Zoonotic parasites in farmed exotic animals in China: Implications to public health

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1. Introduction

Enteric parasites such as Cryptosporidium spp., Giardia duodenalis, and Enterocytozoon bieneusi are important causes of diarrhea (DuPont, 2016). They exert the highest tolls in young children and neonatal animals (Cho and Yoon, 2014; Collaborators, 2017). As these parasites have a broad host range, they are considered major zoonotic pathogens (Thompson and Smith, 2011). Therefore, the One Health approach has been suggested as a tool in the prevention and control of diseases caused by these pathogens (Kreek et al., 2020; Thompson, 2013). This becomes especially important in the era of COVID-19, when increased attention has been directed to emerging zoonotic pathogens.

Molecular diagnostic tools have been used extensively in studies of the transmission of these pathogens (Li et al., 2020c; Xiao and Feng, 2017). Results from characterizations of isolates from humans and various isolates have identified species/genotypes and subtypes with broad host ranges as well as those with host adaptation (Caccio et al., 2018; Feng et al., 2018; Li and Xiao, 2019). As a result, the cross-species transmission and public health potentials of various Cryptosporidium species, G. duodenalis genotypes (known as assemblages), and E. bieneusi genotypes are different. For example, among the over 40 known Cryptosporidium species and an equal number of genotypes of unknown species status, only C. parvum, C. hominis, C. meleagridis, C. canis, and C. felis are major human pathogens (Zahedi and Ryan, 2020). Similarly, among the at least seven assemblages (A to H) of G. duodenalis from mammals, only assemblages A and B are major human pathogens (Caccio et al., 2018). Furthermore, only Group 1 genotypes among the nearly 500 E. bieneusi genotypes in 11 genogroups are major human pathogens (Li et al., 2019b). Therefore, not all species, genotypes, and subtypes of these pathogens have zoonotic potentials.

Wildlife has been suggested to play important roles in the ecology and transmission of Cryptosporidium spp., G. duodenalis, and E. bieneusi (Appelbee et al., 2005; Li and Xiao, 2021). The similar distribution of Cryptosporidium species and G. duodenalis and E. bieneusi genotypes between humans and wild mammals indicates that there could be frequent cross-species transmission of these pathogens (Lesnianska and
Perec-Matsyiak, 2017; Thompson and Ash, 2016). Some of the wildlife of major concern are rodents, nonhuman primates, and carnivores, as they are in closer contact with humans than other animals. As a result, numerous studies have been conducted on the molecular characterization of *Cryptosporidium* spp., *G. duodenalis*, and *E. bieneusi* in these animals (Innes et al., 2020; Lesnianska and Perec-Matsyiak, 2017). Many such studies were from China because of the increased awareness of wildlife as potential reservoirs of zoonotic parasites (Chen et al., 2019a, 2019b; Huang et al., 2019; Karim et al., 2014c, 2015b; Li et al., 2016a; Lv et al., 2009; Song et al., 2018; Ye et al., 2012; Zhao et al., 2015b, 2020).

Terrestrial wild mammals are bred and farmed in China as part of the national policy for rural development and poverty alleviation. The value of commercial breeding and farming of terrestrial wildlife in China was estimated to be $11.4 billion in 2018 (You, 2020). In northern China, several species of fur animals such as blue and silver foxes, raccoon dogs, and minks are farmed in China (Zhao et al., 2015a). Similarly, some nonhuman primates such as crab-eating and rhesus macaques are estimated to be farmed as laboratory animals and bamboo rats for food (Chen et al., 2019a, 2019b; Huang et al., 2019; Karim et al., 2014c, 2015b; Li et al., 2016a; Lv et al., 2009; Song et al., 2018; Ye et al., 2012; Zhao et al., 2015b, 2020).

