

PARASITIC INFECTIONS IN MALAYSIA: CHANGING AND CHALLENGES

V Nissapatorn¹, YAL Lim¹, I Jamaiah¹, LSH Agnes², K Amyliana², C Chian Wen², H Nurul², S Nizam², CT Quake², C Valartmathi², C Ying Woei² and A Khairul Anuar¹

¹Department of Parasitology, University of Malaya Medical Center, Kuala Lumpur; ²Faculty of Medicine's Medical Students, University of Malaya, Kuala Lumpur, Malaysia

Abstract. A total of 1,885 blood and stool samples of four main protozoan parasitic infections were retrospectively reviewed from January, 2000 to April, 2004. Eleven of the 1,350 stool samples were shown positive for *Cryptosporidium* and *Giardia* infections; one of the 5 cases was clinically diagnosed as gastrointestinal cryptosporidiosis, while 6 cases were giardiasis. In patients with giardiasis, children were among the high-risk groups, making up 66.7% of these patients. The common presenting signs and symptoms were: diarrhea (83.3%), loss of appetite (83.3%), lethargy (83.3%), fever (66.7%), nausea/vomiting (50.0%), abdominal pain (16.7%), dehydration (16.7%) and rigor and chills (16.7%). Metronidazole was the drug of choice and was given to all symptomatic patients (83.3%). For the blood samples, 28 of the 92 peripheral smears for *Plasmodium* spp infection were diagnosed as malaria. The age range was from 4 to 57, with a median of 32.5 years. The sex ratio (M:F) was 3.6:1, while the age group of 30-44 years was the most commonly affected in both sexes. The majority of patients were foreigners (60.7%) and non-professional (39%). *Plasmodium vivax* (71%) infection was the most common pathogen found in these patients, along with a history of traveling to an endemic area of malaria (31%). The predominant presenting signs and symptoms were: fever (27%), rigor and chills (24%), nausea/vomiting (15%) and headache (8%). Chloroquine and primaquine was the most common anti-malarial regimen used (78.6%) in these patients. The seroprevalence of toxoplasmosis in different groups was 258/443 (58%): seropositive for IgG 143 (32.3%); IgM 67 (15%); and IgG + IgM 48 (10.8%). The age range was from 1 to 85, with a mean of 34 (\pm SD 16.6) years. The predominant age group was 21 to 40 years (126; 28.4%). The sex ratio (M:F) was 1.2:1. Subjects were predominantly male (142; 32%) and the Malay (117; 26.4%). Of these, 32 cases were clinically diagnosed with ocular toxoplasmosis. The range of age was from 10 to 56 years with a mean of 30.5 (\pm SD 12.05) years. The sex ratio (M:F) was 1:1.7. The majority were in the age group of 21 to 40 years, female (20; 62.5%), and Malay (17; 53%). They were also single (16; 50%), unemployed (12; 37%), and resided outside Kuala Lumpur (21; 65.6%). The more common clinical presentations were blurring of vision (25; 78%), floaters (10; 31%) and pain in the eye (7; 22%). We found that funduscopic examination (100%) and seropositivity for anti-*Toxoplasma* antibodies (93.7%) were the main reasons for investigation. Choroïdoretinitis was the most common clinical diagnosis (69%), while clindamycin was the most frequently used antimicrobial in all cases. Among HIV-infected patients, 10 cases were diagnosed as AIDS-related toxoplasmic encephalitis (TE) (9 were active and 1 had relapse TE). In addition, 1 case was confirmed as congenital toxoplasmosis.

INTRODUCTION

Infectious diseases, once expected to be eliminated as public health problems, remain the leading cause of death worldwide (Marshall *et al*, 1997). To our knowledge, parasitic infections remain highly prevalent in the global arena, particularly in developing countries. Among tropical diseases, malaria has been identified as one of the most important public health problems (Moe Lwin and Umenai, 1999) and is the most important human parasitic disease, affecting over 200 million people and causing more than one million

deaths each year (Suyaphun *et al*, 2002). Given this information, we conducted this study to determine the prevalence of four common protozoan parasitic infections: *Cryptosporidium parvum*, *Giardia lamblia*, *Plasmodium* spp and *Toxoplasma gondii*. We also aimed to determine the incidence of clinically evident cases of these diseases in the UMMC, Kuala Lumpur. These data will help to update our knowledge and implement standard strategies in terms of prevention and proper management of these diseases.

MATERIALS AND METHODS

Patients

This retrospective and descriptive study was carried out in the University of Malaya Medical Center (UMMC), Kuala Lumpur, a 863-bed facility and the oldest university tertiary referral hospital in Malaysia.

Correspondence: Dr Veeranoot Nissapatorn, Department of Parasitology, University of Malaya Medical Center, 50603 Kuala Lumpur, Malaysia.
Tel: 603-7967 6618
E-mail: nissapat@hotmail.com

UMMC mainly serves as a public hospital and teaching Center. A total of 1,885 records from January, 2000 to April, 2004 in the Department of Parasitology were reviewed for the 4 main protozoan infections. There were 297 (15.8%) cases found to be positive by samples (blood, serum and stool): 5 cases of gastrointestinal cryptosporidiosis, 6 cases of giardiasis, 28 cases of malaria and 258 (of 443) individuals seropositive for anti-*Toxoplasma* (IgM, IgG or both) antibodies. All positive cases were further investigated from the medical record office, University of Malaya Medical Center, based on the patients' demographic profiles, clinical presentations, relevant laboratory data and treatment outcome. The patients' information was enlisted in the standard data collection sheet.

