworms (Cestoda: Taeniidae): An inference from nuclear protein-coding genes. Molecular Phylogenetics and Evolution 61: 628–638. doi: 10.1016/j.ympev.2011.07.022

Konyaev, S. V., T. Yanagida, M. V. Ivanov, V. V. Ruppel, et al. 2012. The first report on cystic echinococcosis in a cat caused by *Echinococcus granulosus* sensu stricto (G1). Journal of Helminthology 86: 391–394. doi: 10.1017/S0022149X1100054X

Konyaev, S. V., T. Yanagida, M. Nakao, G. M. Ingovatova, et al. 2013. Genetic diversity of *Echinococcus* spp. in Russia. Parasitology 140: 1,637–1,647. doi: 10.1017/S0031182013001340

Kouguchi, H., T. Irie, J. Matsumoto, R. Nakao, et al. 2016. The timing of worm exclusion in dogs repeatedly infected with the cestode *Echinococcus multilocularis*. Journal of Helminthology 90: 766–772. doi: 10.1017/S0022149X15001169

Lass, A., B. Szostakowska, P. Myjak, and K. Korzeniewski. 2016. Fresh fruits, vegetables and mushrooms as transmission vehicles for *Echinococcus multilocularis* in highly endemic areas of Poland: Reply to concerns. Parasitology Research 113: 3,637–3,642. doi: 10.1007/s00436-016-5149-4

Laurimäe, T., L. Kinker, V. Andresiuk, K. L. Haag, et al. 2016. Genetic diversity and phylogeography of highly zoonotic *Echinococcus granulosus* genotype G1 in the Americas (Argentina, Brazil, Chile, and Mexico) based on 8279 bp of mtDNA. Infection, Genetics and Evolution 45: 290–296. doi: 10.1016/j.meegid.2016.09.015

Laurimäe, T., L. Kinker, E. Moks, T. Romig, et al. 2018. Molecular phylogeny based on six nuclear genes suggests that *Echinococcus granulosus* sensu lato genotypes G6/G7 and G8/G10 can be regarded as two distinct species. Parasitology 145: 1,929–1,937. doi: 10.1017/S0031182018000719

Li, J., L. Li, Y.-L. Fan, B.-Q. Fu, et al. 2018. Genetic diversity in *Echinococcus multilocularis* from the plateau vole and plateau pika in Jiuzhu County, Qinghai Province, China. Frontiers in Microbiology 9: 2,632. doi: 10.3389/fmicb.2018.02632

Liccioli, S., P. Giraudoux, P. Deplazes, and A. Massolo. 2015. Wilderness in the 'City' revisited: Different urbes shape transmission of *Echinococcus multilocularis* by altering predator and prey communities. Trends in Parasitology 31: 297–305. doi: 10.1016/j.pt.2015.04.007

Lightowlers, M. W. 2006. Cestode vaccines: Origins, current status, and future prospects. Parasitology 133 (Supplement): S27–S42. doi: 10.1017/S003118200600179X

Lightowlers, M. W. 1996. Vaccination against cestode parasites. International Journal for Parasitology 26: 819–824. doi: 10.1016/s0020-7519(96)80048-8

Lightowlers, M. W., A. L. Colebrook, C. G. Gauci, S. M. Gauci, et al. 2003. Vaccination against cestode parasites: Anti-helminth vaccines that work and why. Veterinary Parasitology 115: 83–123. doi: 10.1016/s0304-4017(03)00202-4

Lightowlers, M. W., S. B. Lawrence, C. G. Gauci, J. Young, et al. 1996. Vaccination against hydatidosis using a defined recombinant antigen. Parasite Immunology 18: 457–462. doi: 10.1111/j.1365-3024.1996.tb01029.x

Losson, B. J., and F. Coignoul. 1997. Larval *Echinococcus multilocularis* infection in a dog. Veterinary Record 141: 49–50. doi: 10.1136/vr.141.2.49

Lymbery, A. J., R. P. Hobbe, and R. C. A. Thompson. 1989. The dispersion of *Echinococcus granulosus* in the intestine of dogs. Journal of Parasitology 75: 562–570.

