Public health and ecological significance of rodents in *Cryptosporidium* infections

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ARTICLE INFO

ABSTRACT

Cryptosporidium is one of the most important genera of intestinal zoonotic pathogens that cause diarrhea in both humans and animals. Rodents are common and important hosts or carriers of pathogens with public health importance, and rodents play an important role in the ecology of zoonotic transmission. The overall worldwide prevalence of *Cryptosporidium* spp. in rodents is 19.8% (4589/23142). Twenty-five known *Cryptosporidium* species and 43 genotypes have been identified, and *C. parvum* is the dominant species in rodents worldwide. Rodents transfer pathogens to humans by the direct route or by serving as intermediate hosts transmitting the pathogens to other animals. We review the epidemiology, diversity, and transmission routes of *Cryptosporidium* spp. in rodents. The main purpose of this review is to highlight *Cryptosporidium* infection in rodents and its transmission, associated risk factors, and prevention; in addition, we assess the public health and ecological significance of *Cryptosporidium* infections from the One Health perspective.

1. Introduction

Cryptosporidium spp. are foodborne and waterborne parasites with zoonotic potential. The parasites cause watery diarrhea in both humans and animals (domestic animals, mammals, rodents, birds, fish, marsupials, reptiles, and amphibians). Drinking source water, coastal water, recreational use water, wastewater, and market vegetables have been found to contain *Cryptosporidium* spp. in field investigations [1,5,9,11,12]. At least 44 valid *Cryptosporidium* species and approximately 120 genotypes have been described to date. Cryptosporidiosis is a global parasitic disease that usually presents as self-limiting diarrhea, abdominal pain, low-grade fever, nausea, vomiting, and weight loss [1,5]. The condition can be fatal in immunosuppressed individuals (e.g., persons infected with HIV/AIDS) [1]. The current treatment for cryptosporidiosis, nitazoxanide (NTZ), has only moderate clinical efficacy, and no vaccines are available [1,5].

The life cycle of *Cryptosporidium* involves several developmental stages (schizogamy, gametogenesis, and spore stages). The oocysts are ingested by susceptible hosts through contaminated food or water, after which they invade the epithelial cells lining the gastrointestinal gland mucosa and replicate intracellularly [11,53]. Fresh oocysts are excreted from the host with the feces and can cause infections in other susceptible hosts by contaminating food or water [11,12,53]. The rigid spore wall may play a vital role in the survival of the parasite in hostile environments, thus being responsible for large waterborne as well as foodborne outbreaks of the disease [4,53,92–94].

Rodents are an abundant and diversified order of mammals [92,99]. Since the Middle Ages, it has been recognized that rodents can contribute to human disease [9,11,98,99]. In modern times, rodents are also recognized as carriers of many pathogens with public health importance. Almost 10% of the global rodent population is either a carrier or reservoir of pathogens with public health importance [11,98]. Rodents have high population densities and live close to the ground, so they are frequently infected with *Cryptosporidium* spp. While much progress has been made in *Cryptosporidium* research, no retrospective analyses have been done on the epidemiology, diversity, or transmission routes of this parasite in rodents. This review aims to explore the current situation for cryptosporidiosis in rodents and to assess the potential risks posed to human and animal populations.

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2. Molecular characteristics of *Cryptosporidium* in rodents

2.1. Prevalence of Cryptosporidium in rodents

To date, *Cryptosporidium* infection in rodents has been documented in 19 countries, with the prevalence ranging from 0.7% to 100%. The overall average infection rate is 19.8% (4589/23142). Regarding the geographical distribution, the prevalence across different regions ranges from 2.2% to 28.0%. Europe has a higher prevalence (28.0%) (1860/6638) than other documented regions. The overall prevalence values in Asia, North America, South America, Africa, and Oceania are 18.6% (1394/7510), 15.2% (1265/8299), 7.3% (11/150), 2.2% (3/135), and 13.7% (56/410), respectively (Table 1).

It is difficult to explain the discrepancies in the prevalence of *Cryptosporidium* spp. among studies because prevalence is affected by many factors, including the host species composition, host species gender, host species age, season, the geographical distribution of the sample population, the sample size, and the ecological conditions. However, according to current data, the major rodent species vary among regions; the prevalence of *Cryptosporidium* and the major *Cryptosporidium* species in different species of rodents are also different, and the types of rodents studied may influenced the differences in prevalence (Table 3, Supplementary Table S1). However, the reported prevalence of *Cryptosporidium* in Africa and Oceania is possibly related to the relative lack of research data.

2.2. Cryptosporidium species distributions in rodents

To date, 25 known *Cryptosporidium* species (*C. parvum*, *C. hominis*, *C. muris*, *C. tyzzeri*, *C. andersoni*, *C. meleagridis*, *C. suis*, *C. ditrichi*, *C. apodemi*, *C. scrofarum*, *C. alticolis*, *C. microti*, *C. myocastoris*, *C. ubiquitum*, *C. occultus*, *C. homai*, *C. wrairi*, *C. varanii*, *C. erinacei*, *C. canis*, *C. viatorum*, *C. proliferans*, *C. rubeyi*, *C. ratti*, and *C. ryanae*) and 43 genotypes (rat genotype II-V, bamboo rat genotype I-III, mouse genotype II, muskrat genotype I-II, skunk genotype, hamster genotype, ferret genotype, chipmunk genotype I-V, vole genotype I-VII, apodemus genotype I-II, muskrat genotype I-II, squirrel genotypes I-III, deer mouse genotype I-IV, *Cryptosporidium* sp. 1, *Cryptosporidium* sp. 2, Naruko genotype, Qinghai vole genotype, *C. muris* novel genotype, and the *C. environment* isolate) have been identified in rodents (Table 2).

Cryptosporidium species and dominant distributions differ by region. In Asia, 19 species and 15 genotypes have been identified; *C. parvum* is the dominant species. In Europe, 15 species and 16 genotypes have been identified, and *C. parvum* is the dominant species. In North America, three species and four genotypes have been identified, and *C. parvum* is the dominant species. In South America, only *C. parvum* has been detected. In Africa, two species and one genotype have been identified, and *C. andersoni* is the dominant species. In Oceania, four species and five genotypes have been identified, and *C. homai* is the dominant species (Fig. 1). The species and genotypes of *Cryptosporidium* infecting rodents in Asia and Europe are very diverse; this may be due to the comparatively large number of studies and the species richness of rodents studied. *C. parvum* has been shown to be common in rodents throughout the world; the species is similarly prevalent in humans and cattle.

2.3. Cryptosporidium in rodent types

Cryptosporidium infections have been documented 54 rodent species. According to the descriptions of the environment of the sample collection sites and details concerning rodents' living habitats listed in 86 epidemiological articles, the types of rodents can be divided into wild, domestic pet, farm, and laboratory animals. The overall prevalence rates in wild, pet, farm, and laboratory animals are 20.5% (3848/18804), 27.0% (373/1381), 14.5% (354/2439), and 2.7% (14/518), respectively (Table 1).

Table 1
Cryptosporidium species and genotypes identified in rodents in the world.

Factors			Positive/total samples (%)	Zoonotic *Cryptosporidium* spp. Positive no.
Location	Asia	China	16.8% (1010/6010)	*C. parvum* (189); *C. muris* (21); *C. tyzzeri* (13); *C. andersoni* (42); *C. suis* (1); *C. ubiquitum* (125); *C. occultus* (7); *C. erinacei* (1); *C. canis* (1); *C. viatorum* (36)
		Korea	34% (64/188)	*C. muris* (13); *C. ubiquitum* (9); Chipmunk genotype I (8)
		Philippines	26.3% (51/194)	*C. muris* (3); *C. suis* (5); *C. scrofarum* (4); *C. occultus* (1)
		Japan	25.9% (171/661)	*C. parvum* (1); *C. muris* (4); *C.meleagridis* (1); *C. ubiquitum* (14)
		Malaysia	30.9% (69/223)	*C. parvum* (12); *C. muris* (7); *C. meleagridis* (1)
		Iran	12.4% (29/234)	*C. parvum* (3); *C. muris* (21)
		Subtotal	18.6% (1394/7510)	*C. parvum* (205); *C. muris* (69); *C. meleagridis* (2); *C. tyzzeri* (13); *C. andersoni* (42); *C. suis* (6); *C. scrofarum* (4); *C. ubiquitum* (148); *C. occultus* (8); *C. erinacei* (1); *C. canis* (1); *C. viatorum* (36); Chipmunk genotype I (8)
	Europe	Poland	50.3% (863/1715)	*C. parvum* (687); *C. ubiquitum* (1)
		Finland	0.7% (2/272)	–
		Czech Republic	15.5% (219/1409)	*C. parvum* (3); *C. muris* (4); *C. tyzzeri* (44); *C. ditrichi* (21); *C. andersoni* (4); *C. ubiquitum* (1); *C. occultus* (3)
		Slovak Republic	19.4% (97/499)	*C. parvum* (15); *C. muris* (1); *C. ditrichi* (5); *C. suis* (4); *C. scrofarum* (28); *C. hominis* (2); *C. ubiquitum* (4)
		Spain	25.1% (156/621)	*C. parvum* (108); *C. muris* (18); *C. meleagridis* (1); *C. tyzzeri* (2)
		Italy	27.7% (36/130)	Chipmunk genotype I (2)
		England	27.0% (427/1580)	*C. parvum* (263); *C. muris* (73)
		Unkonw	14.6% (69/412)	*C. parvum* (2); *C. muris* (2); *C. tyzzeri* (2); *C. ditrichi* (22)
		Subtotal	28.0% (1860/6638)	*C. parvum* (1078); *C. muris* (98); *C. meleagridis* (1); *C. tyzzeri* (48); *C. ditrichi* (48); *C. andersoni* (4); *C. suis* (4); *C. scrofarum* (28); *C. hominis* (2); *C. ubiquitum* (6); *C. occultus* (3); Chipmunk genotype I (2)
	North America	America	15.2% (1265/8299)	*C. parvum* (510); *C. ubiquitum* (19); Muskrat genotype I (24); Muskrat genotype II (6); Skunk genotype (4)
		Brazil		*C. parvum* (8)

(continued on next page)

Table 1 (*continued*)