Diagnosis of diseases

Various investigations were carefully reviewed according to our study's objective and the following standard criteria:

1. Diagnosis of giardiasis was made by stool examination (concentration technique) for the presence of *Giardia* cysts or trophozoites.
2. Diagnosis of cryptosporidiosis was made by stool examination for the presence of *Cryptosporidium* oocysts and confirmed by modified Ziehl-Neelsen staining techniques.
3. Diagnosis of malaria was made by microscopic identification (either thick or thin peripheral blood smear) of the parasites in peripheral blood smears.
4. Diagnosis of seropositivity for *Toxoplasma* infection was via detection of anti-*Toxoplasma* IgG, IgM or both by either one of the standard ELISA commercial kits (Trinity Biotech, Bray, Ireland, and Veda-lab, Alencon Cedex, France) in accordance with the manufacturer's instructions. Positive results of these 4 parasitic infections were identified and confirmed by experienced technicians.
5. Clinical toxoplasmosis was detected in different groups of patients and the diagnoses were made as follows: (1) Ocular toxoplasmosis was diagnosed by presenting signs and symptoms, ophthalmoscopic examination, serologic evidence of *Toxoplasma* infection and response to anti-*Toxoplasma* therapy. (2) Congenital toxoplasmosis was diagnosed by clinical signs and symptoms, relevant investigations such as ultrasonography, CT scan findings and serologic evidence of *Toxoplasma* infection. (3) Toxoplasmic encephalitis (TE) was empirically diagnosed by HIV-positive status, CD4 <200 cells/mm³,

neurological signs and symptoms, serologic evidence of anti-*Toxoplasma* antibodies and response to anti-*Toxoplasma* therapy.

Statistical analysis

All findings were entered, edited and analyzed using statistical software SPSS version 10 (SPSS Inc, Chicago, Ill, USA). Data with quantitative variables were expressed as median and range, whereas qualitative variables were expressed as frequency and percentage.

RESULTS

Total of 5 cases were positive for *Cryptosporidium* infection; however, only 1 case was symptomatic for gastrointestinal cryptosporidiosis. A one-year old child presented with fever, diarrhea, and vomiting for 2 days prior to admission. Her condition was diagnosed as acute gastroenteritis, then stool examination confirmed the presence of *Cryptosporidium* cysts. However, she recovered with supportive treatment. In six patients with clinical evidence of giardiasis, children (67%) less than 6 years-old were among the high-risk groups. Five out of 6 patients (83.3%) were male. Diarrhea, loss of appetite and lethargy were the most common presentations. Metronidazole was the drug of choice for treatment of giardiasis. In this study, there was a case of a 2-year-old patient whose parents were found to harbor *Giardia* cysts when a routine laboratory investigation was performed; however, he was asymptomatic. No recurrence or deaths were noted during the time of this study.

The demographic and clinical characteristics of 28 patients with malaria are listed in Table 1. The most common species for malaria was *Plasmodium vivax* (71%), followed by *Plasmodium falciparum* (14%), *Plasmodium malariae* (4%) and mixed infections between *Plasmodium falciparum* and *Plasmodium malariae* (11%). There were no cases of malaria caused by *Plasmodium ovale* found in this study. The age range was from 4 to 57 years with a median of 32.5 years. The ratio between male to female was 3.6:1 and the preponderant age group was 21 to 40 years. The majority of them were foreign patients (17; 60.7%) from Australia, Bangladesh, India, Indonesia, Myanmar, Pakistan, Sudan and Thailand. The distribution among Malaysian patients (11; 39.3%) was: Indian (6; 21%), Chinese (4; 14%), and Malay (1; 4%). In addition, we found that 13 (46%) of these patients were laborers and 14 (50%) of them had history of traveling to endemic area of malaria. The three common presenting signs and symptoms were: fever (96.4%), chills and rigor (85.7%) and nausea with

Table 1
Demographic characteristics and clinical relevant of
28 patients with malaria.

