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Incidence of paragonimiasis in Chongqing China: a 6-year retrospective case review

Xiaohong Peng[1,2], Jingru Zhang[2], Jian Zhang[2], Ying Wang[3] and Xilin Zhang[2]

[1]Department of Parasitology, Guilin Medical University, Guilin, Guangxi 541004, China; [2]Department of Pathogenic Biology, Third Military Medical University, Chongqing 400038, China and [3]Institute of Tropical Medicine, Third Military Medical University, Chongqing 400038, China

Research Article

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Authors for correspondence:
Xiaohong Peng, E-mail: pxh815@163.com and Xilin Zhang, E-mail: jsczxl@tmmu.edu.cn

Abstract

Paragonimiasis is an important infectious disease in Chongqing, China. However, no epidemiological surveys of paragonimiasis have been carried out in Chongqing since it became a municipality in 1997. We conducted a retrospective case review of 683 patients who were referred to our laboratory and diagnosed as having paragonimiasis during 2010–2015. Patients were diagnosed with paragonimiasis based on immunodiagnostic tests in addition to clinical and laboratory findings. Patient data extracted from the epidemiologic form were analysed. The majority of patients were distributed on the east side of the Wujiang River, which belongs to the Three Gorges Reservoir region. Consumption of raw or undercooked freshwater crab or crayfish in the family *Cambaridae* was the main reason for infection. Notably, more than 50·0% of patients were diagnosed between March and July, indicating that serious clinical symptoms only appear approximately 6 months post-infection. Paragonimiasis remains a public health issue in Chongqing, and an epidemiological study of *Paragonimus* in the Three Gorges region is strongly recommended.

Introduction

Paragonimiasis, or infection with lung flukes, is an important water-borne zoonosis caused by infection with a number of trematode species belonging to the genus *Paragonimus*. In China, two species, *Paragonimus westermani* and *Paragonimus skrjabini*, cause human paragonimiasis, with the former being strongly dominant (Liu *et al.* 2008). Infections are caused by consumption of freshwater crustaceans containing *Paragonimus* metacercariae. In Chongqing, *Sinopotamon denticulatum* and *Sinopotamon nanum* are important sources of human infections. Moreover, crayfish in the family *Cambaridae*, which were introduced for crayfish farming, are an increasingly significant host of this parasite.

Few epidemiological studies of paragonimiasis have been carried out since Chongqing separated from Sichuan province in 1997. Our laboratory has focused on the epidemiology of paragonimiasis Chongqing since 1999. Our 2002 epidemiological survey showed that the rate of paragonimiasis infection in migration areas of the Three Gorges Reservoir was 21·96% (Yang *et al.* 2002). Another serum study carried out from 2006 to 2009 indicated that the population infection rate was 14·36 or 7·46%, as determined by intradermal test or enzyme-linked immunosorbent assay (ELISA), respectively (Zhang *et al.* 2012).

Most of our previous studies have focused on the Three Gorges Reservoir in Chongqing. Little epidemiological information is available on paragonimiasis in the wider Chongqing area. In the present study, we analysed patient records collected between 2010 and 2015. A total of 638 patients were diagnosed with paragonimiasis in our laboratory. We summarized the distribution and clinical characteristics of these patients. Our records likely represent a substantial portion of the paragonimiasis cases that occurred in Chongqing within the past 6 years and provide the opportunity to elucidate the clinical features of current cases of paragonimiasis.

Materials and methods

Subjects and samples

A total of 1309 clinical cases referred to our laboratory from 1 January 2010 to 30 December 2015 were diagnosed as paragonimiasis. Patients suspected to have a *Paragonimus* infection by their clinician were recommended to our laboratory for further testing. Case data were collected by our technicians using a paragonimiasis epidemiological form, including clinical symptoms, dietary history, radiographic findings and laboratory data in addition to the results of immunodiagnostic tests performed in our laboratory. This study was approved by the Ethics Committee of the Third Military Medical University.

Immunodiagnostic methods

A rapid *Paragonimus* test kit produced by Zhejiang Academy of Medical Sciences and ELISA were used in parallel for diagnosis, as previously described (Zhang *et al.* 2012).