Table 1 Distribution of *Cryptosporidium* species/genotype in farmed exotic animals in various studies in China.

| Host                   | Location          | No. of specimens | No. positive for *Cryptosporidium* (%) | Species/genotype (no.) | Reference          |
|------------------------|-------------------|------------------|---------------------------------------|------------------------|--------------------|
| Mink                   | Xinjiang          | 214              | 26 (12.1%)                            | Mink genotype (17), *C. canis* (7); *C. parvum* (2) | Qian et al. (2020)  |
|                        | Heilongjiang, Jilin, Liaoning | 114            | 8 (7.0%)                               | *C. canis* (6), mink genotype (2) | Yang et al. (2018) |
|                        | Heilongjiang      | 162              | 48 (20.6%)                             | *C. canis* (19), mink genotype (18) *C. meleagridis* (3) | Zhang et al. (2016a) |
|                        | Hebei             | 469              | 6 (1.3%)                               | Mink genotype (6)      | Wang et al. (2008) |
| Raccoon dog            | Xinjiang          | 39               | 8 (20.5%)                              | *C. canis* (8)         | Qian et al. (2020) |
|                        | Heilongjiang, Jilin | 40              | 0                                       | –                      | Yang et al. (2018) |
|                        | Heilongjiang      | 162              | 17 (10.5%)                             | *C. canis* (15)        | Zhang et al. (2016a) |
| Fox                    | Xinjiang          | 35               | 1 (2.9%)                               | *C. canis* (1)         | Qian et al. (2020) |
|                        | Heilongjiang, Jilin, Liaoning | 213            | 12 (5.6%)                              | *C. canis* (11) *C. meleagridis* (1) | Yang et al. (2018) |
|                        | Heilongjiang      | 191              | 3 (1.6%)                               | *C. canis* (3)         | Zhang et al. (2016a) |
|                        | Hebei, Jilin, Heilong | 302            | 48 (15.9%)                             | *C. canis* (48)        | Zhang et al. (2016c) |
| Crab-eating macaque    | Hainan            | 1452             | 132 (9.1%)                             | *C. hominis* (86), *C. parvum* (30), *C. muris* (15), *C. ubiquitum* (1) | Chen et al. (2019a) |
|                        | Hainan            | 193              | 11 (5.7%)                              | *C. hominis* (11)      | Zhao et al. (2019)  |
|                        | Guangxi           | 205              | 1 (0.5%)                               | *C. hominis* (1)       | Ye et al. (2014)    |
|                        | Guangdong         | 57               | 1 (1.8%)                               | *C. hominis* (1)       | Karim et al. (2014c) |
| Rhesus macaque         | Hainan, Guangxi   | 1144             | 9 (0.8%)                               | *C. hominis* (9)       | Karim et al. (2014c) |
|                        | Hainan            | 30               | 0                                       | –                      | Zhao et al. (2019)  |
| Bamboo rat             | Sichuan           | 92               | 3 (3.3%)                               | *C. parvum* (3)        | Liu et al. (2015)   |
|                        | Hunan, Jiangxi, Chongqing, Guangxi, Guangdong | 435          | 9 (2.1%)                               | Bamboo rat genotype I (5), *C. parvum* (2), *C. occultus* (1), bamboo rat genotype II (1) | Wei et al. (2019) |
|                        | Jiangxi, Guangxi, Hainan | 709         | 209 (29.4%)                            | Bamboo rat genotype I (85), *C. parvum* (78), bamboo rat genotype III (45), *C. occultus* (1) | Li et al. (2020a) |
|                        | Guangdong         | 724              | 88 (12.2%)                             | Bamboo rat genotype I (49), *C. parvum* (31), bamboo rat genotype III (5), *C. occultus* (2), *C. muris* (1) | Li et al. (2020b) |

2. *Cryptosporidium* spp. in farmed exotic animals

*Cryptosporidium* spp. have been commonly identified in farmed fur animals, bamboo rats, and macaque monkeys in China (Table 1). The reported infection rates varied greatly among studies for each species of the animals examined (Table 1). This has been attributed to levels of hygiene in the study facilities (Li et al., 2020b). The highest infection rates were reported as 9.1% in crab-eating macaques, 15.9% in foxes, 20.5% in raccoon dogs, 29.4% in bamboo rats, and 29.6% in minks (Table 1). They are much higher than infections rates of *Cryptosporidium* spp. obtained from wild populations of these animals in China and other countries, possibly due to the short history of domestication and congregations of many susceptible animals in confined spaces. As expected, young animals were reported to have higher prevalence of *Cryptosporidium* spp. than older animals (Chen et al., 2019a; Li et al., 2020a, 2020b; Qian et al., 2020; Zhang et al., 2016a; Zhao et al., 2019).