Characteristics	Number of patients (%)
The age range = 4 to 57 years	
Median = 32.5 years	
The sex ratio (M:F) = 3.6:1	
Age group	
≤ 20	2 (7)
21-40	16 (57)
41-60	10 (35.7)
Sex	
Male	22 (78.6)
Female	6 (21.4)
Races	
Malay	1 (3.6)
Chinese	4 (14.3)
Indian	6 (21.4)
Foreigner	17 (60.7)
Marital status	
Single	7 (25)
Married	19 (68)
Not recorded	2 (7)
Occupation	
Laborer	13 (46.4)
Nonlaborer	0
Unemployed	8 (28.6)
Not recorded	7 (25)
Address	
Kuala Lumpur	10 (35.7)
Outsider	18 (64.3)
Risk factors	
History of traveling to endemic area	14 (50)
Migration	6 (21.4)
History of blood transfusion	2 (7.2)
History of previous malaria	1 (3.6)
Clinical signs and symptoms	
Fever	27 (96.4)
Chill and rigor	24 (85.7)
Nausea/vomitting	15 (53.6)
Headache	8 (28.6)
Organomegaly	7 (25)
Diarrhea	6 (21.4)
Sweating	5 (17.9)
Loss of weight and/or appetite	4 (14.3)
Joint pain	4 (14.3)
Abdominal pain	3 (10.7)
Myalgia	2 (7.1)
Investigation	
Peripheral blood smear	28 (100)

Continued

Characteristics	Number of patients (%)
Hemoglobin count (range = 10 to 172; mean 95.5 ± 46.7)	
Normal value	6 (21.4)
Anemic condition (mild, moderate and severe)	22 (78.6)
White blood cell count (range = 1.03 to 12.4; mean = 5.9 ± 2.5)	
Normal value	20 (71.4)
Below or above normal value	8 (28.6)
Red blood cell count (range = 1.94 to 5.85; mean = 4.1 ± 0.89)	
Normal	8 (28.6)
Below normal value	20 (71.4)
Diagnosis	
Vivax malaria	20 (71.4)
Falciparum malaria	4 (14.3)
Malariae malaria	1 (3.6)
Mixed infection (<i>P. falciparum</i> and <i>P. malariae</i>)	3 (10.7)
Treatment	
Chloroquine + primaquine	22 (78.6)
Chloroquine + doxycycline	5 (17.9)
Fansidar + quinine	1 (3.6)

vomiting (53.6%). We further found that a peripheral blood smear was the most useful tool in routine investigation; moreover, most patients had anemia with their malarial infection. From this study, chloroquine (3 days) and subsequently primaquine (14 days) was the most common anti-malarial regimen used in treating vivax malaria. For falciparum malaria, chloroquine and doxycycline was the most commonly used combination. There were no reports of anti-malarial drug resistance or deaths in these patient cases.

Overall, the seroprevalence of toxoplasmosis in different groups was 258/443 (58%): IgG (143; 32.3%), IgM (67; 15%), and IgG+IgM (48; 10.8%). The age range was from 1 to 85 with a mean of 34 (\pm SD) 16.6 years. The sex ratio (M:F) was 1.2:1. The predominant age group was 21-40 years and male (202; 45.6% vs 241; 54.4%) particularly in HIV-positive patients (108; 66.7% vs 107; 66%) and in others (47; 38.8% vs 68; 56.2%). Chinese was the major ethnicity found (195; 44%) and most patients were HIV-positive (114; 70.3%); Malay were the dominant ones in ocular disease (85; 52.8%), and other (55; 45.5%) groups as shown in Table 2. Among seropositive (IgG, IgM or

both) individuals, we found that the main age group was 21-40 years (126; 28.4%), male (142; 32%), and Malay (117; 26.4%) (the data were not shown).

In 162 HIV-positive patients, 10 cases were diagnosed as AIDS-related toxoplasmic encephalitis – one patient had a previous history of toxoplasmic encephalitis and later developed relapsing TE, while the other 9 patients had active toxoplasmic encephalitis.

Tables 3 and 4 show the demographic and clinical profiles of 32 cases of ocular toxoplasmosis from this study. The range of age was from 10 to 56 years with a mean of 30.5 (± SD) 12.05 years. The sex ratio (M:F) was 1:1.7. The majority of them were in the age group of 21 to 40 years. They were comprised of males (12; 37.5%) and females (20; 62.5%). The various ethnic groups were: Malay (17; 53%), Chinese (8; 25%),

Indian (5; 15.6%), and foreigners (2; 6%). The majority of them were single (16; 50%), unemployed (12; 37.%), and outsiders (21; 65.6%). The common clinical presentations were: blurring of vision (25; 78%), photophobia (3; 9.4%), floaters (10; 31%), eye redness (2; 6.3%), pain in the eye (7; 22%) and headache (4; 12.5%). The majority of these patients had involvement of the right eye (17; 53%). Funduscopic examination (100%) and seropositivity for anti-*Toxoplasma* (IgG, IgM or both) antibodies (93.7%) were the main investigations found in this study. Choroidoretinitis was the most common clinical diagnosis (22; 68.8%). Clindamycin was the most frequent drug used both in single or combined forms (56.3%) in most cases.

Only 1 case of congenital toxoplasmosis was reported during the time of our study as shown in Table 5.

Table 2
Demographic characteristics of 443 individuals who came to this hospital during January 2000 to April 2004.