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Statistical analysis

Patients were categorized according to their age, gender, place of residence, dietary history and clinical symptoms. Statistical analysis was performed using Prism software version 5·0 (GraphPad). A P value <0·05 was considered statistically significant. Differences in the number of patients in each age group were assessed using a one-tailed t-test.

Results

Distribution of paragonimiasis cases by date of diagnosis

A total of 1309 cases were recorded by our laboratory from 1 January 2010 to 30 December 2015 following the serodiagnosis of *Paragonimus* infection. Of these, 638 patients were diagnosed with paragonimiasis, including 477 males and 161 females. The number of patients diagnosed with paragonimiasis annually from 2010 to 2015 ranged from 63 to 147. Moreover, more than 50·0% of patients were diagnosed between March and July (Fig. 1A). Most patients were diagnosed in April, accounting for 10–20·5% patients each year (Fig. 1B). This indicates that clinical symptoms manifest at approximately 6 months post-infection, as fresh water crabs are usually consumed in October in this region.

Geographical distribution of paragonimiasis cases

The geographical distribution of the cases is shown in Fig. 2. Chongqing is located in southwestern China, and it has become a municipality in 1997. Chongqing is upstream from the Three Gorges Dam, and it composes of 32 counties. Most of the counties are rural areas except Downtown Chongqing. We found that the majority (46·1%) of the patients were residents of northeast Chongqing (Kaixian, 96; Fengjie, 53; Liangping, 36; Wuxi, 29; Yunyang, 26; Wushan, 26; Chengkou, 17; Wanzhou, 11). Outside northeast Chongqing, a relatively large number of patients were diagnosed in Pengshui (49 patients), Shizhu (22), Fengdu (22) and Downtown Chongqing (39). Only a few cases were confirmed from the district around Yongchuan in west Chongqing. Since Downtown is in the western part of Chongqing, we investigated why it showed such a high level of morbidity. We found that 34 of the 39 patients residing in Downtown had visited northwest Chongqing in the previous year.

Dietary history of patients

The dietary history of patients is summarized in Table 1. Approximately two-thirds of patients (420/638, 65·8%) had a history of consuming a second intermediate host or a transported host of the parasite. The proportion of female patients (116/161, 72·5%) was slightly higher than that of male patients (304/477, 63·7%). Only a few patients (16/638, 2·5%) stated that they had consumed the raw or undercooked wild vertebrates meat such as goat and boar, another potential transport host of *Paragonimus*. Among the 420 patients who had confirmed their dietary history, 233 patients belonged to children group. The primary cause of infection was consumption of freshwater crabs or *Cambaridae*.

Age distribution of patients

To analyse the relationship between outdoor activity and morbidity, patients who were confirmed to have a *Paragonimus* infection were divided into four groups by age. The distribution of paragonimiasis cases by age group is displayed in Fig. 3A. Children (5–12 years old) group showed the highest infection rate; 309 of the 638 (48·4%) patients were children. However, youths (13–21 years old) group exhibited the lowest infection rate. Only 56 of 638 (8·8%) patients were youths, perhaps since most individuals in this age group were boarding school residents. Furthermore, infants (<5 years old) and adults groups showed a 17·4% (111/638) and 25·4% (162/638) infection rate, respectively. Notably, there were more male patients than female patients in all age groups ($P = 0·0495$) (Fig. 3B).

Classification of clinical symptoms

Parasitic invasion of different organs caused different clinical symptoms. Cases were divided into five types according to self-reported symptoms: subcutaneous, pleurisy, cerebral, abdominal and asymptomatic types (Table 2). Most patients reported a single symptom type, except four patients who reported multiple symptoms. One hundred and thirty-three (20·9%) cases were asymptomatic. These patients were referred to us due to computed tomography or B ultrasound findings. Only 47 (7·4%) of patients showed abdominal symptoms. A similar number of patients belonged to the subcutaneous, pleurisy and cerebral symptom groups.