Factors			Positive/ total samples (%)	Zoonotic *Cryptosporidium* spp. Positive no.
	South America		7.3% (11/ 150)	
	Africa	Kenya	100% (1/ 1)	–
		Nigeria	1.5% (2/ 134)	*C. andersoni* (1)
		Subtotal	2.2% (3/ 135)	*C. andersoni* (1); *C. ubiquitum* (19); Muskrat genotype I (24); Muskrat genotype II (6); Skunk genotype (4)
	Oceania	New Zealand	20.0% (5/ 25)	–
		Australia	13.2% (51/ 385)	*C. tyzzeri* (6); *C. viatorum* (3)
		Subtotal	13.7% (56/ 410)	*C. tyzzeri* (6); *C. viatorum* (3)
Rodent type	Wild		20.5% (3848/ 18804)	*C. parvum* (1617); *C. muris* (145); *C. meleagridis* (3); *C. tyzzeri* (66); *C. ditrichi* (48); *C. andersoni* (3); *C. suis* (10); *C. scrofarum* (32); *C. hominis* (2); *C. ubiquitum* (37); *C. occultus* (7); *C. erinacei* (1); *C. canis* (1); *C. viatorum* (39); Muskrat genotype I (24); Muskrat genotype II (6); Skunk genotype (4); Chipmunk genotype I (10)
	Farm		14.5% (354/ 2439)	*C. parvum* (169); *C. muris* (10); *C. ubiquitum* (85); *C. occultus* (4)
	Pet		27.0% (373/ 1381)	*C. parvum* (15); *C. muris* (11); *C. andersoni* (42); *C. ubiquitum* (50)
	Lab		2.7% (14/ 518)	*C. muris* (1); *C. tyzzeri* (1); *C. andersoni* (2); *C. ubiquitum* (1)
Total			19.8% (4589/ 23142)	*C. parvum* (1801); *C. muris* (167); *C. meleagridis* (3); *C. tyzzeri* (67); *C. ditrichi* (48); *C. andersoni* (47); *C. suis* (10); *C. scrofarum* (32); *C. hominis* (2); *C. ubiquitum* (173); *C. occultus* (11); *C. erinacei* (1); *C. canis* (1); *C. viatorum* (39); Muskrat genotype I (24); Muskrat genotype II (6); Skunk genotype (4); Chipmunk genotype I (10)

Note: "–" indicates no Zoonotic *Cryptosporidium* spp.

The dominant species of *Cryptosporidium* are different in various animal types. In wild rodents, 21 species and 32 genotypes have been identified, and *C. parvum* is the dominant species. In pet rodents, 11 species and two genotypes have been identified, and *C. wrairi* is the dominant species. In farm rodents, five species and six genotypes have been identified, and *C. parvum* is the dominant species. In laboratory rodents, five species and one genotype have been identified, and *C. homai* is the dominant species. Wild and farm rodents have zoonotic potential. Pet rodents are often in close contact with humans, and the zoonotic species *C. parvum*, *C. muris*, *C. andersoni*, and *C. ubiquitum* have frequently been detected in pet rodents. Therefore, pet rodents pose a certain zoonotic risk that cannot be considered negligible.

3. Public health of zoonotic *Cryptosporidium* spp

3.1. Zoonotic Cryptosporidium spp. in humans

3.1.1. C. hominis

Although humans are the major host species for *C. hominis*, the species has been reported in a number of wildlife hosts, including rodents. To date, *C. hominis* has only been detected in wild striped field mice (*Apodemus agrarius*) in Slovakia [64,87]. Subtyping of *C. hominis* at the *gp60* locus identified nine subtype families (Ia to Ij); only the subtype IbA10G2 of *C. hominis* has been reported in wild striped field mice [64]. The subtype IbA10G2 of *C. hominis* has been identified in humans, cattle, marsupials, and the European hedgehog. This is the main subtype associated with outbreaks of cryptosporidiosis caused by *C. hominis* [64]. Although the source of *C. hominis* in wild rodents is unclear, these animals can clearly serve as potential reservoirs for this pathogen.

3.1.2. C. parvum

C. parvum is one of the two most common *Cryptosporidium* species causing human cryptosporidiosis. The parasite infects a broad range of hosts, including various bovids, camelids, equids, canids, non-human primates, and marine mammals [94]. *C. parvum* is the dominant species in rodents; at least 20 species of rodents such as rats, mice, voles, squirrels, *Rhizomys sinensis*, and *Chinchilla lanigera* are known to be positive for *C. parvum* [8,11,24,28,37,44,64,68,80,87]. *C. parvum* has been detected in wild rodents, pet rodents, and farm rodents in 14 countries [37,80,87,24,64]. Pet rodents and farm rodents have close contact with humans. Therefore, pet rodents and farm rodents are potential reservoirs of *C. parvum* and thus may play an important role in the ecology of the zoonosis.

Subtyping of *C. parvum* at the *gp60* locus identified more than 20 subtype families. Several studies that identified *C. parvum* in rodents have conducted typing at the *gp60* locus; a variety of *C. parvum* subtypes including IIaA15G2R1, IIaA16G2R1, IIaA17G2R1, IIaA18G1R1b, IIaA18G3R1, IIdA15G1, IIiA10, IIpA9, IIpA6, IIoA15G1, and IIoA13G1 have been reported from rodents [37,80,87,24,64]. The IIa, IId, IIi, and IIo subtypes were previously reported in humans [87]. *C. parvum* IIp is genetically related to the IId and IIo subtypes; they have a broad host range and the potential for human infection. Rodents are frequently infected with IIdA15G1, and the most prevalent subtype family IId in rodents is also commonly found in cattle and other livestock.

3.1.3. C. meleagridis

C. meleagridis is a common cause of cryptosporidiosis in avian hosts. This species is the third most common species involved in human cryptosporidiosis [38,80]. To date, only four cases of *C. meleagridis* have been reported in wild rodents. Japan, USA, Spain, and Malaysia have reported the presence of *C. meleagridis* in *R. norvegicus*, *Peromyscus* spp., *Rattus rattus*, and in one unidentified wild rodent species. These findings may indicate a possible role of rodents in the mechanical transmission of this pathogen [38,65,80].

3.1.4. C. viatorum

C. viatorum has been frequently identified in human and urban wastewater; however, there were no reports in any animal species other than humans prior to recent studies reporting its occurrence in wild rodents [52,66,91]. Rodent species include Edward's long-tailed rat (55.3%, 21/38) and wild rats (12.0%, 25/228) in China and swamp rats in (14.3%, 3/21) in Australia [52,66,91]. To date, nine subtypes of *C. viatorum* (XVaA3a–XVaA3g, XVaA6, and XVbA2G1) have been identified globally. Subtypes XVbA2G1, XVaA6, XVaA3g, XVaA3h, XVcA2G1, XVcA2G1a, XVcA2G1b, and XVdA3 have been found in rodents. Interestingly, subtypes XVaA3a to XVaA3f were identified only in humans. XVaA6 was isolated from wastewater, and thus the presence of the XVa subtype family in rodents suggests that wild rats may have the potential for zoonotic transmission and must be considered a potential

Table 2
Recognized *Cryptosporidium* spp. in the rodents.

Species name	Type host(s)	Major host(s)	Reports in humans	Reports in rodents Positive no.	gp60	Reference
*C. hominis**	Human (*Homo sapiens*)	Humans	Most common reported	*Apodemus agrarius* (1)	IbA10G2	[64,87]
*C. parvum**	Cattle (*Bos taurus*)	Ruminants; humans	Second most common reported	*Rattus norvegicus* (164); *Rattus rattus* (1); *Mus musculus* (60); *Apodemus flavicollis* (70); *Clethrionomys glareolus* (442); *Microtus arvalis* (203); *Apodemus sylvaticus* (132); *Mus spretus* (1); *Peromyscus* sp. (165); *Microtus pennsylvanicus* (13); *A. agrarius* (13); *Ondatra zibethicus* (8); *Spermophilus beecheyi* (149); *Sciurus carolinensis* (6); *Tamiasciurus hudsonicus* (9); *Tamias striatus* (38); *Marmota monax* (2); *Castor canadensis* (2); *Castor fiber* (16); *Erethizon dorsatum* (2); *Hydrochoerus hydrochaeris* (8); *Cavia porcellus* (1); *Chinchilla lanigera* (3); *Phodopus sungorus* (4); *Myocastor coypus* (1); *Rhizomys sinensis* (158); *Rattus tanezumi* (3); *Marmota flaviventris* (33); Wild rat (13); Qinghai vole (3)	IIaA15G2R1; IIaA16G2R1; IIaA17G2R1; IIaA18G1R1b; IIaA18G3R1; IIdA15G1; IIiA10; IIpA9; IIpA6; IIoA15G1; IIoA13G1	[5,37,80,87,24,64]
C. meleagridis	Turkey (*Meleagris gallopavo*)	Birds, humans	Commonly reported	*R. norvegicus* (1); *R. rattus* (1); Wild rat (1)	–	[38,65,80]
C. ubiquitum	Cattle (*B. taurus*)	Ruminants, rodents, primates	Commonly reported	*R. norvegicus* (1); *C. lanigera* (49); Siberian flyingsquirrel (1); *M. coypus* (5); *Callosciurus erythraeus* (19); Wild rat (10); Laboratory rats (1); Qinghai vole (1)	XIIa; XIId; XIIi	[5,11,40,42,43,46]
C. viatorum	Human (*Homo sapiens*)	Rodents	Many reported	*leopoldamys edwardsi* (11); swamp rats (3); Wild rats (25)	XVbA2G1; XVaA6; XVaA3g; XVaA3h; XVcA2G1; XVcA2G1a; XVcA2G1b; XVdA3	[52,66,91]
C.muris	House mouse (*Mus musculus*)	Rodents	Commonly reported	*R. norvegicus* (4); *R. rattus* (14); *M. musculus* (61); *A. flavicollis* (3); *C. glareolus* (2); *M. spretus* (5); *A. sylvaticus* (18); *O. zibethicus* (5); *T. striatus* (1); *P. sungorus* (8); *R. sinensis* (1); *R. tanezumi* (3); *Bandicota bengalensis* (9); *Eutamias sibiricus* (9); Wild rat (25); Laboratory rats (−); *Apodemus speciosus* (2); *C. porcellus* (1);	–	[7,8,20,27,52,59,63,87]
C. canis	Dog (*Canis familiaris*)	Dogs	Commonly reported	Qinghai vole (1)	–	[89]
C. tyzzeri	Mouse (*Mus musculus*)	Rodents	Some reported	*R. norvegicus* (1); *M. musculus* (51); *A. sylvaticus* (1); *Hystrix hodgsoni* (3); *Mus domesticus* (6);	IXa; IXb; IXc	[5,37,75]
C. andersoni	Cattle (*B. taurus*)	Cattle	Some reported [c]	*R. norvegicus* (4); *M. monax* (1); *P. sungorus* (40)	–	[40,47,70,78]
C. erinacei	European hedgehog (*Erinaceus europaeus*)	Hedgehogs, horses	Some reported	*R. tanezumi* (1)	–	[5,52]
C. suis	Pig (*Sus scrofa*)	Pig	Some reported	*A. flavicollis* (4); *Microtus brandti* (−)	–	[87]
C. ditrichi	Yellow-necked mouse (*Apodemus flavicollis*)	Rodents	Two reported	*A. flavicollis* (43); *A. sylvaticus* (4); *A. agrarius* (2)	–	[37,64]
C. occultus	Brown rat (*Rattus norvegicus*)	Rodents	Two reported	*R. norvegicus* (5); *R. sinensis* (4); *R. tanezumi* (1); Wild rats (5)	–	[5,46,49,50,52,49]
C. scrofarum	Pig (*S. scrofa*)	Pig	One reported	*A. flavicollis* (5); *M. arvalis* (4); *A. agrarius* (19)	–	[61,87]
C. ryanae	Cattle (*B. taurus*)	Cattle	None reported	*R. norvegicus* (1)	–	[13]
C wrairi	Guinea pig (*Cavia porcellus*)	Rodents	None reported	*C. porcellus* (159); *C. erythraeus* (1);	–	[40,45,47,82]
C. homai	Guinea pig (*Cavia porcellus*)	Rodents	None reported	*C. porcellus* (39)	–	[40,82]
C. apodemi	Striped field mouse (*A. agrarius*)	Rodents	None reported	*A. flavicollis* (11);*A. agrarius* (12); *A. sylvaticus* (2)	–	[37,64]
C. alticolis	Common vole (*M. arvalis*)	Rodents	None reported	*M. arvalis* (7)	–	[35]
C. microti	Common vole (*M. arvalis*)	Rodents	None reported	*M. arvalis* (46); *A. flavicollis* (2);	–	[35,37]