Characteristics	Number of patients			
	HIV-patients (162)	Ocular patients (161)	Others ^a (121)	Total (443)
The range of age = 1 to 85 years				
Mean = 34 (± SD) 16.6 years				
The sex ratio (M:F) = 1.2 : 1				
Age Group				
≤ 20	4 (2.5)	33 (20.5)	41 (34)	77 (17.4)
21-40	108 (66.7)	57 (35.4)	47 (38.8)	212 (48)
≥ 41	47 (29)	69 (43)	25 (20.7)	141 (31.8)
No information	3 (2)	2 (1.2)	8 (6.6)	13 (3)
Sex				
Male	107 (66)	66 (41)	68 (56.2)	241 (54.4)
Female	55 (34)	95 (59)	53 (43.8)	202 (45.6)
Race				
Malay	29 (18)	85 (52.8)	55 (45.5)	168 (38)
Chinese	114 (70.3)	37 (23)	44 (36.4)	195 (44)
Indian	12 (7.4)	37 (23)	20 (16.5)	69 (15.6)
Foreigner	7 (4.3)	2 (1.2)	2 (1.7)	11 (2.5)
Seroprevalence of toxoplasmosis				
No ^b	69 (42.6)	54 (33.5)	63 (52)	185 (41.8)
Yes: IgG	58 (35.8)	50 (31.1)	35 (29)	143 (32.3)
IgM	24 (14.8)	31 (19.3)	12 (10)	67 (15.1)
IgG+IgM	11 (6.8)	26 (16.1)	11 (9.1)	48 (10.8)
Total Ig	93 (57.4)	107 (66.5)	58 (48)	258 (58.2)

^aOthers mean individual with pregnancy, congenital, generalized lymphadenopathy, or any immunosuppressed conditions.

The significant association were found between age group with HIV, ocular patients and others (p<0.05); sex with HIV and ocular patients (p<0.05); and race with HIV, and ocular patients (p<0.05).

^bThere were 2 cases who had no evidence of *Toxoplasma* status but clinically proven of ocular toxoplasmosis.

Table 3
Demographic profiles of 32 cases of ocular toxoplasmosis.

Demographic characteristics	Number of patients (%)
The range of age = 10 to 56 years	
Mean = 30.5 ± 12.05 years	
The sex ratio (M:F) = 1 : 1.7	
Age Group	
≤ 10	1 (3.1)
11-20	7 (22)
21-30	9 (28.1)
31-40	8 (25)
41-50	5 (15.6)
≥ 51	2 (6.3)
Sex	
Male	12 (37.5)
Female	20 (62.5)
Race	
Malay	17 (53.1)
Chinese	8 (25.0)
Indian	5 (15.6)
Foreigner	2 (6.3)
Marital status	
Single	16 (50.0)
Married	11 (34.4)
No information	5 (15.6)
Occupation	
Laborer	3 (9.4)
Non-laborer	6 (18.8)
Unemployed	12 (37.5)
Not recorded	11 (34.4)
Address	
Kuala Lumpur	5 (15.6)
Outsider	21 (65.6)
Not recorded	6 (18.8)

Table 4
Clinical manifestation, investigation and treatment outcome of these patients.

Characteristics	Number of patient (%)
Signs and symptoms	
Blurring of vision	
No	3 (9.4)
Yes	25 (78.1)
Not recorded	4 (12.5)
Photophobia	
No	25 (78.1)
Yes	3 (9.4)
Not recorded	4 (12.5)

Table 4 (continued)

Characteristics	Number of patient (%)
Floaters	
No	18 (56.3)
Yes	10 (31.3)
Not recorded	4 (12.5)
Redness of eye	
No	26 (81.3)
Yes	2 (6.3)
Not recorded	4 (12.5)
Pain in the eye	
No	21 (65.6)
Yes	7 (21.9)
Not recorded	4 (12.5)
Fever	
No	28 (87.5)
Yes	0
Not recorded	4 (12.5)
Headache	
No	24 (75.0)
Yes	4 (12.5)
Not recorded	4 (12.5)
Affected eye(s)	
Left	9 (28.1)
Right	17 (53.1)
Bilateral	3 (9.4)
Not recorded	3 (9.4)
Investigation	
Funduscopy examination	32 (100)
Serology	
IgM	4 (12.5)
IgG	18 (56.3)
Both	8 (25.0)
Not recorded	2 (6.3)
Diagnosis	
Retinochoroiditis	
No	10 (31.2)
Yes	22 (68.8)
Uveitis	
No	22 (68.8)
Anterior uveitis	3 (9.4)
Posterior uveitis	1 (3.1)
Panuveitis	6 (18.8)
Treatment	
Clindamycin	6 (18.8)
Prednisolone	1 (3.1)
Azithromycin	3 (9.4)
Fansidar	1 (3.1)
Combination (clindamycin +prednisolone, fansidar, and azithromycin)	12 (37.5)
Prednisolone + azithromycin	6 (18.8)
Not recorded	3 (9.4)

Table 5
A report of clinically evident case of congenital toxoplasmosis.