Discussion

Paragonimiasis is an important water-borne zoonosis that is endemic in most parts of Asia, including China, Japan (Nagayasu *et al.* 2015; Yatera *et al.* 2015), India (Das *et al.* 2017), Vietnam (Doanh *et al.* 2016), with sporadic case reports

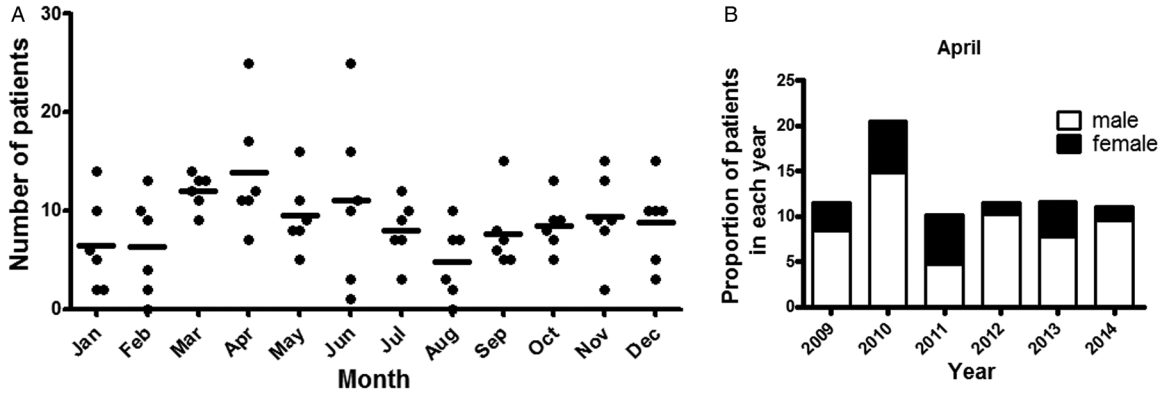

Fig. 1. Distribution of paragonimiasis cases by date of diagnosis. Data were collected from 1 January 2010 to 30 December 2015. Six hundred and thirty-eight patients were diagnosed as paragonimiasis. (A) Distribution of paragonimiasis cases by month. The dot shows patients number each year and the black line represents mean value of each month. (B) Patients diagnosed in April accounted for the proportion of the whole year.

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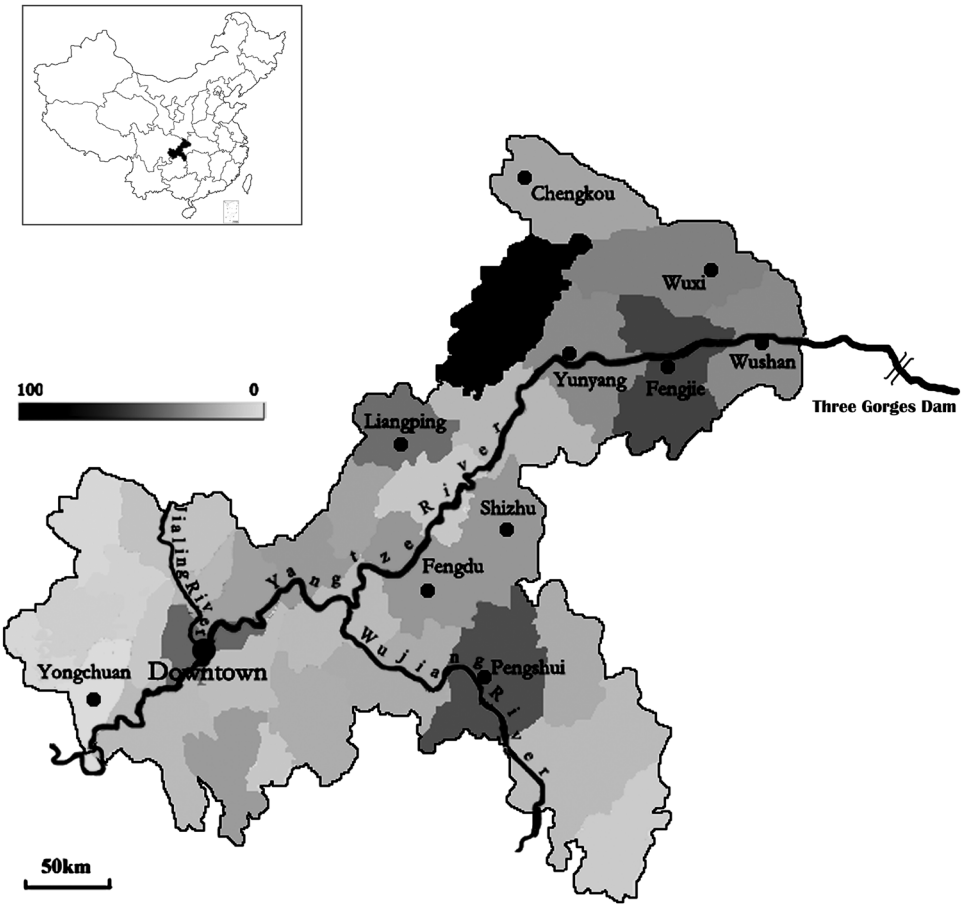