Ma, J., H. Wang, G. Lin, P. S. Craig, et al. 2012. Molecular identification of *Echinococcus* species from eastern and southern Qinghai, China, based on the mitochondrial *cox1* gene. Parasitology Research 111: 179–184. doi: 10.1007/s00436-012-2815-z

Macpherson, C. N. 1983. An active intermediate host role for man in the life cycle of *Echinococcus granulosus* in Turkana, Kenya. American Journal of Tropical Medicine and Hygiene 32: 297–304. doi: 10.4269/ajtmh.1983.32.397

Massolo, A., S. Liccioli, C. Budke, and C. Klein. 2014. *Echinococcus multilocularis* in North America: The great unknown. Parasite 21: 1–13. doi: 10.1051/parasite/2014069

Meyer, A., F. J. Conraths, C. Schneemann, V. Wienrich, et al. 2013. [Lethal alveolar echinococcosis in a dog: Clinical symptoms and pathology.] Berliner und Muchener tierarztliche Wochenschrift 126: 408–414. [In German.]

Morishima, Y., H. Sugiyama, K. Arakawa, and M. Kawanaka. 2006. *Echinococcus multilocularis* in dogs, Japan. Emerging Infectious Diseases 12: 1,292–1,294. doi: 10.3201/eid1708.051241

Morishima, Y., Y. Tomaru, S. Fukumoto, H. Sugiyama, et al. 2016. Canine echinococcosis due to *Echinococcus multilocularis*: A second notifiable case from mainland Japan. Japanese Journal of Infectious Diseases 69: 443–449. doi: 10.7883/yoken.JJID.2015.573

Moro, P. L., and P. M. Schantz. 2009. Echinococcosis: A review. International Journal of Infectious Diseases 13: 125–133. doi: 10.1016/j.ijid.2008.03.037

Moro, P. L., M. Nakao, A. Ito, P. M. Schantz, et al. 2009. Molecular identification of *Echinococcus* isolates from Peru. Parasitology International 58: 184–186. doi: 10.1016/j.parint.2009.01.005

Mulinge, E., J. Magambo, D. Odongo, S. Njenga, et al. 2018. Molecular characterization of *Echinococcus* species in dogs from four regions of Kenya. Veterinary Parasitology 255: 49–57. doi: 10.1016/j.vetpar.2018.03.029

Nakao, M., A. Lavikainen, T. Iwaki, V. Haukisalmi, et al. 2013a. Molecular phylogeny of the genus *Taenia* (Cestoda: Taeniidae): Proposals for the resurrection of *Hydatigera* Lamarck, 1816 and the creation of a new genus *Versteria*. International Journal for Parasitology 43: 427–437. doi: 10.1016/j.ijpara.2012.11.014

Nakao, M., A. Lavikainen, T. Yanagida, and A. Ito. 2013b. Phylogenetic systematics of the genus *Echinococcus* (Cestoda: Taeniidae). International Journal for Parasitology 43: 1,017–1,029. doi: 10.1016/j.ijpara.2013.06.002

Nakao, M., T. Li, X. Han, X. Ma, et al. 2010a. Genetic polymorphisms of *Echinococcus* tapeworms in China as determined by mitochondrial and nuclear DNA sequences. International Journal for Parasitology 40: 379–385. doi: 10.1016/j.ijpara.2009.09.006

Nakao, M., N. Xiao, M. Okamoto, T. Yanagida, et al. 2009. Geographic pattern of genetic variation in the fox tapeworm *Echinococcus multilocularis*. Parasitology International 58: 384–389. doi: 10.1016/j.parint.2009.07.010

Nakao, M., T. Yanagida, S. Konyaev, A. Lavikainen, et al. 2013c. Mitochondrial phylogeny of the genus *Echinococcus* (Cestoda: Taeniidae) with emphasis on relationships among *Echinococcus canadensis* genotypes. Parasitology 140: 1,625–1,636. doi: 10.1017/S0031182013000565

Nakao, M., T. Yanagida, M. Okamoto, J. Knapp, et al. 2010b. State-of-the-art *Echinococcus* and *Taenia*: Phylogenetic taxonomy of human-pathogenic tapeworms and its application to molecular diagnosis. Infection, Genetics and Evolution 10: 444–452. doi: 10.1016/j.meegid.2010.01.011

Nakaya, K., M. Nakao, and A. Ito. 1997. *Echinococcus multilocularis*: Mouse strain difference in hydatid development. Journal of Helminthology 71: 53–56. doi: 10.1017/s0022149x00000791

Nguyen, V. D., and L. V. Duyet. 2017. The first report of two cases of cystic echinococcosis in the lung by *Echinococcus ortleppi* infection, in Vietnam. Research and Reports in Tropical Medicine 8: 45–51. doi: 10.2147/RRTM.S122014