Characteristics	Patient
Age	3 years old
Gender	Male
Ethnic	Malay
Nationality	Malaysian
Antenatal history	His mother was 41 years old with G ₅ P ₄ and all normal children before his birth. During her 6 months pregnancy, she had fever for 1 week with exposed to chicken pox
Ultrasound examination	Ventriculomegaly appeared on the fetal brain
Postnatal history	He was a term baby with normal delivery in November 2001
In 2001: Clinical manifestation	Hydrocephalus
Investigation	
Serodiagnosis	Positive for IgM anti- <i>Toxoplasma</i> antibody in the mother Positive for IgM and IgG anti- <i>Toxoplasma</i> antibodies in the new born baby
CT scan	Hydranencephaly, gross dilatation of lateral and third ventricle, minimal visible brain parenchyma, extensive gyral and basal ganglia calcification
Treatment	Anti- <i>Toxoplasma</i> therapy: spiramycin
In 2002: Clinical manifestation	Quadriplegic cerebral palsy
Investigation	
MRI	Brain is small with dilated lateral ventricle
VEP studies	Severe lesion at visual pathway level
Ophthalmoscopic examination	Rt eye showed macular scar; Lt eye was normal
Serodiagnosis	Both CSF and serum showed positive for IgG and IgM anti- <i>Toxoplasma</i> antibodies
Treatment	Replaced by ventral-peritoneal (VP) shunt Anti- <i>Toxoplasma</i> therapy: fansidar
Follow-up	Yes
Other complications	Recurrent VP shunt infections, resolved MRSE meningitis, urinary tract infection and pneumonia

DISCUSSION

Seven cases of symptomatic gastrointestinal protozoan infections mostly occurred in children. This indicates that parasitic infections are still encountered in our setting, even though in small numbers. The prevalence of these two organisms varied according to geographical distribution (Cross *et al*, 1985; Kamel *et al*, 1994; Gambhir *et al*, 2003). In a case of cryptosporidiosis, no specific treatment was given to the patient; however, her condition spontaneously improved. This could be due to the fact that *Cryptosporidium* is an acute, self-limiting gastro-enteritis in immunocompetent patients, whereas it is a chronic and possibly life-threatening illness in

immunocompromized patients. Moreover, after a literature review, we found no drug to date that has proven to be effective in killing this parasite (Casemore *et al*, 1985; Kadappu *et al*, 2002). Cases of giardiasis can be successfully treated with metronidazole in affected patients. However, a few current studies reported that albendazole alone or in combination with praziquantel could be a promising agent in treating this protozoan parasite and co-existing organisms (Penggabean *et al*, 1998; Pengsaa *et al*, 2002). Outbreaks of food-waterborne giardiasis and/or cryptosporidiosis in day care centers and travelers returning from the tropics have been reported (Combee *et al*, 1986; de Lalla *et al*, 1992; Lee *et al*, 2002); however, no such outbreaks have occurred in the

Malaysian scenario. There is speculation as to whether a vaccine against cryptosporidiosis is a reality or fantasy (de Graaf *et al*, 1999) due to its own virulence and resistance to therapy, whereas vaccination for giardiasis (Olson *et al*, 2000) may become an ultimate tool in eradicating this protozoan parasite. In Malaysia, drinking water contamination with *Giardia* and *Cryptosporidium* oocysts has become one of the top agendas in public health.

We found that *Plasmodium vivax* was the most common cause of malaria in this study. This finding is consistent with those reported earlier in domestic and other regions (Norhayati *et al*, 2001; Kitvatanachai *et al*, 2003; Koh *et al*, 2004) but contrary to others (Sidhu and Ng, 1991; Jamaiah *et al*, 1998). We observed that the majority of these patients were foreign workers, which indicates that imported malaria still exists and there is an urgent need to prevent or control transmission. Fever, chills and rigors were the commonest clinical presentations, similar to another study (Suyaphun *et al*, 2002). This suggests that malaria should be included in the differential diagnoses for any patient with pyrexia of unknown origin (PUO) or a history of traveling in the tropics. The peripheral blood smear is the conventional, reliable gold standard to detect malaria parasites used in our study, even though many novel modified techniques have been discovered in recent years. The treatment of choice for vivax malaria in this study was chloroquine and subsequently primaquine, while one study suggested that the combination of artesunate (5 days) and primaquine (14 days) has proven to be a highly effective and generally well-tolerated treatment regimen (Silachamroon *et al*, 2003). No anti-malarial drug resistance was noted in this study; however, previous studies showed that vivax malaria parasites have developed resistance to chloroquine and other drugs (Longworth, 1995; Kshirsagar *et al*, 2000). Nevertheless, one study showed that the epidemic outbreak has not been due to the presence of chloroquine resistant *P. vivax* (Congpuong *et al*, 2002).