Table 2 (*continued*)

Species name	Type host(s)	Major host(s)	Reports in humans	Reports in rodents Positive no.	gp60	Reference
C. myocastoris	Nutria (*Myocastor coypus*)	Rodents	None reported	*M. coypus* (5)	–	[42]
C. proliferans	East African mole rat (*Tachyoryctes splendes*)	Rodents	None reported	*Tachyoryctes splendens* (−)	–	[46]
C varanii	numerous reptiles	Reptiles	None reported	*C. lanigera* (−)	–	[53]
C. rubeyi	Spermophilus ground squirrel	Rodents	None reported	*C. erythraeus* (2); Spermophilus ground squirrel (−)	–	[55,57]
C. ratti	Brown rats (*Rattus norvegicus*)	Rodents	None reported	*R. norvegicus* (37); *R. rattus* (1); *T. hudsonicus* (4); Wild rats (1)	–	[4]
Chipmunk genotype I	*Peromyscus* spp.	Rodents	Many reported	*Sciurus vulgaris* (2); Wild rat (8)	–	[32,40,44,47,48,76]
Skunk genotype	*Mephitis mephitis*	Fox, human	Many reported	*C. erythraeus* (4)	–	[77]
Muskrat genotype I	*O. zibethicus*	Rodents	One reported	*O. zibethicus* (24)	–	[29,54]
Muskrat genotype II	*O. zibethicus*	Rodents	One reported	*O. zibethicus*(6); *Microtus brandti* (−)	–	[29,54]
rat genotype II	*R. tanezumi*	Rodents	None reported	*R. norvegicus* (1); *R. rattus* (10); *M. musculus* (2); *C. erythraeus* (2); *T. hudsonicus* (8); Wild rat (19)	–	[29,43,45]
rat genotype III	*R. tanezumi*	Rodents	None reported	*R. norvegicus* (1); *R. rattus* (10); *M. musculus* (2); *R. tanezumi* (8); *leopoldamys edwardsi* (2); Muridae (2); Wild rat (23); *Hystrix hodgsoni* (1)	–	[29,43,45]
rat genotype IV	*R. tanezumi*	Rodents	None reported	*R. norvegicus* (35); *R. tanezumi* (24); *leopoldamys edwardsi* (8); Muridae (2); Wild rats (6)	–	[29,43,45]
rat genotype V	*R. tanezumi*	Rodents	None reported	*R. norvegicus* (5)	–	[29,43,45]
Bamboo rat genotypeI	*R. sinensis*	Rodents	None reported	*R. sinensis* (54)	–	[49,50]
Bamboo rat genotype II	*R. sinensis*	Rodents	None reported	*R. sinensis* (1)	–	[49,50]
Bamboo rat genotype III	*R. sinensis*	Rodents	None reported	*R. sinensis* (5)	–	[49,50]
chipmunk genotype II	*T. striatus*	Rodents	None reported	*T. striatus* (28)	–	[50,54]
chipmunk genotype III	*T. striatus*	Rodents	None reported	*T. hudsonicus* (5); *T. striatus* (1)	–	[50,54]
chipmunk genotype IV	*Eutamias sibiricus*	Rodents	None reported	*T. striatus* (−)	–	[50,54]
chipmunk genotype V	*T. striatus*	Rodents	None reported	*T. striatus* (1); *C. lanigera* (1)	–	[50,54]
Mouse genotype II	*M. domesticus*	Rodents	None reported	*M. domesticus* (11)	–	[47,77]
Muskrat genotypes I	*O. zibethicus*	Rodents	None reported	*M. arvalis* (1); *O. zibethicus* (24)	–	[29,54]
Muskrat genotypes II	*O. zibethicus*	Rodents	None reported	*Microtus brandti*(−); *O. zibethicus* (6)	–	[29,54]
Vole genotypes I	*M. pennsylvanicus*	Rodents	None reported	Meadow vole (1)	–	[35]
Vole genotypes II	*M. arvalis*	Rodents	None reported	*M. arvalis* (1)	–	[35]
Vole genotypes III	*M. arvalis*	Rodents	None reported	*M. arvalis* (1)	–	[35]
Vole genotypes IV	*M. arvalis*	Rodents	None reported	*M. arvalis* (3)	–	[35]
Vole genotypes V	*M. arvalis*	Rodents	None reported	*M. arvalis* (2)	–	[35]
Vole genotypes VI	*M. arvalis*	Rodents	None reported	*M. arvalis* (1)	–	[35]
Vole genotypes VII	*M. arvalis*	Rodents	None reported	*M. arvalis* (6)	–	[35]
Apodemus genotypes I	*Apodemus* spp.	Rodents	None reported	*A. flavicollis* (8)	XVIIa	[37]
Apodemus genotypes II	*Apodemus* spp.	Rodents; water	None reported	*A. flavicollis* (4); *A. agrarius* (5)	XVIIIa	[37]
squirrel genotype I	*S. beecheyi*	*Sciuridae* spp.	None reported	*C. erythraeus* (2)	–	[77]
squirrel genotype II	*S. beecheyi*	*Sciuridae* spp.	None reported	*C. erythraeus* (1)	–	[77]
	S. beecheyi	*Sciuridae* spp.		*C. erythraeus* (2)	–	[77]

Table 2 (*continued*)

Species name	Type host(s)	Major host(s)	Reports in humans	Reports in rodents Positive no.	gp60	Reference
squirrel genotype III			None reported			
Deer mouse genotype I	*Peromyscus* spp.	Rodents; water	None reported	Deer mouse (13)	–	[77]
Deer mouse genotype II	*Peromyscus* spp.	Rodents; water	None reported	Deer mouse (3)	–	[77]
Deer mouse genotype III	*Peromyscus* spp.	Rodents; water	None reported	*C. erythraeus* (5); Deer mouse (20)	–	[77]
Deer mouse genotype IV	*Peromyscus* spp.	Rodents; water	None reported	Deer mouse (21)	–	[77]
Cryptosporidium sp. 1	environmental sample; water	–	None reported	*R. rattus* (1)	–	[38]
Cryptosporidium sp. 2	–	–	None reported	*M. musculus* (1)	–	[5]
Qinghai vole genotype	*Microtus fuscus*	Vole	None reported	Qinghai vole (3)	–	[89]
Novel genotype of Brandt's vole	Brandt's vole	Vole	None reported	Brandt vole (−)	–	[54]
Novel genotype	*Apodemus* spp.	Vole	None reported	Wild rat (14); *A. speciosus* (2)	–	[48]
Naruko genotype	Wild rats	Rodents	None reported	Wild rats (1)	–	[79]

Note: "–" indicates unknown information; "*" indicates *Cryptosporidium* spp. that caused the outbreak of human cryptosporidiosis.

threat to human health.

3.1.5. C. ubiquitum

C. ubiquitum is considered an emerging zoonotic pathogen. The species has a broad host range that includes primates, carnivores, ruminants, and various rodents [46,94]. There are increasing research reports of *C. ubiquitum* being detected in rodents, and the host range has been expanding to include rodents such as wild squirrels, chipmunks, field mice, brown rats, *Myocastor coypus*, pet *C. lanigera*, farm bamboo rats, and laboratory mice [40,42,43,46,53,62,67,74,77,81]. In the USA, a study showed that transmission of *C. ubiquitum* to humans from rodents was likely to come from drinking untreated water contaminated by wildlife urine or feces [11].

Subtyping of *C. ubiquitum* at the *gp60* locus identified nine subtype families (XIIa–XIIi). Subtypes XIIa and XIId have been found in pet *C. lanigera* in China (1.8%, 5/280 and 6.7%, 28/420, respectively). Subtype XIID has also been found in pet *C. lanigera* in Japan (20.6%, 13/63), *M. coypus* in the Czech Republic (5.8%, 7/120), *M. coypus* in the Slovak Republic (16.7%, 5/30), and *C. lanigera* in Japan (no data); subtype XIIi has been detected in Siberian flying squirrels in China (100%, 1/1) [40,42,46,53]. Subtype XIId appears to be common in rodents, occurring in *C. ubiquitum* isolates examined in many countries [42]. Subtypes XIIa and XIId have broadly specific and zoonotic potential, but novel subtype XIIi has unknown human infective potential.