Okamoto, M., M. Nakao, D. Blair, M. T. Anataphruti, et al. 2010. Evidence of hybridization between *Taenia saginata* and *Taenia asiatica*. Parasitology International 59: 70–74. doi: 10.1016/j.parint.2009.10.007

Ortlepp, R. J. 1934. *Echinococcus* in dogs from Pretoria and vicinity. Onderstepoort Journal of Veterinary Science 3: 97–108. http://hdl.handle.net/2263/48342

Oudini-M'rad, M., S. M'rad, A. Ksia, R. Lamiri, et al. 2016. First molecular evidence of the simultaneous human infection with two species of *Echinococcus granulosus* sensu lato: *Echinococcus granulosus* sensu stricto and *Echinococcus canadensis*. Parasitology Research 115: 1,065–1,069. doi: 10.1007/s00436-015-4836-x

Pallas, P. S. 1776. Miscellanea zoologica, quibus novae imprimus atque obscurae animalium species describuntur et observationibus iconibusque. Van Cleef, Hagae Comitum, [Netherlands], 224 p. doi: 10.5962/bhl.title.69851

Rausch, R. L. 1993. The biology of *Echinococcus granulosus*. *In* F. L. Anderson, J. Chai, and F. Liu, eds. Compendium on Cystic Echinococcosis with Special Reference to the Xinjiang Uygur Autonomous Regions, the People's Republic of China. Brigham Young University Print Services, Provo, Utah, United States, p. 27–56.

Rausch, R. L. 1967. A consideration of intraspecific categories in the genus *Echinococcus* Rudolphi, 1801 (Cestoda: Taeniidae). Journal of Parasitology 53: 484–491.

Rausch, R. L. 2003. Cystic echinococcosis in the Arctic and Subarctic. Parasitology 127 (Supplement): S73–S85. doi: 10.1017/s0031182003003664

Rausch, R. L. 1995. Life cycle patterns and geographic distribution of *Echinococcus* species. *In* R. C. A. Thompson and A. J. Lymbery, eds. *Echinococcus* and Hydatid Disease. CAB International, Wallingford, United Kingdom, p. 89–134.

Rausch, R. L. 1954. Studies on the helminth fauna of Alaska, XX: The histogenesis of the alveolar larva of *Echinococcus* species. Journal of Infectious Diseases 94: 178–186. doi: 10.1093/infdis/94.2.178

Rausch, R. L., and J. J. Bernstein. 1972. *Echinococcus vogeli* sp. n. (Cestoda: Taeniidae) from the bush dog, *Speothos venaticus* (Lund). Zeitschrift für Tropenmedizin und Parasitologie 23: 25–34. https://digitalcommons.unl.edu/parasitologyfacpubs/477/

Rausch, R. L., and V. L. Jentoft. 1957. Studies on the helminth fauna of Alaska, XXXI: Observations on the propagation of the larval *Echinococcus multilocularis* Leuckart, 1863, in vitro. Journal of Parasitology. 43: 1–8.

Rausch, R. L., and S. H. Richards. 1971. Observations on parasite-host relationships of *Echinococcus multilocularis* Leuckart, 1863, in North Dakota. Canadian Journal of Zoology 49: 1,317–1,330. doi: 10.1139/z71-198

Rausch, R. L., and E. L. Schiller. 1951. Hydatid disease (echinococcosis) in Alaska and the importance of rodent intermediate hosts. Science 113: 57–58. doi: 10.1126/science.113.2925.57

Romig, T., D. Ebi, and M. Wassermann. 2015. Taxonomy and molecular epidemiology of *Echinococcus granulosus* sensu lato. Veterinary Parasitology 213: 76–84. doi: 10.1016/j.vetpar.2015.07.035

Rostami, S., S. Shariat Torbaghan, S. Dabiri, Z. Babaei, et al. 2015. Genetic characterization of *Echinococcus granulosus* from a large number of formalin-fixed, paraffin-embedded tissue samples of human isolates in Iran. American Journal of Tropical Medicine and Hygiene 92: 588–594. doi: 10.4269/ajtmh.14-0585

Santa, M. A., S. A. Pastran, C. Klein, P. Duignan, et al. 2018a. Corrigendum to "Detecting co-infections of *Echinococcus multilocularis* and *Echinococcus canadensis* in coyotes and red foxes in Alberta, Canada using real-time PCR." International Journal for Parasitology: Parasites and Wildlife 7: 463. doi: 10.1016/j.ijppaw.2018.07.006