Fig. 2. Geographical distribution of paragonimiasis patients were residents in Chongqing, China. The patient number in each district was exhibited by different gradation as the grey scale bar shows in the left corner.

Table 1. Dietary history of patients

	Number of patients		Percentage of total patients	
Food species	Male	Female	Male (%)	Female (%)
Freshwater crab	148	59	34·0	36·6
Cambaridae	181	57	37·9	35·4
Wild red meat	11	5	2·3	3·1
No information available	173	45	36·2	30·0

Note that the total number of patients is more than 638, due to the patients who consumed two (38 patients) or three (three patients) food species.

from America (Fischer and Weil, 2015), Africa (Friant *et al.* 2015) and Russia (Besprozvannykh, 1994). Approximately 20 million people are infected with paragonimiasis and 300 million people are at risk of infection (Ahn *et al.* 2015). Nine species of *Paragonimus* can infect humans (Blair *et al.* 2016). *Paragonimus westermani* is the predominant species in Asia, whereas *P. skrjabini* is only found in China. In China, a national epidemiological survey of parasitic diseases published in 2005 (Coordinating Office of the National Survey on the Important Human Parasitic Diseases, 2005) showed that the rate of serological positivity for paragonimiasis was 1·71%. The report indicated that paragonimiasis remains a threat to public health. Chongqing is an important region of paragonimiasis endemism, especially *P. skrjabini*. However, few studies have been carried out to investigate the epidemiology of paragonimiasis in Chongqing after it separated from Sichuan province in 1997. Our laboratory has focused on diagnosis of paragonimiasis in the Chongqing area since 1999. In 2008, we carried out serological testing for paragonimiasis using ELISA and a rapid diagnosis kit produced by Zhejiang Academy of Medical Sciences (Gan *et al.* 2005). Deficiently, this method is hard to identify the *Paragonimus* at species level. However, we had been working on a new *Paragonimus* test kit these years (Yu *et al.* 2017). It will be used in the future. In this study, we performed a retrospective review of cases reported between 1 January 2010 and 30 December 2015. To the best of our knowledge, this is the first report of a systematic epidemiological review of paragonimiasis in Chongqing.

In this 6-year period, 638 patients were confirmed to have paragonimiasis. Based on the geographical distribution analysis, most patients were distributed on the east side of the Wujiang River (Fig. 2). Notably, more than one-third of patients confirmed to be infected lived along the border of Hubei province, which also belongs to the Three Gorges region. We also identified 39 patients from Downtown Chongqing, the region of west Chongqing with the highest infection rate. Further investigation showed that 33/39 patients had travelled to east Chongqing prior to infection. Our previous publication suggested that the rising water level in the Three Gorges region may have produced more streams that are a suitable habitat for freshwater crabs or *Cambaridae*, which could cause an increase in morbidity from paragonimiasis (Zhang *et al.* 2012). The results of this study confirmed our hypothesis that paragonimiasis is increasing in this region. The epidemiology of *Paragonimus* in the Three Gorges

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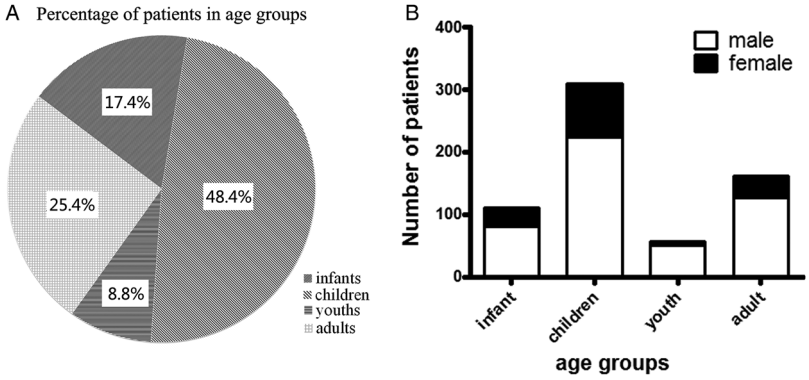