In crab-eating macaques, animals with diarrhea had higher occurrence of *Cryptosporidium* infection (Chen et al., 2019a).

2.1. *Cryptosporidium* species and subtypes in fur animals

Several *Cryptosporidium* species and genotypes were detected in farmed foxes, raccoon dogs, and minks in China. One dominant species in these fur animals is *C. canis*, which was found in most studies conducted in northern China. In addition, *Cryptosporidium* mink genotype appears to be another common pathogen in minks. Other
Cryptosporidium species identified include C. parvum and C. meleagris in a few animals (Table 1). The C. parvum identified in two minks belonged to IIdA15G1, one of the two most common C. parvum subtypes in China (Qian et al., 2020). Four divergent subtype families (Xb-Xe) were found in Cryptosporidium mink genotype, indicating the diverse origins of these animals (Qian et al., 2020; Yang et al., 2018; Zhang et al., 2016a).

2.2. Cryptosporidium species and subtypes in bamboo rats

Similarly, several Cryptosporidium species and genotypes were found in farmed bamboo rats in China. Among them, C. parvum was one of the dominant species in the few studies conducted in southern China. Other common genotypes include Cryptosporidium bamboo rat genotypes I and III, which are genetically related to C. ubiquitum and C. parvum, respectively (Li et al., 2020b). The remaining species and genotypes (C. occultus, C. muris, and bamboo rat genotype II) have been found in only a few animals (Table 1), thus could represent native parasites of other rodents. In the latter, bamboo rat genotype is genetically similar to a genotype in found in a masked palm civet (Yu et al., 2020). The intensity of oocyst shedding was higher when animals were infected with C. parvum and C. parvum-like genotype (bamboo rat genotype II) than with other Cryptosporidium spp. (Li et al., 2020a, 2020b).

The C. parvum subtypes found in bamboo rats belong mostly to two divergent subtype families (Iio and IIp) of C. parvum, which are genetically related to the Ild subtype family and have been thus far reported only in Asia (Li et al., 2020a; Liu et al., 2015; Wei et al., 2019). Two subtypes of each subtype family have been identified in bamboo rats from various areas, including IloA13G1, IloA15G1, IIpA6 and IIpA9 (Li et al., 2020a, 2020b; Liu et al., 2015; Wei et al., 2019). One bamboo rat was identified as having the C. parvum IldA15G1 subtype (Wei et al., 2019).

2.3. Cryptosporidium species and subtypes in macaques

Four Cryptosporidium species have been identified in farmed macaques, mostly in southern China. They include C. hominis, C. parvum, C. muris and C. ubiquitum. The dominant species is C. hominis, which was identified in all studies conducted in farmed crab-eating and rhesus macaques (Table 1). Other Cryptosporidium species were only detected in one study conducted in crab-eating macaques on a large farm in Hainan (Chen et al., 2019a). On that farm, significant numbers of animals were infected with C. parvum and C. muris in addition to C. hominis. The intensity of oocyst shedding was higher in animals infected with C. hominis than those infected with C. parvum and C. muris (Chen et al., 2019a).

The C. hominis subtypes detected in farmed macaques all belong to the unique C. hominis monkey genotype with divergent small subunit (SSU) rRNA gene sequence (Chen et al., 2019a; Feng et al., 2018; Karim et al., 2014c; Zhao et al., 2019). At the g660 locus, they were from three unusual subtype families of Ii (Iia17), Im (ImA18), and In (InA14, InA17, and InA26), and one common subtype family Iib (Chen et al., 2019a; Karim et al., 2014c; Zhao et al., 2019). The Iib subtype identified at the g660 locus was IiA12G3, which at the SSU rRNA locus was identified as C. hominis monkey genotype (Karim et al., 2014c). Other subtypes of the Iib subtype family in humans have the typical SSU rRNA sequences of C. hominis (Feng et al., 2018). The C. parvum identified in crab-eating macaques belong to IioA14G1 (n = 18) and IldA19G1 (n = 2). Of clinical significance, C. hominis ImA18 subtype and C. parvum IloA14G1 subtype were detected in animals with diarrhea whereas the remaining ones were mostly found in asymptomatic animals (Chen et al., 2019a).