Toxoplasmosis is a protozoan disease with a worldwide distribution and most infections in humans are asymptomatic. In our study, we found 10 cases of toxoplasmic encephalitis (TE). TE is the most common intracerebral lesion in AIDS patients and is due to reactivation of latent *Toxoplasma* infection. Interestingly, CT scan and serodiagnosis were the main investigations in all TE cases. However, we also support the existing PCR, which has consistently proven to be useful in TE diagnosis as verified in previous studies (Dupouy-Camet *et al*, 1993; Joseph *et al*, 2002; Vidal *et al*, 2004). The frequency of TE in

AIDS patients varies from about one fourth to one half of cases in the absence of antimicrobial prophylaxis (Cohen, 1999). In the era of HAART, prophylaxis against TE is cost-effective (Yazdanpanah *et al*, 2003), and lessens the burden of hospitalization (Khetsuriani *et al*, 2002). Therefore, recommendations on prophylaxis and maintenance therapy need to be redefined (Furrer *et al*, 2002). HAART has improved the outcome of patients with AIDS who have CNS infections, and the initiation of this therapy is mandatory if effective therapy is not available (Collazos, 2003); moreover, there is no increase in the risk of developing TE after beginning HAART if the TE patient discontinues anti-*Toxoplasma* prophylaxis (Pozio, 2004). We found one confirmed case of TE relapse, the cause of which may have been due to side effects or non-compliance to anti-*Toxoplasma* therapy. In this context, atovaquone containing regimens are well tolerated, safe, and may be useful for patients intolerant of standard regimens for TE (Chirgwin *et al*, 2002). Nonetheless, the development of novel anti-*Toxoplasma* drugs may prove to be more effective against *Toxoplasma* infection, particularly its cyst form.

Ocular toxoplasmosis (OT) was the most common clinical manifestation of *Toxoplasma* infection in this study. The majority of OT patients were in the 2nd and 3rd decades of life. Ocular toxoplasmosis is either due to congenital or acquired infection, and it is possible to show that many cases are congenital and others are acquired (Ho-Yen, 1992). The typical clinical presentations found in these patients correlated with previous studies (Zurainee *et al*, 2000; Suhardjo *et al*, 2003). This indicates that toxoplasmosis should be included in the differential diagnoses for any highly suspected ocular cases. It showed that serodiagnosis for anti-*Toxoplasma* antibodies was the confirmatory investigation. Congenital ocular toxoplasmosis does not always show an increase in anti-*Toxoplasma* (IgM) antibody, especially in the case of chorioretinal scarring – a finding which most cases with positive IgG also encountered in our study; furthermore, anti-*Toxoplasma* titer positivity has been an important factor in determining whether the lesion found was active or not (Suhardjo *et al*, 2003). Clindamycin was the most common antibiotic used, either single or combined therapy – a promising agent in the management of ocular toxoplasmosis. Most cases of OT were recurrent in this study. The risk of recurrent ocular disease appeared to be greatest during the first year after an initial episode of toxoplasmic retinochoroiditis (Holland, 2003). A few studies showed that long-term intermittent trimethoprim/sulfamethoxazole or chemoprophylaxis reduced the rate of recurrent

toxoplasmic retinochoroiditis in immunocompetent cases and high-risk patients (Silveira *et al*, 2002; Kopec *et al*, 2003; Holland, 2004). This indicates that OT cases are still common in clinical practice.

Only one case of congenital toxoplasmosis was encountered in this study. The incidence of congenital toxoplasmosis has been more widely reported in Europe (Munoz Batet *et al*, 2004), whereas the true incidence of congenital toxoplasmosis in Malaysia is unknown. Serological surveys conducted in pregnant women have shown that toxoplasmosis is a common infection in this country as reported in earlier studies (23% to 49%) (Cheah *et al*, 1975; Nissapatorn *et al*, 2003). Therefore, it is most likely that toxoplasmosis is an important cause of congenital infection in Malaysia. Our data also showed that this pediatric patient had obvious brain and eye involvement at first detection during antenatal examination. This finding is consistent with one previous study (Mets *et al*, 1996) but not consistent with another from Malaysia (Tan and Mak, 1985). This suggests the importance of imaging in diagnosing congenital toxoplasmosis. Serodiagnosis – particularly IgM for *Toxoplasma* infection – plays a very important role to confirm the diagnosis, as shown in one previous study (Lebech *et al*, 1999). We strongly recommend the possibility of early prenatal diagnosis of congenital *Toxoplasma* infection using an approach based on PCR (Grover *et al*, 1990; Hohlfeld *et al*, 1994) performed on amniotic fluid – which is rapid, sensitive, safe, and accurate. In addition, the pyrimethamine-sulfa drug combination given to mothers of proven infected fetuses, and extended to well-documented seroconverted mothers can be effective (Couvreur *et al*, 1991).

In conclusion, these common parasitic infections are still viable and prevalent in Malaysia. We therefore suggest the following agenda: firstly more epidemiological studies need to be carried out in larger scales and in different target populations; secondly, the appropriate routine diagnosis, particularly novel laboratory techniques, should be well equipped, easy, cheap, and not time consuming – especially when screening a mass community; lastly, standard strategies including health education should be consistently implemented throughout the country. We would then expect that the incidence of parasitic infections would be markedly reduced or eradicated from this region in the future.

REFERENCES

Casemore DP, Sands RL, Curry A. *Cryptosporidium* species a “new” human pathogen. *J Clin Pathol*

1985;38:1321-36.

Cheah WC, Fah CS, Fook CW. Pattern of *Toxoplasma* antibodies in Malaysian pregnant women. *Med J Malaysia* 1975;29:275-9.