Fig. 3. Distribution of paragonimiasis cases by age of patients. Patients were divided into four groups by age. Infants group represents patients under 5 years old; children group equal to 5–12 years old patients; youths group means 13–21 years old patients and adults group shows patients over 21 years old. (A) The percentage of patients in age groups. (B) The number of patients in different age groups.

Table 2. Clinical symptoms classification of patients

Types	Symptoms	Number	Percentage (%)
Subcutaneous type	Subcutaneous migratory mass	130	20·4
Pleurisy type	Chest pain, cough, pleural effusion, haemoptysis	179	28·1
Cerebral type	Headache, nausea, vomiting, hemiplegia, epilepsy	149	23·4
Abdominal type	Abdominal pain, diarrhoea, hepatomegaly	47	7·4
Asymptomatic type	None	137	21·5

Note that the total number of patients is more than 638, due to four patients who consumed two types of food species.

region should be investigated further, and a public health education initiative is strongly recommended to control this disease.

After ingestion of metacercariae, juvenile worms excyst from the metacercariae and migrate to the target organ, where they settle and develop into adult worms in 2–3 months (Keiser and Utzinger, 2009). However, limited data are available on how long it takes for patients to become symptomatic. In this study, we found that more than 50% of patients were diagnosed between March and July. In 2011, 20·5% of patients were diagnosed in April (Fig. 1B). Considering crabs were always harvested around October, and crabs consumption concentrate on October in China, we speculate that approximately 6 months is required for manifestation of serious clinical symptoms post-infection.

We observed an age distribution pattern among the patients; paragonimiasis occurs predominantly in children (Fig. 3A), with almost half of patients being children. Children of this age typically live with their grandparents, and they spend considerable time outdoors without adult supervision. They tend to eat raw or undercooked crabs, and they are thus at highest risk of infection. However, only 8·8% of patients were youths. This is likely because most youths are boarding school residents, with few opportunities for unsupervised outdoor activity. Notably, 17·4% of patients were infants. Infant patients show more serious symptoms but early detection is difficult.

Approximately 70% of patients had eaten raw crab, *Cambaridae*, or wild vertebrate meat. Raw crab or *Cambaridae* consumption was the main reason for infection. A recent study confirmed that deer can also host *P. westermani* (Yoshida *et al.* 2016), and indicated that other vertebrates may also be unreported paratenic hosts of *Paragonimus*. Hence, although only approximately 3% of patients had a history of eating wild vertebrate meat, consumption of undercooked wild game cannot be ignored as a source of infection, and should be investigated further.

In conclusion, paragonimiasis remains a public health issue in Chongqing, especially the Three Gorges region. Many publications show that the risk of paragonimiasis infection is high in the Three Gorges region (Wang *et al.* 2009; Zhang *et al.* 2012, 2014), and we strongly recommend that an in-depth survey be carried out in this area, and that a public health education initiative be started to help control this disease.

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Conflict of interests. The authors declare no conflict of interests.

References

Ahn CS, Na BK, Chung DL, Kim JG, Kim JT and Kong Y (2015) Expression characteristics and specific antibody reactivity of diverse cathepsin F members of *Paragonimus westermani*. *Parasitology International* **64**, 37–42.

Besprozvannykh VV (1994) [The epizootiological problems of trematodiases in the Maritime Territory]. *Meditsinskaia Parazitologiia i Parazitarnye Bolezni* **3**, 28–31.

Blair D, Nawa Y, Mitreva M and Doanh PN (2016) Gene diversity and genetic variation in lung flukes (genus *Paragonimus*). *Transactions of the Royal Society of Tropical Medicine and Hygiene* **110**, 6–12.

Coordinating Office of the National Survey on the Important Human Parasitic Diseases (2005) A national survey on current status of the important parasitic diseases in human population. *Chinese Journal of Parasitology and Parasitic Diseases* **23**, 332–340.