3.2. Zoonotic Cryptosporidium spp. in rodents

A number of other zoonotic *Cryptosporidium* spp. have been identified in rodents, and several have been identified in humans. Of these, *C. muris* and *C. andersoni* are gastric parasites. *C. muris* has a wide host range that includes various mammals (rodents, canids, felids, suids, equids, NHPs, and marsupials) and birds, but *C. andersoni* primarily infects cattle, while the human infectivity is controversial. *C. tyzzeri* mostly infects domestic mice and small rodents, and it has been found in several non-specific hosts such as humans, pandas, black leopards, voles, snakes, and horses, among others [94]. Subtyping of *C. tyzzeri* at the *gp60* locus identified three subtype families (IXa–IXc) that coevolved with hosts, each type having different natural host specificities [75]. Subtype IXa was restricted to the house mouse subspecies; subtype IXb was restricted to *Mus musculus domesticus*, and subtype IXc was detected only in *A. sylvaticus*.

C. suis and *C. scrofarum* are potential zoonotic species that are commonly detected in pigs. These species have been detected in rodents in Slovakia, China, and the Philippines; rodents may not be natural hosts for *C. scrofarum* and may have been infected as a result of mechanical transmission. *C. occultus* has a wide host range, mostly parasitizing rats genetically related to bamboo rats [46,49,50,52]. *C. canis* is the predominant species responsible for companion animal cryptosporidiosis, and the species has recently been reported in humans. *C. ditrichi* seems to be quite restricted to *Apodemus* spp. in Europe. The chipmunk genotype I has been identified in many rodents and in water [32,40,44,47,48,76]; this genotype is considered an emerging human pathogen. In *C. erinacei*, the skunk and muskrat genotypes I and II have also been reported in a few human cases of cryptosporidiosis.

3.3. Other Cryptosporidium species identified in rodents

Most rodent species and genotypes are host-specific or have narrow host ranges. Specific associations include *C. myocastoris* in nutrias [42]; *C. proliferans* in moles [46]; *C. alticolis*, *C. microti*, and vole genotypes I–VII in voles [29,35,37,54]; *C. apodemi* in mice [37,64]; *C. homai* and *C. wrairi* in guinea pigs [40,45,47,82]; *C. rubeyi* and squirrel genotypes I–III in ground squirrels [55,77]; *C. ratti* and mouse genotype II in rats [29,43–45]; hamster genotype in pet hamsters [40,47]; bamboo rat genotypes I–III in bamboo rats [49,50], and apodemus genotypes I and II in *Apodemus* spp. [37,48]. However, with increasing research effort, the host species ranges of these genotypes (rat genotypes II–V, ferret genotype, chipmunk genotypes II–V, muskrat genotypes I and II, and deer mouse genotypes I–IV) have gradually been extended [13,32,40,44,45,47,52,54,61,65,70,73,77].

C. varanii and *C. scrofarum* have mostly been isolated from reptiles and pigs; the presence in rodents may have been the result of mechanical transmission [53,61,87]. *Cryptosporidium* environmental has been found in wild *Apodemus* spp., suggesting that the environment plays an important role in transmission dynamics of the parasites [87]. Future studies aiming to characterize *Cryptosporidium* in environmental samples from areas with rodents are needed. The potential of these *Cryptosporidium* species and genotypes to cause disease in humans or animals is unknown, but *C. ratti*, rat genotype III, rat genotype IV, apodemus genotype II, and *Cryptosporidium* sp. 1 have been detected in streams in the USA and in raw sewage water in the UK, China, Japan, and USA [13,29,37,94]. To date, these species and genotypes have not been reported in humans, suggesting that they are unlikely to be of public health significance. However, more research is needed to confirm this.

Table 3

The prevalence of *Cryptosporidium* and *Cryptosporidium* spp. in the rodents.

Animal species	Locations total samples no.	Positive/ total samples (%)	*Cryptosporidium* species/genotypes positive no.	*gp60* subtypes
Brown Rat (*Rattus norvegicus*)	Japan (206); England (511); China (491); Iran (106); Nigeria (134); Czech Republic (−)	17.2% (249/ 1448)	*C. parvum* (164); *C. ubiquitum* (1); *C. ratti* (37); rat genotype IV (35); *C. occultus* (5); *C. tyzzeri* (1); rat genotype III (1); rat genotype V (5); *C. muris* (4); *C. andersoni* (4); rat genotype II (1); *C. meleagridis* (1); *C. ryanae* (1);	IIdA15G1
House Rat (*Rattus rattus*)	Japan (346); New Zealand (8); Spain (102); Iran (40); Australia (85)	26.3% (153/ 581)	*C. parvum* (1); rat genotype II/III (10); *C. muris* (14); *C. meleagridis* (1); *C. ratti* (1); *C.* sp. 1 (1)	–
House mouse (*Mus musculus*)	England (715); New Zealand (17); USA (303); Spain (78); Iran (63); China (31); Czech Republic (45)	22.0% (276/ 1252)	*C. muris* (61); *C. parvum* (60); *C. tyzzeri* (51); *C.* sp. 2 (1); rat genotype II (2); rat genotype III (2)	Ixa; Ixb
Yellow-necked mouse (*Apodemus flavicollis*)	Poland (331); Spain (2); Belgium (2); Czech Republic (274); Finland (2); France (16); Germany (10); Serbia (14); Slovakia (35); Slovak Republic (196)	26.2% (66/ 252)	*C. parvum* (70); *C. ditrichi* (43); *C. apodemi* (11); apodemus genotype I (8); *C. tyzzeri* (1); apodemus genotype II (4); *C. microti* (2); *C. muris* (3); *C. scrofarum* (5); *C. environment* (3); *C. suis* (4)	IXaA8; XVIIIa; XVIIa; IIaA16GlRlb; IIaA18G3R1; IIiA10
Myod glareolus (*Clethrionomys glareolus*)	Poland (836); Finland (141); Spain (49); England (123); USA (301)	30.7% (445/ 1450)	*C. parvum* (442); *C. muris* (2)	–
Common Vole (*Microtus arvalis*)	Poland (274); Czech Republic (328); Slovak Republic (75)	42.8% (290/ 677)	*C. parvum* (203); *C. alticolis* (7); *C. microti* (46); vole genotype II (1); vole genotype III (1); vole genotype IV (3); vole genotype V (2); vole genotype VI (1); vole genotype VII (6); *C. scrofarum* (4); *C. environment* (4); muskrat genotype I (3)	IIaA18G3R1; IIaA10G1R1
Common field vole (*Microtus agrestis*)	Finland (131)	0.8% (1/ 131)	–	–
Wood mice (*Apodemus sylvaticus*)	England (230); Spain (278); Czech Republic (25); France (4); Netherlands (6); Serbia (3); Slovakia (8)	30.0% (166/ 554)	*C. parvum* (132); *C. muris* (18); *C. ditrichi* (3); *C. tyzzeri* (1); *C. apodemi* (2)	IXcA6
Algerian mouse (*Mus spretus*)	Spain (22)	27.3% (6/ 22)	*C. parvum* (1); *C. muris* (5)	–
Apodemus speciosus	Japan (33)	12.1% (4/ 33)	*C. muris* (2); *C. muris* novel genotype (2)	–
White-footed mice (*Peromyscus* sp.)	USA (2706)	8.2% (222/ 2706)	*C. parvum* (165)	–
Red-backed vole (*Myodes gapperi*)	USA (5)	80.0% (4/5)	–	–
Prairie vole (*Microtus pennsylvanicus*)	USA (307)	5.2% (16/ 307)	*C. parvum* (13)	–
Striped field mouse (*Apodemus agrarius*)	Slovak Republic (107)	31.8% (34/ 107)	*C. scrofarum* (19); *C. environment* (2); muskrat genotype II (3); *C. parvum* (8); *C. hominis* (1)	IbA10G2; IIcA5G3a; IIaA18G3R1; IIiA10
Muskrat (*Ondatra zibethicus*)	Poland (9); USA (353); Spain (90)	26.3% (119/ 452)	*C. parvum* (85); *C. muris* (5); muskrat genotype I (24); muskrat genotype II (6)	–
California Ground Squirrels (*Spermophilus beecheyi*)	USA (1162)	12.8% (149/ 1162)	*C. parvum* (149)	–
Eastern Gray Squirrel (*Sciurus carolinensis*)	USA (106)	17.0% (18/ 106)	*C. parvum* (6)	–
Red squirrels (*Tamiasciurus hudsonicus*)	USA (80); China (333)	9.4% (39/ 413)	*C. parvum* (9); rat genotype II (8); ferret genotype (13); chipmunk genotype III (5); *C. ratti* (4);	–
Eurasian Red Squirrel (*Sciurus vulgaris*)	Italia (70); USA (2)	25.0% (18/ 72)	ferret genotype (15); chipmunk genotype I (2)	–
Eastern chipmunks (*Tamias striatus*)	USA (268); China (20)	23.0% (66/ 288)	*C. parvum* (38); ferret genotype (3); ferret genotype + *C. parvum* (1); *C. muris* + *C. parvum* + chipmunk genotype III (1); chipmunk genotype II (28); chipmunk genotype IV (−)	–
Woodchuck (*Marmota monax*)	USA (38); Czech Republic (−)	7.9% (3/38)	*C. parvum* (2); *C. andersoni* (1)	–
American Beaver (*Castor canadensis*)	USA (170)	4.1% (7/ 170)	*C. parvum* (2)	–
Eurasian Beaver (*Castor fiber*)	Poland (82); Slovak Republic (19)	19.8% (20/ 101)	*C. parvum* (16)	–
North American Porcupine (*Erethizon dorsatum*)	USA (18)	11.1% (2/ 18)	*C. parvum* (2)	–
Capybara (*Hydrochoerus hydrochaeris*)	Brazil (145)	5.5% (8/ 145)	*C. parvum* (8)	–
Root rat (*Tachyoryctes splendens*)	Kenya (−)	–	*C. proliferans*	–
Striped field mouse (*A. agrarius*)		16.8% (21/ 125)	apodemus genotype II (5); *C. ditrichi* (2); *C. apodemi* (12); *C. parvum* (1); *C. hominis* (1)	XVIIIa; IIaA16G1R1b; IbA10G2