Santa, M. A., S. A. Pastran, C. Klein, P. Duignan, et al. 2018b. Detecting co-infections of *Echinococcus multilocularis* and *Echinococcus canadensis* in coyotes and red foxes in Alberta, Canada using real-time PCR. International Journal for Parasitology: Parasites and Wildlife 7: 111–115. doi: 10.1016/j.ijppaw.2018.03.001

Schantz, P. M., J. Chai, P. S. Craig, J. Eckert, et al. 1995. Epidemiology and control of hydatid disease. *In* R. C. A. Thompson and A. J. Lymbery, eds. *Echinococcus* and Hydatid Disease. CAB International, Wallingford, United Kingdom, p. 233–331.

Shirmen O., B. Batchuluun, A. Lkhamjav, T. Tseveen, et al. 2018. Cerebral cystic echinococcosis in Mongolian children caused by *Echinococcus canadensis*. Parasitology International 67: 584–586. doi: 10.1016/j.parint.2018.05.006

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

Storandt, S. T., and K. R. Kazacos. 1993. *Echinococcus multilocularis* identified in Indiana, Ohio, and east-central Illinois. Journal of Parasitology 79: 301–305.

Storandt, S. T., D. R. Virchow, M. W. Dryden, S. E. Hygnstrom, et al. 2002. Distribution and prevalence of *Echinococcus multilocularis* in wild predators in Nebraska, Kansas, and Wyoming. Journal of Parasitology 88: 420–422. doi: 10.1645/0022-3395(2002)088[0420:DAPOEM]2.0.CO;2

Tang, C.-T., Y.-C. Quian, Y.-M. Kang, G.-W. Cui, et al. 2004. Study on the ecological distribution of alveolar *Echinococcus* in Hulunbeier Pasture of Inner Mongolia, China. Parasitology 128: 187–194. doi: 10.1017/s0031182003004438

Tang, C.-T., Y.-H. Wang, W.-F. Peng, L. Tang, et al. 2006. Alveolar *Echinococcus* species from *Vulpes corsac* in Hulunbeier, Inner Mongolia, China, and differential development of the metacestodes in experimental rodents. Journal of Parasitology 92: 719–724. doi: 10.1645/GE-3526.1

Thompson, R. C. A. 1986. Biology and systematics of *Echinococcus*. *In* R. C. A. Thompson, ed. The Biology of *Echinococcus* and Hydatid Disease. Allen and Unwin, Boston, Massachusetts, United States, p. 5–43.

Thompson, R. C. A., and J. Eckert. 1983. Observations on *Echinococcus multilocularis* in the definitive host. Zeitschrift für Parazitenkunde 69: 335–345. doi: 10.1007/BF00927875

Thompson, R. C. A., and D. P. McManus. 2002. Towards a taxonomic revision of the genus *Echinococcus*. Trends in Parasitology 18: 452–457. doi: 10.1016/s1471-4922(02)02358-9

Thompson, R. C. A., P. Deplazes, and A. J. Lymbery, eds. 2017a. *Echinococcus* and echinococcosis, Part A. Advances in Parasitology 95, 525 p.

Thompson, R. C. A., P. Deplazes, and A. J. Lymbery, eds. 2017b. *Echinococcus* and echinococcosis, Part B. Advances in Parasitology 96, 405 p.

Umhang, G., J. Knapp, V. Hormaz, F. Raoul, et al. 2015. Using the genetics of *Echinococcus multilocularis* to trace the history of expansion from an endemic area. Infection, Genetics and Evolution 22: 141–149. doi: 10.1016/j.meegid.2014.01.018

Wang, X., J. Liu, Q. Zuo, Z. Mu, et al. 2018. *Echinococcus multilocularis* and *Echinococcus shiquicus* in a small mammal community on the eastern Tibetan Plateau: Host species composition, molecular prevalence, and epidemiological implications. Parasites and Vectors 11: 302. doi: 10.1186/s13071-018-2873-x

Xiao, N., T.-Y. Li, J.-M. Qiu, M. Nakao, et al. 2004. The Tibetan hare *Lepus oiostolus*: A novel intermediate host for *Echinococcus multilocularis*. Parasitology Research 92: 352–353. doi: 10.1007/s00436-003-1048-6

Xiao, N., J. Qiu, M. Nakao, T.-Y. Li, et al. 2006. *Echinococcus shiquicus*, a new species from the Qinghai-Tibet plateau region of China: Discovery and epidemiological implications. Parasitology International 55: S233–S236.