3. Giardia duodenalis in farmed exotic animals

Several studies were conducted to assess the prevalence and genotype identity of G. duodenalis in farmed raccoon dogs, bamboo rats, and macaque monkeys in China. Low infections rates were obtained from most studies (Table 2). Two studies, however, showed common occurrence of G. duodenalis in farmed crab-eating macaques (32.3%) in Hainan and bamboo rats (10.8%) in Hunan. Younger animals and animals with diarrhea had higher infection rates than older animals and animals with normal stools (Chen et al., 2019b; Ma et al., 2018). Infected raccoon dogs mostly had assemblage C, while macaque monkeys and bamboo rats mostly had assemblage B (Table 2). There was a high genetic diversity among assemblage B and C isolates in all these studies (Chen et al., 2019b; Karim et al., 2014c; Ma et al., 2018; Ye et al., 2014; Zhang et al., 2016d). In one study of G. duodenalis in crab-eating macaques on one farm, 53 multi-locus genotypes were found. Most of them were genetically related to those previously seen in Old-World monkeys (Chen et al., 2019b; Karim et al., 2014c).

4. Enteroocytozoon bieneusi in farmed exotic animals

The transmission of E. bieneusi in farmed exotic animals in China has been examined in numerous studies. E. bieneusi was commonly detected in farmed fur animals in northern China and bamboo rats and macaque monkeys in southern China (Table 3). The reported infection rates were mostly above 10%. This was especially the case with macaque monkeys (Table 3). Unlike the case with Cryptosporidium spp. and G. duodenalis, there were no consistent age-associated differences in infection rates of E. bieneusi, which was detected at high frequency in all age groups of animals sampled in most studies (Chen et al., 2019b; Ma et al., 2020a, 2020b; Yang et al., 2015; Ye et al., 2014; Zhang et al., 2016b, 2018). Crab-eating macaques with diarrhea were reported to have higher infections rates than those with normal stools (Chen et al., 2019b).

4.1. E. bieneusi genotypes in farmed fur animals

A high genetic diversity is present in E. bieneusi isolates from farmed minks, foxes, and raccoon dogs. Most of these studies have reported multiple genotypes in each species of animals on each farm (Table 3). Altogether, 25 E. bieneusi genotypes have been found in the small numbers of foxes, raccoon dogs and minks examined in northern China. They all belong to Group 1, and many occur in multiple animal species. D, however, appears to be the dominant genotype in farmed fur animals, being found in all but one study (Table 3). Although concerns have been raised regarding the public health significance of E. bieneusi from fur animals based on the wide occurrence of the well-known zoonotic genotype (Yang et al., 2015), multilocus characterization of E. bieneusi of ITS genotypes A, D and Type IV at four micro and minisatellites (MS1, MS3, MS4 and MS7) had shown clear genotypic and phylogenetic divergences between isolates of ITS genotype D from fur animals and humans. In fact, in phylogenetic analysis of the multilocus sequence data, genotype D isolates from fur animals formed their own cluster, while human isolates of genotype D clustered together with Type IV from humans from several countries. A third cluster was formed by isolates of the anthropoconic genotype A. While the first two populations had clonal genetic structure, the third population had an epidemic genetic structure (Li et al., 2016b). The presence of host-segregated E. bieneusi genotypes was supported by MLST analysis of additional isolates from other hosts (Li et al., 2019a; Liu et al., 2020). These data indicate significant population differentiation of E. bieneusi between fur animals and humans within some of the so-called zoonotic ITS genotypes.

4.2. E. bieneusi genotypes in bamboo rats

There were only two studies of E. bieneusi in bamboo rats in southern China. Altogether, eight genotypes were found among the small number of positive samples. The dominant genotype was D. Other Group 1 genotypes included the well-known Peru11, EbpA, and PigEBITS57. Two novel genotypes of Group 2, however, were detected in a few animals.
4.3. E. bieneusi genotypes in farmed monkeys

E. bieneusi infections are especially common in farmed monkeys. Studies conducted in three species of farmed monkeys have identified 15 E. bieneusi genotypes, all belonging to Group 1. Macaque3 (synonym of CM1) was the dominant genotype in most studies (Table 3). Other common genotypes include Type IV, D and Peru8, all well-known zoonotic ITS genotypes. There are no apparent differences in the distribution of E. bieneusi genotypes among the three species of farmed monkeys examined. This contrasts with the dominance of Peru11 and absence of Macaque3 in free-range monkeys in a public park in Guiyang, China (Ye et al., 2012). Similarly, in a study of various nonhuman primates in zoos in China, D was the dominant E. bieneusi genotype in most animals, while Macaque3 was only seen in macaque monkeys (Karim et al., 2015a). In another study conducted in a zoo in Zhengzhou, Henan, all three species of monkeys were mainly infected with HenanV. Therefore, the distribution of E. bieneusi genotypes in farmed monkeys appears to be different from that in captive monkeys kept in zoos and parks.