Table 3 (*continued*)

Animal species	Locations total samples no.	Positive/ total samples (%)	*Cryptosporidium* species/genotypes positive no.	*gp60* subtypes
	Latvia (11); Lithuania (3); Romania (2); Serbia (4); Slovakia (33); Slovak Republic (72)			
Guinea pig (*Cavia porcellus*)	China (350); Australia (29); Italia (60); Brazil (5); England (1)	50.8% (226/445)	*C.rairi* (159); *C. homai* (39); *C. muris* (1); *C. parvum* (1)	–
Chinchillas (*Chinchilla lanigera*)	China (420); Japan (63)	11.0% (53/483)	*C. ubiquitum* (49); *C. parvum* (3); chipmunk genotype V (1); *C. varanii* (−)	–
Djungarian Hamster (*Phodopus sungorus*)	China (226)	38.9% (88/226)	hamster genotype (31); *C. andersoni* (40); *C. muris* (8); *C. parvum* (4); *C. andersoni* + *C. parvum* (2); *C. muris* + *C. parvum* (2);	–
Chipmunk (*Tamias*)	China (4)	75.0% (3/4)	ferret genotype (2); chipmunk genotype V (1)	–
Pteromys volans (*Siberian flyingsquirrel*)	China (1)	100% (1/1)	*C. ubiquitum* (1)	XIIi
Cricetid rodents	USA (586); Czech Republic (493)	33.2% (362/1089)	–	–
Nutria (*Myocastor coypus*)	Czech Republic (120); Slovak Republic (30)	8.0% (12/150)	*C. parvum* (1); *C. ubiquitum* (5); *C. myocastoris* (5)	IIa; XXIIb; XXIIa; XIId;
Red-bellied treesquirrels (*Callosciurus erythraeus*)	China (287); USA (302)	23.1% (136/589)	*C. parvum* (1); *C. wrairi* (1); rat genotype II (2); *C. rubeyi* (2); squirrel genotypes I (2); squirrel genotypes II (1); squirrel genotypes III (2); *C. ubiquitum* (19); skunk genotype (4); deer mouse genotype III (5)	–
Bamboo rat (*Rhizomys sinensis*)	China (1960)	15.8% (309/1960)	*C. parvum* (158); *C. occultus* (4); *C. ubiquitum* (85); bamboo rat genotype I (54); bamboo rat genotype II (1); bamboo rat genotype III (5); *C. muris* (1)	IIpA9; IIpA6; IIoA15G1; IIoA13G1
Porcupine (*Hystrix hodgsoni*)	China (147)	6.8% (10/147)	*C. tyzzeri* (3); rat genotype III (1)	–
Asian house rat (*Rattus tanezumi*)	China (79)	50.6% (40/79)	rat genotype IV (24); rat genotype III (8); *C. occultus* (1); *C. erinacei* (1); *C. parvum* (3); *C. muris* (3)	–
Edward's long-tailed rat (*leopoldamys edwardsi*)	China (38)	55.3% (21/38)	*C. viatorum* (11); rat genotype IV (8); rat genotype III (2)	XVcA2G1a (4); XVcA2G1b (1); XVdA3 (1)
Muridae	China (10)	40.0% (4/10)	rat genotype III (2); rat genotype IV (2)	–
Brandt vole (*Microtus brandti*)	China (678)	18.7% (127/678)	*C. suis*, *C. environmental*; muskrat genotype II; novel genotype of Brandt's vole	–
Spermophilus ground squirrel	USA (−)	–	*C. rubeyi* (−)	–
White-footed Mouse (*Peromyscus maniculatus*)	USA (1071)	6.9% (74/1071)	–	–
Yellow-bellied Marmot (*Marmota flaviventris*)	USA (224)	14.7% (33/224)	*C. parvum* (33)	–
Australian Mice (*Mus domesticus*)	Australia (250)	7.6% (19/250)	*C. tyzzeri* (6); mouse genotype II (11)	–
Indian mole rat (*Bandicota bengalensis*)	Iran (25)	36.0% (9/25)	*C. muris* (9)	–
Asian chipmunk (*Eutamias sibiricus*)	Czech Republic (−)	–	*C. muris* (−)	–
Qinghai vole (*Lasiopodomys fuscus*)	China (90)	8.9% (8/90)	*C. parvum* (3); *C. canis* (1); *C. ubiquitum* (1); Qinghai vole genotype (3)	–
Swamp rats	Australia (21)	14.3% (3/21)	*C. viatorum* (3)	XVbA2G1
Prairie vole (*Meadow vole*)	USA (10)	10.0% (1/10)	Vole genotype I (1)	–
Deer mouse	USA (177)	32.2% (57/177)	Deer mouse I (13); Deer mouse II (3); Deer mouse III (20); Deer mouse IV (21);	–
Laboratory rats	China (355); Czech Republic (−)	0.6% (2/355)	*C. ubiquitum* (1); *Cryptosporidium* spp. (1); *C. muris* (−)	
Wild rats	Philippines (194); Japan (14); China (228); Poland (266); Malaysia (223); Korea (188)	33.0% (387/1173)	*C. muris* (25); *C. scrofarum* (4); *C. ratti* (1); rat genotypes II (19); rat genotypes III (23); rat genotypes IV (6); *C. occultus* (5); *C. ubiquitum* (10); Naruko genotype (1); *C. viatorum* (25); *C. parvum* (13); *C. meleagridis* (1); chipmunk genotype I (8); bear genotype (14).	XVaA6; XVaA3g; XVaA3h; XVcA2G1; IIaA15G2R1; IIaA17G2R1; IIaA16G3R1

Note: "-" indicates unknown information.

4. Ecological significance from a One Health perspective

Rodents are essential components of many terrestrial ecosystems. Their beneficial activities in nature are well known, as is their transmission potential of pathogens to humans [92,98–101]. Rodent transfer of pathogens to humans occurs by direct contact with humans and animals or through contamination of human or animal food and water by rodent stools, hair, and urine [9,98,99]. Rodents live in close
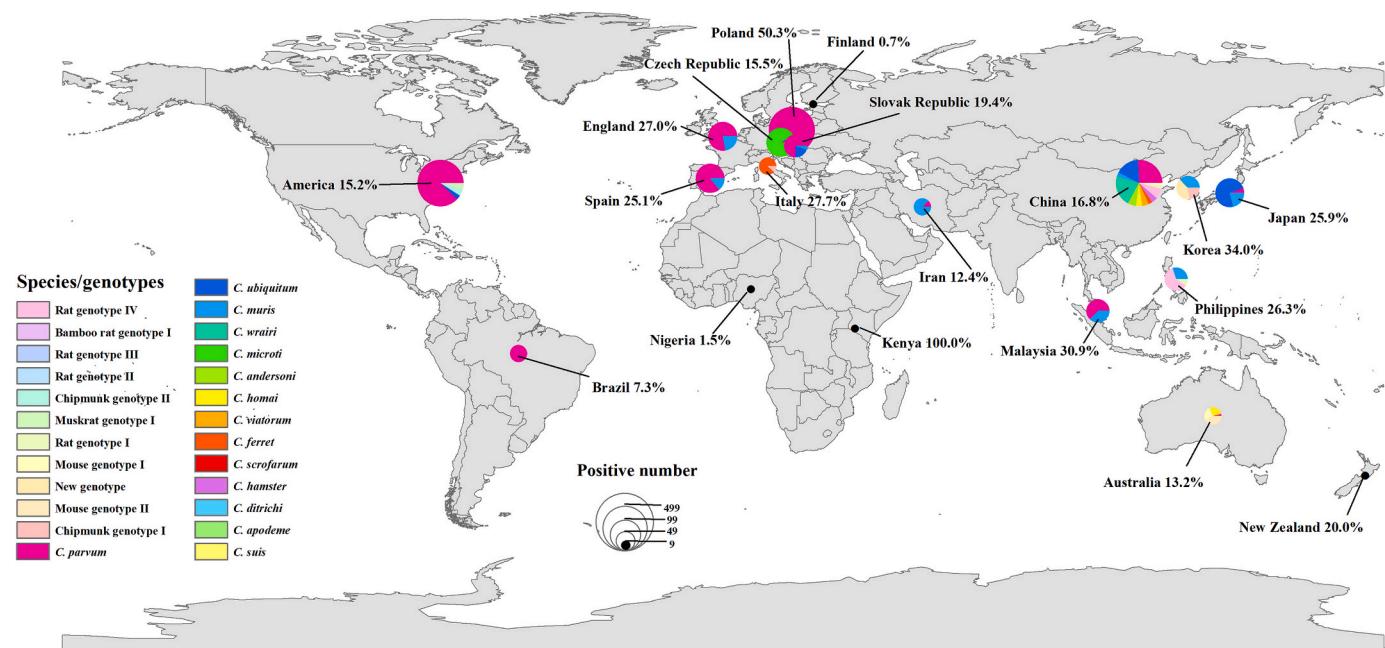
Fig. 1. Prevalence and geographic distribution of *Cryptosporidium* spp. in rodents. The figure was originally designed by the authors using ArcGIS 10.2 software. The original vector diagram imported in ArcGIS was adapted from Natural Earth (http://www.naturalearthdata.com).

contact with human populations; farm animals, pets, and peri-urban rodents provide a nexus between wildlife communities and humans, exposing humans to some zoonoses circulating in these natural ecosystems [99]. Rodent-borne diseases are associated with the rodent population and human socioeconomic lifestyle factors [11]. Human migration, travel, trade, urbanization, and agricultural activities can be facilitating factors in transferring rodent-borne pathogens from one community to another.

4.1. Possible direct transmission of rodent-borne Cryptosporidium at the human–animal–environment interface

Data obtained thus far suggest that rodents may play a role in the transmission of zoonotic *Cryptosporidium* spp. The first pathway is the direct route in which humans come in contact with *Cryptosporidium* present in rodent excrement or in an environmental component (food, water, or soil) that is contaminated with rodent urine. Moreover, humans may consume food products or water that is contaminated with rodent feces. Wild rodents are commonly found in urban and rural areas, thus providing a link between rural and urban disease foci [99]. Rodents often occur in the streets of cities or are hidden in food stores, granaries, and kitchens in rural areas, and they inhabit farmland, forests, and other natural environments. Their fecal droppings may be left wherever they forage, thus contaminating human and animal feed stores and accommodations. This can contribute to many of the sporadic human cases of cryptosporidiosis in urban and rural areas [99,98].