Das M, Doleckova K, Shenoy R, Mahanta J, Narain K, Devi KR, Konyak T, Mansoor H and Isaakidis P (2017) Paragonimiasis in tuberculosis patients in Nagaland, India. *Global Health Action* **9**, 32387.

Doanh NP, Tu AL, Bui TD, Loan TH, Nonaka N, Horii Y, Blair D and Nawa Y (2016) Molecular and morphological variation of *Paragonimus westermani* in Vietnam with records of new second intermediate crab hosts and a new locality in a northern province. *Parasitology* **143**, 1639–1646.

Fischer PU and Weil GJ (2015) North American paragonimiasis: epidemiology and diagnostic strategies. *Expert Review of Anti-Infective Therapy* **13**, 1–8.

Friant S, Brown K, Saari MT, Segel NH, Slezak J and Goldberg TL (2015) Lung fluke (*Paragonimus africanus*) infects Nigerian red-capped mangabeys and causes respiratory disease. *International Journal for Parasitology. Parasites and Wildlife* **4**, 329–332.

Gan XX, Shi SX, Wang Y, Wang PP, Shen HY, Zhu MD, Tang Y and Zhang S (2005) Development of rapid diagnostic Kit (Dot Immunogold

https://doi.org/10.1017/S003118201700172X Published online by Cambridge University Press

Filtration Assay) for detection of antibodies against *Paragonimus westermani*. *Chinese Journal of Zoonoses* **21**, 988–990.

Keiser J and Utzinger J (2009) Food-borne trematodiases. *Clinical Microbiology Reviews* **22**, 466–483.

Liu Q, Wei F, Liu W, Yang S and Zhang X (2008) Paragonimiasis: an important food-borne zoonosis in China. *Trends in Parasitology* **24**, 318–323.

Nagayasu E, Yoshida A, Hombu A, Horii Y and Maruyama H (2015) Paragonimiasis in Japan: a twelve-year retrospective case review (2001–2012). *Internal Medicine* **54**, 179–186.

Wang CQ, Yang SJ, Wang DJ, Pan HM, Lv QY, Qiu MS, Li XF and Gan YQ (2009) Investigation on the etiology of *Paragonimiasis skrjabini* in Xingshan County locating the Reservoir Area of Three Gorges. *Journal of Pathogen Biology* **4**, 36–39.

Yang S, Liu JP, Song JY, Lin H, Huang Y, Zhu FA, Tan CX and Shi L (2002) Seroepidemiological investigation on paragonimiasis at migration areas of the Three-Gorge Reservoir Chongqing region of Yangtze River. *Acta Academiae Medicine Militaris Tertiae* **24**, 1070–1072.

Yatera K, Hanaka M, Hanaka T, Yamasaki K, Nishida C, Kawanami T, Kawanami Y, Ishimoto H, Kanazawa T and Mukae H (2015) A rare case of *Paragonimiasis miyazakii* with lung involvement diagnosed 7 years after infection: a case report and literature review. *Parasitology International* **64**, 274–280.

Yoshida A, Matsuo K, Moribe J, Tanaka R, Kikuchi T, Nagayasu E, Misawa N and Maruyama H (2016) Venison, another source of *Paragonimus westermani* infection. *Parasitology International* **65**, 607–612.

Yu S, Zhang X, Chen W, Zheng H, Ai G, Ye N and Wang Y (2017) Development of an immunodiagnosis method using recombinant PsCP for detection of *Paragonimus skrjabini* infection in human. *Parasitology Research* **116**, 377–385.

Zhang X, Peng L, Liu W, Fan L, Zhang Q, Chen G, He P, Wu R, Liu A, Yang Y, Yu X and Yun L (2014) Response of primary vectors and related diseases to impoundment by the Three Gorges Dam. *Tropical Medicine & International Health* **19**, 440–449.

Zhang XL, Wang Y, Wang GX, Chen WB, He X, Niu H, Li ZL, Chen L and Wang LF (2012) Distribution and clinical features of *Paragonimiasis skrjabini* in Three Gorges Reservoir Region. *Parasitology International* **61**, 645–649.

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