Multilocus sequence typing (MLST) of 85 of E. bieneusi isolates from diverse nonhuman primates produced 59 multilocus genotypes. They contained mainly ITS genotype Type IV, sub-population 2 contained all with an epidemic genetic structure. Among them, sub-population 1 contained mixed genotypes, while sub-population 4 contained genotype Peru11. The other 3 sub-populations contained ITS genotype D/Peru11.

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### Table 2

| Host          | Location       | No. of specimens | No. positive for G. duodenalis (%) | Assemblage (no.) | Reference          |
|---------------|----------------|------------------|-----------------------------------|------------------|-------------------|
| Raccoon dog   | Heilongjiang, Jilin, Liaoning, Hebei, Shandong | 305               | 22 (7.2%)                         | C (22)           | Zhang et al. (2016d) |
| Crab-eating macaque | Hainan | 1452            | 469 (32.3%)                      | B (469)          | Chen et al. (2019b)  |
|                | Guangxi       | 205              | 5 (2.4%)                          | A (2), B (3)     | Ye et al. (2014)   |
|                | Guangdong     | 57               | 1 (1.8%)                          | B (1)            | Karim et al. (2014c) |
| Rhesus macaque | Hainan, Guangxi | 1144             | 20 (1.7%)                         | B (20)           | Karim et al. (2014c) |
| Bamboo rat    | Hunan         | 480              | 52 (10.8%)                        | B (52)           | Ma et al. (2018)   |

### Table 3

| Host          | Location       | No. of specimens | No. positive for E. bieneusi (%) | Genotype (no.)               | Reference          |
|---------------|----------------|------------------|---------------------------------|---------------------------|-------------------|
| Mink          | Heilongjiang, Jilin, Liaoning, Hebei, Shandong | 298              | 30 (10.1%)                       | D (12), Peru11 (5), EbpC (7), NCM-1 (5), NCM-2 (1) | Yang et al. (2015) |
| Raccoon dog   | Shandong       | 356              | 23 (6.5%)                        | Type IV (11), D (8), Peru8 (3), CHG1 (1) | Ma et al. (2020a)  |
| Heilongjiang, Jilin, Liaoning, Hebei, Shandong | 305              | 68 (22.3%)       | NCF2 (33), CHN-F1 (10), D (9), CHN-DC1 (9), NCR2 (5), NCR1 (2) | Ye et al. (2016) |
| Heilongjiang  | 49             | 2 (4.1%)         | D (1), CHN-R1 (1)               | Zhao et al. (2015a)       |
| Heilongjiang  | 162            | 17 (10.5%)       | D (14), CHN-DC1 (1), CHN-DC1/WildBoar3 (1) | Zhao et al. (2015a) |
| Fox           | Shandong       | 344              | 31 (9.0%)                        | HND-1 (10), NCF2 (5), Type IV (3), Hum-q1 (1), SF1 (1), SF2 (1) | Ma et al. (2020b)  |
| Heilongjiang, Jilin, Hebei | 302          | 37 (12.3%)       | NCF2 (13), Peru8 (4), Type IV (5), D (4), NCF1 (3), CHN-DC1 (2), NCF5 (2), NCF3 (1), NCF4 (1), NCF6 (1), NCF7 (1) | Zhao et al. (2016b) |
| Heilongjiang  | 110            | 18 (16.4%)       | D (12), EbpC (5), CHN-F1 (1)    | Zhao et al. (2015a)       |
| Heilongjiang  | 191            | 53 (27.7%)       | D (44)                           | Yang et al. (2015)       |
| Crab-eating macaque | Hainan     | 1452            | 461 (31.7%)                      | Type IV (236), Macaque3 (119), Peru8 (42), Pongo2 (27), CM2 (17), Peru11 (12), D (4) | Chen et al. (2019b) |
|                | Hainan        | 133             | 34 (25.6%)                      | Type IV (10), Macaque3 (9), CM2 (4), D (3), Peru11 (3), Peru8 (2), WL21 (1), CC4 (1), D/Peru11 (1), Peru8/Type IV (1), CMB1 (1), CMB2 (1) | Yang et al. (2017) |
|                | Guangxi       | 205             | 38 (18.5%)                      | Type IV (15), Macaque3 (14), Peru3 (3), CM2 (3), D (2), Peru11 (2), CM3 (1) | Ye et al. (2014) |
|                | Guangdong     | 57              | 40 (70.2%)                      | Type IV (15), Macaque3 (25), Type IV (15), D (9), Peru8 (4) | Karim et al. (2014a) |
| Rhesus macaque | Sichuan, Guangxi, Yunan | 427             | 53 (12.4%)                      | Macaque3 (25), Type IV (15), D (9), Peru8 (4) | Karim et al. (2014a) |
| White-headed langur | Guangxi   | 143             | 19 (13.3%)                      | D (11), Macaque3 (4), Peru8 (2), CM2 (1), Peru11 (1) | Karim et al. (2014c) |
| Bamboo rat    | Hainan        | 117             | 18 (15.4%)                      | D (15), Peru11 (1), HNR-IV (1), HNR-V (1) | Zhao et al. (2020) |
|                | Hunan, Jiangxi, Chongqing, Guangxi, Guangdong | 435            | 22 (5.1%)                      | D (17), J (1), BR1 (1), BR2 (2), EbpA (1), PigEBITS7 (1) | Wang et al. (2019) |