C. ditrichi oocysts were detected in the feces of decoration workers in Sweden. Epidemiological data indicated that the workers shared the same room with wild mice when they were working and thus had contact with mouse feces [37]. Humans can be directly infected with *Cryptosporidium* through contact with rodent feces. Humans often live closely with pet rodents; feeding, handling of rodents, close contact with feces, or playing with rodents can directly cause humans to be infected with *Cryptosporidium* (Fig. 2). At the same time, pet rodents excrete feces during family activities and thus contaminate the home environment (food, water, and the ground). Humans can become infected with *Cryptosporidium* by contact with an environment that is contaminated with rodent excrement. Laboratory and farm rodents have close contact

with the breeder, and thus the breeder may be directly infected with *Cryptosporidium* by contacting rodent feces.

4.2. Possible waterborne transmission of rodent-borne Cryptosporidium at the human–animal–environment interface

Cryptosporidium is one of the most prevalent waterborne parasitic infections. *Cryptosporidium* spores can be transported into water bodies and become waterborne pathogens [94,95]. *C. ubiquitum* has been found in untreated drinking water in the USA. *C. viatorum*, the chipmunk genotype I, and the muskrat genotypes I and II have also been found in water [4,11,29,32,54]. These species and genotypes have zoonotic potential, and they can be transmitted to humans through drinking water or recreational waters (Fig. 2). To date, *C. parvum* and *C. hominis* have been responsible for all typed waterborne outbreaks [94]. Although *C. parvum* and *C. hominis* have not been detected in surface water contaminated by rodents or in the watershed within the living range of rodents, this may be due to fewer relevant studies; it is still a public health problem that cannot be ignored. Rodents contributing to *Cryptosporidium* contamination in water may have major public health significance since rodents are generally infected with human-pathogenic species and genotypes.

4.3. Possible foodborne transmission of rodent-borne Cryptosporidium at the human–animal–environment interface

Foodborne illnesses are any infections or diseases caused by consuming contaminated foods or drinks. Almost all reported *Cryptosporidium* cases of foodborne diseases are caused by *C. parvum* [5,97]. *Cryptosporidium* foodborne illnesses commonly involve contaminated water supplies, fresh fruits, and vegetables [10,11,92]. Polluted waters may contaminate food through the process of irrigating crops and washing vegetables, thereby causing foodborne transmission [3] (Fig. 2). Rats within fields excrete feces ubiquitously, thereby increasing the risk for human foodborne illness, particularly if harvested products are to be consumed raw [3]. It is difficult to remove *Cryptosporidium* oocysts from the surfaces of vegetables and fruits using common cleaning methods. Humans may ingest *Cryptosporidium* under unknown
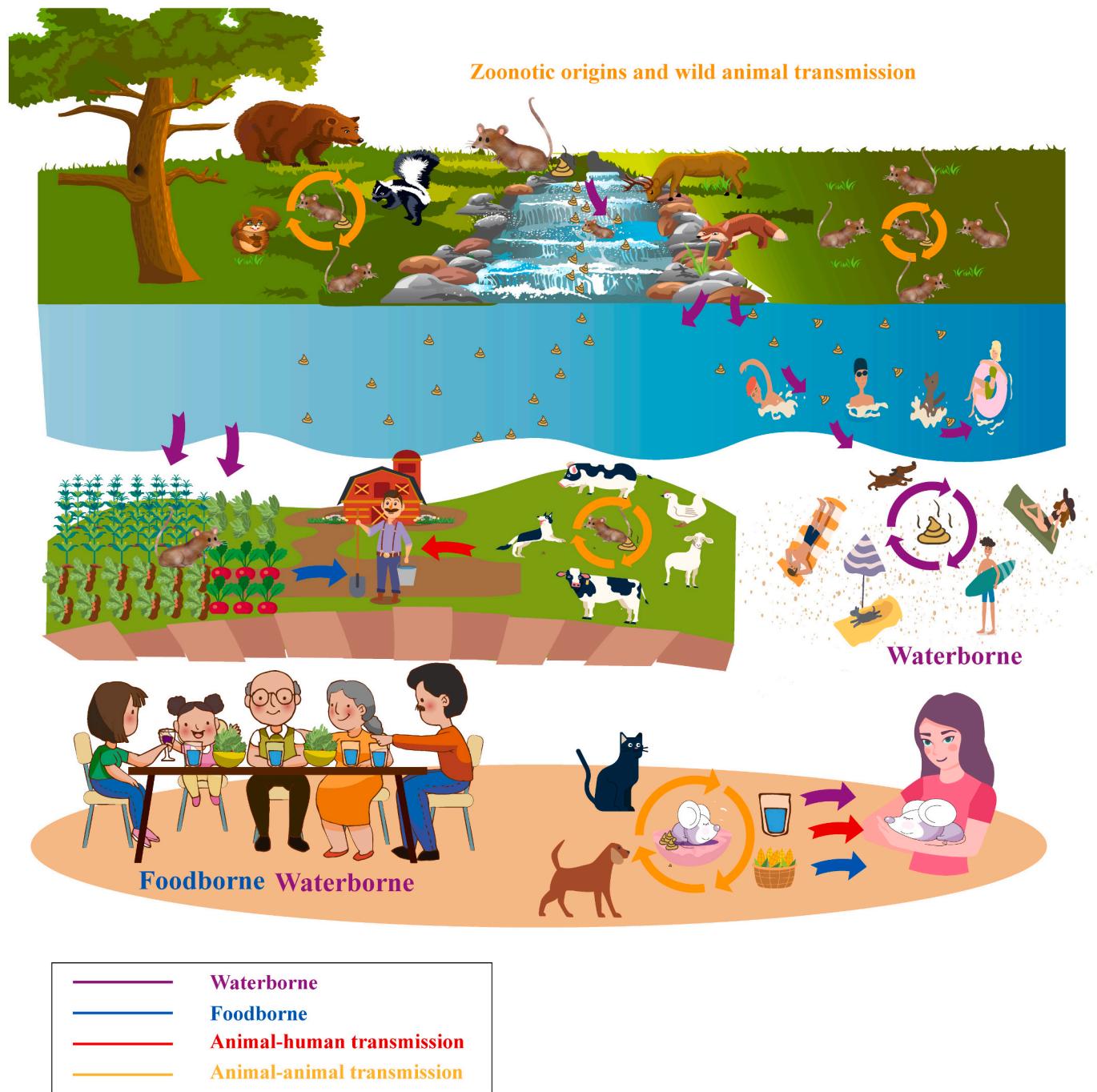
Fig. 2. Schematic diagram showing the ecological and public health significance of *Cryptosporidium* in rodents and the major routes of transmission. Possible direct, indirect, waterborne, and foodborne transmission of rodent-borne *Cryptosporidium* at the human–animal–environment interface.

circumstances. Unfortunately, there is little relevant research in this area, and thus more research is needed to better understand the potential health risks.

4.4. Possible indirect transmission of rodent-borne Cryptosporidium at the human–animal–environment interface

Rodent-borne pathogens can also be spread indirectly to humans. At least 25 species and 43 genotypes of *Cryptosporidium* have been detected in rodents; some are zoonotic and can cross the species barrier. In addition to humans, rodent-related zoonotic species and genotypes of *Cryptosporidium* are present among wildlife, livestock, farm captive animals, and companion animals (Fig. 2). Moreover, rodents can maintain

pathogen transmission cycles in different environments. Rodents can serve as potential mediators of *Cryptosporidium* and can transmit the parasites to wildlife, livestock, farm captive animals, and companion animals.

The risk of *Cryptosporidium* spreading within a rodent colony is elevated in rodent farms (*Cavia porcellus*, *R. sinensis*, and *Rattus tanezumi*) and laboratory rats that achieve high rodent densities whereby collective fecal production by a cohort, social behaviors (grooming and licking), and close interactions can promote intraspecific transmission, fecal shedding, and environmental persistence of *Cryptosporidium*. Coprophagia, a common behavior in a variety of rodent species, is a significant route for autoinfection of fecal-orally transmitted *Cryptosporidium* and can amplify *Cryptosporidium* shedding and disease spread

within a rodent colony [92,99]. Wild rats leave many small droppings wherever they forage (including watersheds) in wild areas. Wildlife and domestic animals can become infected with *Cryptosporidium* by ingesting contaminated food, water, and rodents (possible in carnivores) and thereby transfer the pathogens. At the same time, pet rodents excrete feces during family activities, possibly causing dogs or cats to be infected with *Cryptosporidium*. Ultimately, humans may be indirectly infected with *Cryptosporidium* through contact with wildlife, livestock, and companion animals or contaminated environments.

Wild rodents may spread *Cryptosporidium* on farms. This risk may be even greater on captive animal farms where wild rats can share the habitat with farm animals or travel through grazing land used by domestic animals where contact with livestock is more likely, thus providing ample opportunity for transmission of *Cryptosporidium* to the livestock. Infected wild rodents on livestock farms can potentially transmit pathogens to the livestock by contaminating animal feed and water sources with fecal pellets. Horizontal transmission by infected captive animals on farms can amplify *Cryptosporidium* shedding and disease spread. Additionally, rodenticides are used less often on farms, further increasing the possibility of *Cryptosporidium* spreading. Rodents may also acquire enteric microbes from livestock and amplify and mechanically vector the pathogens across agricultural landscapes, thereby facilitating the spread of disease [2]. Ultimately, breeders may be indirectly infected with *Cryptosporidium* through contact with farm animals and contaminated environments.