Chirgwin K, Hafner R, Leport C, *et al*. Randomized phase II trial of atovaquone with pyrimethamine or sulfadiazine for treatment of toxoplasmic encephalitis in patients with acquired immunodeficiency syndrome: ACTG 237/ANRS 039 Study. AIDS Clinical Trials Group 237/Agence Nationale de Recherche sur le SIDA, Essai 039. *Clin Infect Dis* 2002;34:1243-50.

Cohen BA. Neurologic manifestations of toxoplasmosis in AIDS. *Semin Neurol* 1999;19:201-11.

Collazos J. Opportunistic infections of the CNS in patients with AIDS: diagnosis and management. *CNS Drugs* 2003;17:869-87.

Combee CL, Collinge ML, Britt EM. Cryptosporidiosis in a hospital-associated day care center. *Pediatr Infect Dis* 1986;5:528-32.

Congpuong K, Na-Bangchang K, Thimasarn K, Tasanor U, Wernsdorfer WH. Sensitivity of *Plasmodium vivax* to chloroquine in Sa Kaeo Province, Thailand. *Acta Trop* 2002;83:117-21.

Couvreur J, Thulliez P, Daffos F, *et al*. Fetal toxoplasmosis. In utero treatment with pyrimethamine sulfamides. *Arch Fr Pediatr* 1991;48:397-403 (in French).

Cross JH, Alcantara A, Alquiza L, Zaraspe G, Ranoa C. Cryptosporidiosis in Philippine children. *Southeast Asian J Trop Med Public Health* 1985;16:257-60.

de Graaf DC, Spano F, Petry F, Sagodira S, Bonnin A. Speculation on whether a vaccine against cryptosporidiosis is a reality or fantasy. *Int J Parasitol* 1999;29:1289-306.

de Lalla F, Rinaldi E, Santoro D, Nicolin R, Tramarin A. Outbreak of *Entamoeba histolytica* and *Giardia lamblia* infections in travelers returning from the tropics. *Infection* 1992;20:78-82.

Dupouy-Camet J, de Souza SL, Maslo C, *et al*. Detection of *Toxoplasma gondii* in venous blood from AIDS patients by polymerase chain reaction. *J Clin Microbiol* 1993;31:1866-9.

Furrer H, Cohort Study Ts t. Management of opportunistic infection prophylaxis in the highly active antiretroviral therapy era. *Curr Infect Dis Rep* 2002;4:161-74.

- Gambhir IS, Jaiswal JP, Nath G. Significance of *Cryptosporidium* as an aetiology of acute infectious diarrhoea in elderly Indians. *Trop Med Int Health* 2003;8:415-9.
- Grover CM, Thulliez P, Remington JS, Boothroyd JC. Rapid prenatal diagnosis of congenital *Toxoplasma* infection by using polymerase chain reaction and amniotic fluid. *J Clin Microbiol* 1990;28:2297-301.
- Hohlfeld P, Daffos F, Costa JM, Thulliez P, Forestier F, Vidaud M. Prenatal diagnosis of congenital toxoplasmosis with a polymerase-chain-reaction test on amniotic fluid. *N Engl J Med* 1994;331:695-9.
- Holland GN. Ocular toxoplasmosis: a global reassessment. Part I: epidemiology and course of disease. *Am J Ophthalmol* 2003;136:973-88.
- Holland GN. Ocular toxoplasmosis: a global reassessment. Part II: disease manifestations and management. *Am J Ophthalmol* 2004;137:1-17.
- Ho-Yen DO. Ocular disease. In: Ho-Yen DO, Joss AWL, eds. Human toxoplasmosis. New York: Oxford University Press, 1992:65-8.
- Jamaiah I, Anuar AK, Najib NA, Zurainee MN. Imported malaria: a retrospective study in University Hospital, Kuala Lumpur, a ten-year experience. *Med J Malaysia* 1998;53:6-9.
- Joseph P, Calderon MM, Gilman RH, *et al.* Optimization and evaluation of a PCR assay for detecting toxoplasmic encephalitis in patients with AIDS. *J Clin Microbiol* 2002;40:4499-503.
- Kadappu KK, Nagaraja MV, Rao PV, Shastry BA. Azithromycin as treatment for cryptosporidiosis in human immunodeficiency virus disease. *J Postgrad Med* 2002;48:179-81.
- Kamel AG, Maning N, Arulmainathan S, Murad S, Nasuruddin A, Lai KP. Cryptosporidiosis among HIV positive intravenous drug users in Malaysia. *Southeast Asian J Trop Med Public Health* 1994;25:650-3.
- Khetsuriani N, Holman RC, Anderson LJ. Burden of encephalitis-associated hospitalizations in the United States, 1988-1997. *Clin Infect Dis* 2002;35:175-82.
- Kitvatanachai S, Janyapoon K, Rhongbuttsri P, Thap LC. A survey on malaria in mobile Cambodians in Aranyaprathet, Sa Kaeo Province, Thailand. *Southeast Asian J Trop Med Public Health* 2003;34:48-53.
- Koh KH, Chew PH, Kiyu A. A retrospective study of malaria infections in an intensive care unit of a general hospital in Malaysia. *Singapore Med J* 2004;45:28-36.
- Kopec R, De Caro G, Chapnick E, Ghitan M, Saffra N. Prophylaxis for ocular toxoplasmosis. *Clin Infect Dis* 2003;37:e147-8.
- Kshirsagar NA, Gogtay NJ, Rajgor D, Dalvi SS, Wakde M. An unusual case of multidrug-resistant *Plasmodium vivax* malaria in Mumbai (Bombay), India. *Ann Trop Med Parasitol* 2000;94:189-90.
- Lebech M, Andersen O, Christensen NC, *et al.* Feasibility of neonatal screening for *Toxoplasma* infection in the absence of prenatal treatment, Danish Congenital Toxoplasmosis Study Group. *Lancet* 1999;353:1834-7.
- Lee SH, Levy DA, Craun GF, Beach MJ, Calderon RL. Surveillance for waterborne-disease outbreaks-United States, 1999-2000. *MMWR Surveill Summ* 2002;51:1-47.
- Longworth DL. Drug-resistant malaria in children and in travelers. *Pediatr Clin North Am* 1995;42:649-64.
- Marshall MM, Naumovitz D, Ortega Y, Sterling CR. Waterborne protozoan pathogens. *Clin Microbiol Rev* 1997;10:67-85.
- Mets MB, Holfels E, Boyer KM, *et al.* Eye manifestations of congenital toxoplasmosis. *Am J Ophthalmol* 1996;122:309-24.
- Moe Lwin AM, Umenai T. Cost analysis of malaria patients in Taikkyi Township Mymmar. *Asia-Pacific J Public Health* 1999;11:94-100.
- Munoz Batet C, Guardia Llobet C, Juncosa Morros T, *et al.* Toxoplasmosis and pregnancy. Multicenter study of 16,362 pregnant women in Barcelona. *Med Clin (Barc)* 2004;123:12-6 (in Spanish).
- Nissapatorn V, Nor Azmi MA, Cho SM, *et al.* Toxoplasmosis: prevalence and risk factors. *J Obstetr Gynecol* 2003;23:618-24.
- Norhayati M, Rohani AK, Hayati MI, *et al.* Clinical features of malaria in Orang Asli population in Pos Piah, Malaysia. *Med J Malaysia* 2001;56:271-4.
- Olson ME, Ceri H, Morck DW. *Giardia* vaccination. *Parasitol Today* 2000;16:213-7.
- Penggabean M, Norhayati, Oothuman P, Fatmah MS. Efficacy of albendazole in the treatment of *Trichuris trichiura* and *Giardia intestinalis* infection in rural Malay communities. *Med J Malaysia* 1998;53:408-12.