a Bolded ones are Group 1 genotypes.

b Reported as CM1.
5. Public health perspectives of zoonotic protists in farmed exotic animals

Data accumulated thus far have shown a prevalence of Cryptosporidium spp., G. duodenalis, and E. bieneusi in farmed exotic animals. Molecular characterizations of isolates from these animals have identified the occurrence of human-pathogenic species/genotypes and subtypes. The public health significance of these enteric protists depends on the distribution of genotypes and/or subtypes. This is further impacted by the species of animals under consideration. Therefore, data from individual pathogens and farm animals are needed for accurate assessment of public health potential of pathogens in farmed exotic animals.

While we appreciate the human-infective potential of enteric protists from farmed animals, host specificity in pathogens might have reduced the likelihood for zoonotic infections in humans and cross-species transmission of pathogens among animals. For example, the dominant C. canis species in farmed fur animals is unlikely to cause major outbreaks in humans, which thus far are caused almost exclusively by the more virulent and infectious C. parvum and C. hominis. The canine-adapted nature of C. canis suggests that it is also unlikely to be a major pathogen in macaque monkeys and bamboo rats, which are farmed in southern China. The same is likely true for the assemblage C of G. duodenalis identified in farmed fur animals, which is not an established pathogen in humans and has rarely been found in monkeys and bamboo rats.

Host adaptation within pathogen species or genotypes could further reduce the occurrence of cross-species transmission. For example, the C. hominis variants infecting monkeys are not the subtypes commonly found in humans. The two differ from each other in the SSU rRNA gene, which is also unlikely to be a major pathogen in macaque monkeys and bamboo rats, which are farmed in southern China. Similarly, although monkeys and other nonhuman primates are commonly infected with assemblage B subtypes of G. duodenalis, results of the MLST analyses indicate that they differ from those found in humans genetically. Host-adapted subpopulations have further been found in E. bieneusi isolates from farmed monkeys. While fur animals, monkeys, and bamboo rats appear to be commonly infected with human-pathogenic genotypes of E. bieneusi, the presence of host-adapted subpopulations in some of the zoonotic ITS genotypes such as D implies that cross-species transmission might not occur as widely as believed.