5. Conclusions

Cryptosporidium spp. are common in rodents. To date, 25 *Cryptosporidium* species and 43 genotypes have been identified in rodents, including the species that cause outbreaks of human cryptosporidiosis, *C. parvum* and *C. hominis*. *C. parvum* is the dominant species in rodents. The fact that zoonotic *C. parvum*, *C. hominis*, *C. meleagridis*, and *C. ubiquitum*, particularly subtypes IbA10G2 and IIdA15G1, have been found in rodents suggests that rodents infected with *Cryptosporidium* have significant zoonotic potential. For *Cryptosporidium* at the human–animal–environment interface, rodents can be a direct route or can become potential mediators in parasite transmission. There is no direct evidence with which to illustrate the transmission pathways of *Cryptosporidium* at the human–animal–environment interface. In addition to rodents, dogs, cats, wild animals, and livestock animals can be involved in the transmission cycle. Studies are required to investigate *Cryptosporidium* among the diverse human population, livestock, pet animals, and rodents in various ecosystems. Researchers should pursue a multidisciplinary One Health approach with contributions from zoologists, ecologists, veterinarians, and public health experts to understand rodent-related *Cryptosporidium* and possible transmission routes.

Search strategy

We conducted a systematic literature search from June 20, 2021 to June 26, 2021 through four databases: PubMed, Scopus, Science Direct, and Web of Science. The search included original field epidemiological articles in English for each of the 86 rodent-*Cryptosporidium* diseases individually, with no time limit of publication (Supplementary Table S1). The search terms included *Cryptosporidium* or Cryptosporidiosis and scientific names of animal species We screened the searches as "Title/Abstract" in PubMed, "Find articles with these terms" in Science Direct, "TITLE-ABS-KEY" in Scopus, and "Topic" in Web of Science.

Funding

Supplementary data to this article can be found online at https://doi.org/10.1016/j.onehlt.2021.100364.

Declaration of Competing Interest

The authors declare that no competing interests exist.

Acknowledgments

References

[1] C. Tallant, P. Huddleston, A. Alshanberi, S. Misra, Acute, Severe Cryptosporidiosis in an Immunocompetent Pediatric Patient, Clin. Pract. 6 (2) (2016) 837.

[2] K. Donskow, A. Bajer, M. Bednarska, E. Siński, Experimental transmission of *Cryptosporidium parvum* isolates from wild rodents and calves to laboratory bred common voles (*Microtus arvalis*), Acta Parasitol. 50 (1) (2005) 19–24.

[3] C. Kilonzo, Epidemiology of Foodborne Pathogens in Wild Rodents in a Major Agricultural Region of the California Central Coast, University of California, Davis, 2015.

[4] Y. Feng, K.A. Alderisio, W. Yang, L.A. Blancero, W.G. Kuhne, C.A. Nadareski, *Cryptosporidium* Genotypes in Wildlife from a New York Watershed, Appl. Environ. Microbiol. 73 (20) (2007) 6475.

[5] R. Åberg, M. Sjöman, K. Hemminki, A. Pirnes, S. Räsänen, A. Kalanti, et al., *Cryptosporidium* parvum Caused a Large Outbreak Linked to Frisée Salad in Finland, 2012, Zoonoses Public Health 62 (8) (2015) 618–624.

[7] R.M. Chalmers, A.P. Sturdee, S.A. Bull, A. Miller, S.E. Wright, The prevalence of *Cryptosporidium parvum* and *C. muris* in *Mus domesticus*, *Apodemus sylvaticus* and *Clethrionomys glareolus* in an agricultural system, Parasitol. Res. 83 (5) (1997) 478–482.

[8] J. Torres, M. Gracenea, M.S. Gómez, A. Arrizabalaga, O. González-Moreno, The occurrence of *Cryptosporidium parvum* and *C. muris* in wild rodents and insectivores in Spain, Vet. Parasitol. 92 (4) (2000) 253–260.

[9] T.M. Strand, Å. Lundkvist, Rat-borne diseases at the horizon. A systematic review on infectious agents carried by rats in Europe 1995-2016, Infect. Ecol. Epidemiol. 9 (1) (2019) 1553461.

[10] A. Rzezutka, R.A. Nichols, L. Connelly, A. Kaupke, I. Kozyra, N. Cook, et al., *Cryptosporidium* oocysts on fresh produce from areas of high livestock production in Poland, Int. J. Food Microbiol. 139 (1–2) (2010) 96–101.

[11] K. Hamidi, How do Rodents Play Role in Transmission of Foodborne Diseases, Nutr Food Sci, Int. J. 6 (2018) 1–4.

[12] S.P. O'Hara, X.M. Chen, The cell biology of *Cryptosporidium* infection, Microbes Infect. 13 (8–9) (2011) 721–730.

[13] J. Ježková, J. Prediger, N. Holubová, B. Sak, R. Konečný, Y. Feng, et al., *Cryptosporidium ratti* n. sp. (Apicomplexa: Cryptosporidiidae) and genetic diversity of *Cryptosporidium* spp. in brown rats (*Rattus norvegicus*) in the Czech Republic, Parasitol. 148 (1) (2020) 1–45.

[20] P.H. Klesius, T.B. Haynes, L.K. Malo, Infectivity of *Cryptosporidium* sp. isolated from wild mice for calves and mice, J. Am. Vet. Med. Assoc. 189 (2) (1986) 192–193.

[24] E. Siński, M. Bednarska, A. Bajer, The role of wild rodents in ecology of Cryptosporidiosis in Poland, Folia Parasitol. 45 (2) (1998) 173–174, https://doi.org/10.1006/expr.1998.4215.

[27] Y. Nakai, K. Hikosaka, M. Sato, T. Sasaki, Y. Kaneta, N. Okazaki, Detection of *Cryptosporidium muris* Type Oocysts from Beef Cattle in a Farm and from Domestic and Wild Animals in and around the Farm (Parasitology), J. Vet. Med. Sci. 66 (8) (2004) 983–984.

[28] J.F. Perz, S. Blancq, *Cryptosporidium* parvum Infection Involving Novel in Wildlife from Lower New York State, Appl. Environ. Microbiol. 67 (3) (2001) 1154–1162, https://doi.org/10.1128/AEM. 67.3.1154-1162.2001.

[29] L. Zhou, R. Fayer, J.M. Trout, U.M. Ryan, F.W. Schaefer, L. Xiao, Genotypes of *Cryptosporidium* species infecting fur-bearing mammals differ from those of species infecting humans, Appl. Environ. Microbiol. 70 (12) (2004) 7574–7577.

[32] M. Kvác, L. Hofmannová, S. Bertolino, L. Wauters, G. Tosi, D. Modrý, Natural infection with two genotypes of *Cryptosporidium* in red squirrels (*Sciurus vulgaris*) in Italy, Folia Parasitol. 55 (2) (2008) 95–99.

[35] M. Horčičková, Š. Čondlová, N. Holubová, B. Sak, D. Květoňová, L. Hlásková, et al., Diversity of *Cryptosporidium* in common voles and description of *Cryptosporidium alticolis* sp. n. and *Cryptosporidium microti* sp. n. (Apicomplexa: Cryptosporidiidae), Parasitol. 146 (2) (2008) 220–233.

[37] Š. Čondlová, M. Horčičková, N. Havrdová, B. Sak, L. Hlásková, A. Perec-Matysiak, et al., Diversity of *Cryptosporidium* spp. in *Apodemus* spp. in Europe, Eur. J. Protistol. 69 (2019) 1–13, https://doi.org/10.1016/j.ejop.2019.02.005.

[38] L.K. García, A.A. Martín, P. Foronda, Diversity of *Cryptosporidium* spp. in wild rodents from the Canary Islands, Spain, Parasit. Vectors 13 (1) (2020) 445.

[40] J. Chen, W. Wang, Y. Lin, L. Sun, N. Li, Y. Guo, et al., Genetic characterizations of *Cryptosporidium* spp. from pet rodents indicate high zoonotic potential of pathogens from chinchillas, One Health. 13 (2021), 100269.

[42] J. Ježková, Z. Limpouchová, N. Prediger, N. Holubová, B. Sak, R. Konečný, et al., *Cryptosporidium myocastoris* n. sp. (Apicomplexa: Cryptosporidiidae), the Species Adapted to the Nutria (*Myocastor coypus*), Microorganisms. 9 (4) (2021) 813.

[43] W. Zhao, J. Wang, G. Ren, Z. Yang, F. Yang, W. Zhang, et al., Molecular characterizations of *Cryptosporidium* spp. and *Enterocytozoon bieneusi* in brown rats (*Rattus norvegicus*) from Heilongjiang Province, China, Parasit. Vectors 11 (1) (2018) 313.

[44] L. Deng, Y. Chai, R. Luo, L. Yang, J. Yao, Z. Zhong, et al., Occurrence and genetic characteristics of *Cryptosporidium* spp. and *Enterocytozoon bieneusi* in pet red squirrels (*Sciurus vulgaris*) in China, Sci. Rep. 10 (1) (2020), 1026.

[45] Y. Chai, L. Deng, H. Liu, J. Yao, Z. Zhong, L. Xiang, et al., First detection of *Cryptosporidium* spp. in red-bellied tree squirrels (*Callosciurus erythraeus*) in China, Parasite. 26 (2019) 28.

[46] F. Li, Z. Zhang, S. Hu, W. Zhao, J. Zhao, M. Kváč, et al., Common occurrence of divergent *Cryptosporidium* species and *Cryptosporidium parvum* subtypes in farmed bamboo rats (*Rhizomys sinensis*), Parasit. Vectors 13 (1) (2020) 149.

[47] C. Lv, L. Zhang, R. Wang, F. Jian, S. Zhang, C. Ning, et al., *Cryptosporidium* spp. in Wild, Laboratory, and Pet Rodents in China: prevalence and molecular characterization, Appl. Environ. Microbiol. 75 (24) (2009) 7692–7699.

[48] J. Song, C.Y. Kim, S.N. Chang, T.S. Abdelkader, J. Han, T.H. Kim, et al., Detection and Molecular Characterization of *Cryptosporidium* spp. from Wild Rodents and Insectivores in South Korea, Korean J. Parasitol. 53 (6) (2015) 737–743.

[49] Z. Wei, Q. Liu, W. Zhao, X. Jiang, Y. Zhang, A. Zhao, et al., Prevalence and diversity of *Cryptosporidium* spp. in bamboo rats (*Rhizomys sinensis*) in South Central China, Int. J. Parasitol. Parasites Wildl. 9 (2019) 312–316.

[50] F. Li, W. Zhao, C. Zhang, Y. Guo, N. Li, L. Xiao, et al., *Cryptosporidium* Species and *C. parvum* Subtypes in Farmed Bamboo Rats, Pathogens 9 (12) (2020) 1018.