- Pengsaa K, Limkittikul K, Pojjaroen-anant C, *et al.* Single-dose therapy for giardiasis in school-age children. *Southeast Asian J Trop Med Public Health* 2002;33:711-7.
- Pozio E. Highly active antiRetroviral therapy and opportunistic protozoan infections. *Parassitologia* 2004;46:89-93 (in Italian).
- Sidhu PS, Ng SC. A retrospective study on malaria cases admitted to the University Hospital, Kuala Lumpur, 1984-1988. *Med J Malaysia* 1991;46:177-82.
- Silachamroon U, Krudsood S, Treeprasertsuk S, *et al.* Clinical trial of oral artesunate with or without high-dose primaquine for the treatment of vivax malaria in Thailand. *Am J Trop Med Hyg* 2003;69:14-8.
- Silveira C, Belfort R Jr, Muccioli C, *et al.* The effect of long-term intermittent trimethoprim/sulfamethoxazole treatment on recurrences of toxoplasmic retinochoroiditis. *Am J Ophthalmol* 2002;134:41-6.
- Suyaphun A, Wiwanitkit V, Suwansaksri J, *et al.* Malaria among hilltribe communities in northern Thailand: a review of clinical manifestations. *Southeast Asian J Trop Med Public Health* 2002;33 (suppl 3):14-5.
- Suhardjo, Utomo PT, Agni AN. Clinical manifestations of ocular toxoplasmosis in Yogyakarta, Indonesia: a clinical review of 173 cases. *Southeast Asian J Trop Med Public Health* 2003;34:291-7.
- Tan DS, Mak JW. The role of toxoplasmosis in congenital disease in Malaysia. *Southeast Asian J Trop Med Public Health* 1985;16:88-92.
- Vidal JE, Colombo FA, Penalva de Oliveira AC, Focaccia R, Pereira-Chioccola VL. PCR assay using cerebrospinal fluid for diagnosis of cerebral toxoplasmosis in Brazilian AIDS patients. *J Clin Microbiol* 2004;42:4765-8.
- Yazdanpanah Y, Goldie SJ, Paltiel AD, *et al.* Prevention of human immunodeficiency virus-related opportunistic infections in France: a cost-effectiveness analysis. *Clin Infect Dis* 2003;36:86-96.
- Zurainee MN, Khairul Anuar A, Fong MY, Hoh HB, Choon J, Rahmah N. Ocular presentations and *Toxoplasma* serology. *J Univ Malay Med Center* 2000;2:98-102.