Results of genotype analyses suggest that most of the enteric protists in farmed wildlife were probably brought from their native habitats. The C. hominis identified in farmed macaque monkeys all belong to several subtype families (II, Im, and In) of the monkey genotype, which have not been found in other farm animals. Similarly, the dominant genotype of E. bieneusi in nonhuman primates in China, Macaque3, has rarely been found in other animals and never in humans (Chen et al., 2020b). As discussed above, the assemblage B of G. duodenalis from farmed macaques formed a cluster with sequences from Old World monkeys. A similar situation is seen with pathogen families in farmed bamboo rats, which are commonly infected with very divergent Cryptosporidium spp. (bamboo genotypes I, II, and III) and occasionally infected with Cryptosporidium spp. from other rodents (C. marsi and C. occultus). When they are infected with C. parvum, the subtypes involved are mostly IId and IId subtype families. These distinct families have not been found in other farm animals. As there are divergent subtype families within C. canis, it would be interesting to see whether the C. canis isolates in farmed fur animals belong to host-adapted subtype families, as suggested recently on C. canis isolates from foxes in the United States (Jiang et al., 2020).

The farm environment appears to promote the transmission of Cryptosporidium spp. with high transmissibility. This is reflected by the difference in the distribution of Cryptosporidium species and subtypes between farmed and wild animals. For example, farmed raccoon dogs, foxes, and minks are most infected with C. canis (Table 1), which in native habitats are only found in dogs, foxes and other canine animals (Zhou et al., 2004). Wild raccoon dogs, foxes, and minks, in contrast, are infected with a range of Cryptosporidium species such as C. parvum, C. hominis, C. ubiquitum, C. andersoni, C. felis, C. suis, and muskrat genotype I, which are rarely seen in farmed fur animals (Barrera et al., 2020; Gomez-Couso et al., 2007; Kellnerova et al., 2017; Mateo et al., 2017; Matsubayashi et al., 2005; Nagano et al., 2007; Stuart et al., 2013; Zhou et al., 2004). As minks, raccoon dogs and foxes are frequently kept in proximity, it is possible that foxes might have transmitted C. canis to minks and raccoon dogs in captivity. There could be cross-species transmission of C. parvum between farmed bamboo rats and macaque monkeys as well. Both are commonly infected with IId and Ilp subtypes of C. parvum, which are divergent subtype families rarely found in other animals (Chen et al., 2019a; Li et al., 2020a, 2020b; Liu et al., 2015; Wei et al., 2019). This was supported by the dominance of G. duodenalis assemblage B in both group of animals (Table 2). Further studies using advanced molecular typing and comparative genomics are needed to validate these suggestions.

Measures should be developed to prevent the spillover of the enteric protists from the farmed exotic animals to humans and other farm animals. As discussed above, some of the divergent C. parvum subtypes such as IId and Ilp, have already been spread from bamboo rats to macaque monkeys. Between them, two IId subtypes have been identified in seven human patients in Thailand and New Zealand (Garcia et al., 2020; Insulander et al., 2013; Sannella et al., 2019). Previously, rodents were suggested to play a major role in the dissemination of C. parvum IId subtypes to farm animals and humans in China (Feng and Xiao, 2017). Among C. hominis detected in farmed macaque monkeys, the IIA17 subtype has been reported in a few human cases (Elwin et al., 2012; Lebbad et al., 2018). Another subtype commonly detected in nonhuman primates, Iba12G3, is emerging as a major subtype for human cryptosporidiosis in the United Kingdom, Ireland, Canada, Mexico, and Australia (Chalmers et al., 2019; Guy et al., 2021; Millan et al., 2019; O’Leary et al., 2020; Urrea-Quezada et al., 2018). This subtype could be a recombinant as isolates from farmed macaques differed from human isolates at the SSU rRNA locus. Genetic recombination has been implicated in the emergence of hyper-transmissible C. hominis subtypes in humans (Guo et al., 2015).

Since the beginning of COVID-19, the Chinese government has tightened regulations on the breeding and farming of exotic animals (You, 2020). Captive wild animals are no longer farmed for meat and consumption of exotic meat becomes illegal. As a result, the farming of bamboo rats has been forbidden in China and the breeding of other animals requires special licenses and is subject to more stringent monitoring. Another newly established biosafety law has set specific guidelines on the surveillance of major and emerging diseases in farmed exotic animals. The implementation of these new legislations would probably reduce the emergence of new pathogens in farmed exotic animals. One Health measures, including molecular surveillance systems and better training and education of farmers, should be developed to control the transmission of indigenous pathogens among farmed terrestrial wildlife and spillover of infections to other farmed animals and humans.

Declaration of competing interest

The authors declared that they have no conflicts of interest with this work.

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