[52] W. Zhao, H. Zhou, Y. Huang, L. Xu, L. Rao, S. Wang, et al., *Cryptosporidium* spp. in wild rats (*Rattus* spp.) from the Hainan Province, China: Molecular detection, species/genotype identification and implications for public health, Int. J. Parasitol. Parasites Wildl. 9 (C) (2019) 317–321.

[53] J. Melicherová, J. Ilgová, M. Kváč, B. Sak, B. Koudela, A. Valigurová, Life cycle of *Cryptosporidium muris* in two rodents with different responses to parasitization, Parasitol. 141 (2) (2014) 287–303.

[54] S. Feng, H. Chang, Y. Wang, C. Huang, S. Han, H. He, Molecular Characterization of *Cryptosporidium* spp. in Brandt's Vole in China, Front. Vet. Sci. 7 (2020) 300.

[55] X. Li, M.D. Pereira, R. Larsen, C. Xiao, R. Phillips, K. Striby, et al., *Cryptosporidium rubeyi* n. sp. (Apicomplexa: Cryptosporidiidae) in multiple Spermophilus ground squirrel species, Int. J. Parasitol. Parasites Wildl. 4 (3) (2015) 343–350.

[57] L.D. Montecino, X. Li, C. Xiao, E.R. Atwill, Elevation and vegetation determine *Cryptosporidium* oocyst shedding by yellow-bellied marmots (*Marmota flaviventris*) in the Sierra Nevada Mountains, Int. J. Parasitol. Parasites Wildl. 4 (2) (2015) 171–177.

[59] S.K. Brar, L.D. Singla, Concurrent infection of *Cryptosporidium* and *Giardia* in synanthropic rodents: First report from Punjab, India, Indian J. Vet. Sci. Biotechnol. 17 (1) (2021) 1–3.

[61] J.S. Ng-Hublin, G.R. Singleton, U. Ryan, Molecular characterization of *Cryptosporidium spp.* from wild rats and mice from rural communities in the Philippines, Infect. Genet. Evol. 16 (2013) 5–12.

[62] F. Murakoshi, Y. Fukuda, R. Matsubara, Y. Kato, T. Sato, T. Sasaki, et al., Detection and genotyping of *Cryptosporidium* spp. in large Japanese field mice, *Apodemus speciosus*, Vet. Parasitol. 196 (1−2) (2013) 184–188.

[63] Z. Zhao, R. Wang, W. Zhao, M. Qi, J. Zhao, L. Zhang, et al., Genotyping and subtyping of *Giardia* and *Cryptosporidium* isolates from commensal rodents in China, Parasitology. 142 (6) (2015) 800–806.

[64] Š. Čondlová, M. Horčičková, B. Sak, D. Květoňová, L. Hlásková, R. Konečný, et al., *Cryptosporidium apodemi* n. sp. and *Cryptosporidium ditrichi* sp. n. (Apicomplexa: Cryptosporidiidae) in *Apodemus* spp, Eur. J. Protistol. 63 (2018) 1–12.

[65] T.K. Tan, V.L. Low, W.H. Ng, J. Ibrahim, D. Wang, C.H. Tan, et al., Occurrence of zoonotic *Cryptosporidium* and *Giardia duodenalis* species/genotypes in urban rodents, Parasitol. Int. 69 (2019) 110–113.

[66] Y.W. Chen, W.B. Zheng, N.Z. Zhang, B.Z. Gui, Q.Y. Lv, J.Q. Yan, et al., Identification of *Cryptosporidium viatorum* XVa subtype family in two wild rat species in China, Parasit. Vectors 12 (1) (2019) 502.

[67] A.P. Matysiak, G.K. Buńkowska, G. Zaleśny, J. Hildebrand, Small rodents as reservoirs of *Cryptosporidium* spp. and *Giardia* spp. in south-western Poland, Ann. Agric. Environ. Med. 22 (1) (2015) 1–5.

[68] J. Bystrianska, I. Papajová, Ľ. Šmiga, J. Šoltys, V. Majláthová, I. Majláth, et al., First report on parasites of European beavers in the Slovak Republic, Parasitol. Res. 120 (1) (2020) 355–358.

[70] A.B. Ayinmode, N.F. Ogbonna, G. Widmer, Detection and molecular identification of *Cryptosporidium* species in laboratory rats (*Rattus norvegicus*) in Ibadan, Nigeria, Ann. Parasitol. 63 (2) (2017) 105–109.

[73] A. Paparini, B. Jackson, S. Ward, S. Young, U. Ryan, Multiple *Cryptosporidium* genotypes detected in wild black rats (*Rattus rattus*) from northern Australia, Exp. Parasitol. 131 (4) (2012) 404–412.

[74] M. Qi, N. Luo, H. Wang, F. Yu, R. Wang, J. Huang, et al., Zoonotic *Cryptosporidium* spp. and *Enterocytozoon bieneusi* in pet chinchillas (*Chinchilla lanigera*) in China, Parasitol. Int. 64 (2015) 339–341.

[75] X. Ren, J. Zhao, L. Zhang, C. Ning, F. Jian, R. Wang, et al., *Cryptosporidium tyzzeri* n. sp. (Apicomplexa: Cryptosporidiidae) in domestic mice (*Mus musculus*), Exp. Parasitol. 130 (3) (2012) 274–281.

[76] B.L. Stenger, M.E. Clark, M. Kváč, E. Khan, C.W. Giddings, N.W. Dyer, et al., Highly divergent 18S rRNA gene paralogs in a *Cryptosporidium* genotype from eastern chipmunks (*Tamias striatus*), Infect. Genet. Evol. 32 (2015) 113–123.

[77] B.L.S. Stenger, M.E. Clark, M. Kváč, E. Khan, C.W. Giddings, J. Prediger, North American tree squirrels and ground squirrels with overlapping ranges host different *Cryptosporidium* species and genotypes, Infect. Genet. Evol. 36 (2015) 287–293.

[78] U. Ryan, L. Xiao, C. Read, L. Zhou, A.A. Lal, I. Pavlasek, Identification of Novel *Cryptosporidium* Genotypes from the Czech Republic, Appl. Environ. Microbiol. 69 (7) (2003) 4302–4307.

[79] K. Hikosaka, Y. Nakai, A novel genotype of *Cryptosporidium muris* from large Japanese field mice, *Apodemus speciosus*, Parasitol. Res. 97 (5) (2005) 373–379.

[80] A. Kimura, A. Edagawa, K. Okada, A. Takimoto, S. Yonesho, P. Karanis, et al., Detection and genotyping of *Cryptosporidium* from brown rats (*Rattus norvegicus*) captured in an urban area of Japan, Parasitol. Res. 100 (6) (2007) 1417–1420.

[81] Y. Koyama, M. Satoh, K. Maekawa, K. Hikosaka, Y. Nakai, Isolation of *Cryptosporidium andersoni* Kawatabi type in a slaughterhouse in the northern island of Japan, Vet. Parasitol. 130 (3–4) (2005) 323–326.

[82] A. Zahedi, Z. Durmic, A.W. Gofton, S. Kueh, J. Austen, M. Lawson, et al., *Cryptosporidium homai* n. sp. (Apicomplexa: Cryptosporidiidae) from the guinea pig (*Cavia porcellus*), Vet. Parasitol. 245 (2017) 92–101.

[87] O. Danišová, A. Valenčáková, M. Stanko, L. Luptáková, E. Hatalová, A. Čanády, Rodents as a reservoir of infection caused by multiple zoonotic species/genotypes of *C. parvum, C. hominis, C. suis, C. scrofarum*, and the first evidence of *C. muskrat* genotypes I and II of rodents in Europe-Science Direct, Acta Trop. 172 (2017) 29–35.

[89] X. Zhang, Y. Jian, X. Li, L. Ma, G. Karanis, P. Karanis, The first report of *Cryptosporidium* spp. in *Microtus fuscus* (Qinghai vole) and *Ochotona curzoniae* (wild plateau pika) in the Qinghai-Tibetan Plateau area, China, Parasitol. Res. 117 (5) (2018) 1401–1407, https://doi.org/10.1007/s00436-018-5827-5.

[91] A.V. Koehler, T. Wang, S.R. Haydon, R.B. Gasser, *Cryptosporidium viatorum* from the native Australian swamp rat *Rattus lutreolus* - An emerging zoonotic pathogen, Int. J. Parasitol. Parasites Wildl. 7 (1) (2018) 18–26.

[92] Kunz, Mammal species of the world: a taxonomic and geographic reference, Mastozool. Neotropical. 13 (2) (2006) 290–293.

[93] S.H. Ranjbar-Bahadori, A. Mostoophi, B. Shemshadi, Study on *Cryptosporidium* contamination in vegetable farms around Tehran, Trop. Biomed. 30 (2) (2013) 193–198.

[94] A. Zahedi, A. Paparini, F. Jian, I. Robertson, U. Ryan, Public health significance of zoonotic *Cryptosporidium* species in wildlife: critical insights into better drinking water management, Int. J. Parasitol. Parasites Wildl. 5 (1) (2016) 88–109.

[95] P.A. Rochelle, G. Giovanni, *Cryptosporidium* Oocysts in Drinking Water and Recreational Water, Springer Vienna, 2014, pp. 489–513.

[97] A. Pönka, H. Kotilainen, R. Rimhanen-Finne, P. Hokkanen, M.L. Hänninen, A. Kaarna, et al., A foodborne outbreak due to *Cryptosporidium parvum* in Helsinki, November 2008, Euro Surveill. 14 (28) (2009) 19269.

[98] B.A. Han, J.P. Schmidt, S.E. Bowden, J.M. Drake, Rodent reservoirs of future zoonotic diseases, Proc. Natl. Acad. Sci. 112 (2015) 7039–7044.

[99] B.G. Meerburg, G.R. Singleton, A. Kijlstra, Rodent-borne diseases and their risks for public health, Crit. Rev. Microbiol. 35 (2009) 221–270.

[100] R. Khaghani, The economic and health impact of rodent in urban zone and harbours and their control methods, Ann. Mil. Health Sci. Res. 4 (2007) 1071–1078.

[101] M.H. Rabiee, A. Mahmoudi, R. Siahsarvie, B. Kryštufek, E. Mostafavi, Rodent-borne diseases and their public health importance in Iran, PLoS Negl. Trop. Dis. 12 (4) (2018), e0006256.