Xiao, N., J. Qiu, M. Nakao, T.-Y. Li, et al. 2005. *Echinococcus shiquicus* n. sp., a taeniid cestode from Tibetan fox and plateau pika in China. International Journal for Parasitology 35: 693–701. doi: 10.1016/j.ijpara.2005.01.003

Yamane, K., T. Yanagida, T.-Y. Li, X. Chen, et al. 2013. Genotypic relationships between *Taenia saginata*, *Taenia asiatica*, and their hybrids. Parasitology 140: 1,595–1,601. doi: 10.1016/j.parint.2005.11.035

Yamasaki, H., M. Nakao, K. Nakaya, P. M. Schantz, et al. 2008. Genetic analysis of *Echinococcus multilocularis* originating from a patient with alveolar echinococcosis occurring in Minnesota in 1977. American Journal of Tropical Medicine and Hygiene 79: 245–247.

Yanagida, T., J.-F. Carod, Y. Sako, M. Nakao, et al. 2014. Genetics of the pig tapeworm in Madagascar reveal a history of human dispersal and colonization. PLoS One 9: e109002. doi: 10.1371/journal.pone.0109002

Yanagida, T., T. Mohammadzadeh, S. Kamhawi, M. Nakao, et al. 2012. Genetic polymorphisms of *Echinococcus granulosus* sensu stricto in the Middle East. Parasitology International 61: 599–603. doi: 10.1016/j.parint.2012.05.014

Supplemental Reading

Bold, B., F. Boué, C. Schindler, B. Badmaa, et al. 2018. Evidence for camels (*Camelus bactrianus*) as the main intermediate host of *Echinococcus granulosus* sensu lato G6/G7 in Mongolia. Parasitology Research 118: 2,583–2,590. doi: 10.1007/s00436-019-06391-x

Bonelli, P., G. Masu, S. Dei Giudici, D. Pintus, et al. 2018. Cystic echinococcosis in a domestic cat (*Felidis catus*) in Italy. Parasite 25: 25. doi: 10.1051/parasite/2018027

Ito, A., T. Dorjsuren, A. Davaasuren, T. Yanagida, et al. 2014. Cystic echinococcosis in Mongolia: Molecular identification, serology, and risk factors. PLoS Neglected Tropical Diseases 8: e2937. doi: 10.1371/journal.pntd.0002937

Ito, A., T. Yanagida, and M. Nakao. 2016. Recent advances and perspectives in molecular epidemiology of *Taenia solium* cysticercosis. Infection, Genetics and Evolution 40: 357–367. doi: 10.1016/j.meegid.2015.06.022

Massolo, A., D. Valli, M. Wassermann, S. Cavallero, et al. 2018. Unexpected *Echinococcus multilocularis* infections in shepherd dogs and wolves in south-western Italian Alps: A new endemic area? International Journal for Parasitology: Parasites and Wildlife 7: 309–316. doi: 10.1016/j.ijppaw.2018.08.001

Nakao, R., Y. Kameda, H. Kouguchi, J. Matsumoto, et al. 2011. Identification of genetic loci affecting the establishment and development of *Echinococcus multilocularis* in mice. International Journal for Parasitology 41: 1,121–1,128. doi: 10.1016/j.ijpara.2011.06.007

Romig, T., P. Deplazes, D. Jenkins, P. Giraudoux, et al. 2017. Ecology and life cycle patterns of *Echinococcus* species. Advances in Parasitology 95: 213–314. doi: 10.1016/j.vetpar.2015.07.035

Schurer, J. M., E. Bouchard, A. Bryant, S. Revell, et al. 2018. *Echinococcus* in wild canids in Québec (Canada) and Maine (USA). PLoS Neglected Tropical Diseases 12: e0006712. doi: 10.1371/journal.pntd.0006712

Thompson, R. C. A., C. M. Kapel, R. P. Hobbs, and P. Deplazes. 2006. Comparative development of *Echinococcus multilocularis* in its definitive hosts. Parasitology 132: 709–716. doi: 10.1017/S0031182005009625

Wassermann, M., D. Woldeyes, B. M. Gerbi, D. Ebi, et al. 2016. A novel zoonotic genotype related to *Echinococcus granulosus* sensu stricto from southern Ethiopia. International Journal for Parasitology 46: 663–668. doi: 10.1016/j.ijpara.2016.04.005