



Research Journal of
Parasitology

ISSN 1816-4943



Academic
Journals Inc.

www.academicjournals.com

Toxoplasmosis: A Silent Threat in Southeast Asia*

Veeranoot Nissapatorn
Department of Parasitology, University of Malaya Medical Centre,
50603 Kuala Lumpur, Malaysia

Abstract: Toxoplasmosis represents the most prominent parasitic disease found in humans. The seroprevalence of toxoplasmosis was estimated to vary from <2% up to 70% in the Southeast Asian population. Contact with cat and consumption of uncooked meat were the most common risk factors in acquiring high rate *Toxoplasma* infection profusely. However, there were a very few reports of toxoplasmosis contracted through blood product or organ transplantation. In view of the clinical scenario, toxoplasmosis was an etiological factor in pregnant women related to factors such as abortion, stillbirth and bad obstetric history and required a consideration differential diagnosis of patients with unexplained lymphadenopathy. Moreover, toxoplasmosis was found to be a common cause in patients with infectious posterior uveitis. With the concurrent HIV/AIDS pandemic, toxoplasmosis was shown to be highly prevalent in HIV-infected patients, with substantial incidence of toxoplasmic encephalitis (TE) in AIDS patients being reported mainly from Malaysia, Singapore and Thailand. Majority of active TE patients presented with typical neurological manifestations with CD4 cell count of less than 100 cells/mm³. The laboratory investigations in the diagnosis to be taken into consideration included a positive *Toxoplasma* serodiagnosis and CT scan finding. Anti-*Toxoplasma* therapy was shown to be quite effective in treating TE, nonetheless, relapse of TE cases were still reported. Moreover, no outbreak in food and water borne toxoplasmosis has been documented in this subcontinent.

Key words: Toxoplasmosis, epidemiology, clinical perspective, health issue and Southeast Asia

INTRODUCTION

Toxoplasma gondii is a ubiquitous, intracellular protozoan parasite and zoonotic in nature. Toxoplasmosis is still prevalent in every part of the world even today and is a public health problem capable of causing a broad spectrum of diseases in different groups of population found in Southeast Asia (Iverarity *et al.*, 2002; Suhardjo *et al.*, 2003; Subsai *et al.*, 2004; Nissapatorn *et al.*, 2005). This literature review therefore aims to highlight epidemiological surveillances and clinical perspectives on toxoplasmosis in Southeast Asian people. Toxoplasmosis is definitely a subject of challenge in the field of infectious diseases that still need more efforts in its initial elimination and further steps should also be taken in eradicating this disease from this well known region.

MATERIALS AND METHODS

This literature review was carried out at the Department of Parasitology, University of Malaya Medical Centre from October to December, 2004. Since 1900, the first observation of *Toxoplasma* was found in a section of the spleen and bone marrow of Java sparrows and was given its definitive description by Nicolle and Manceaux in 1908. However, the first case of congenital toxoplasmosis in man was diagnosed in 1928. Later, *Sabin* and *Feldman* developed the first reliable serological assay

*Originally Published in Research Journal of Parasitology, 2007

the Dye test to detect *Toxoplasma* serology in 1948. From these historical events, all related-data of this human pathogen were intentionally reviewed and obtained from the initial phases of its literature during the late 50s (1959), up to the new era (2005) from the prime and hi-tech search Medline, which is a systematic, informative and a very useful source in conducting this review. The abstracts of these previous works were collected from each country in Southeast Asia. Subsequently, all accessible original articles were carefully read and they highlighted the importance of its content. From this search, it is presumed that some works could not be traced due to the fact that they were either published by local journals that could not be accessed or were written in the native language, which might not be widely understood by others. Unfortunately, no study on toxoplasmosis has been reported in Brunei Darussalam, although it is a small but a rich country. Therefore, other 9 Southeast Asian countries were alphabetically included; Cambodia (2001-2003), Indonesia (1965-2003), Laos PDR (1992), Malaysia (1973-2005), Myanmar (1977), Philippines (1991-2000), Singapore (1967-2003), Thailand (1967-2004) and Viet Nam (1959-2003). Overall, a total number of 103 publications were successfully reported, which portrayed to the native people an awareness of this scientific documentation in the beginning of 21st century.

RESULTS

Table 1 shows that the seroprevalence of toxoplasmosis seems to increase with the time duration as particularly seen in Indonesia; 2 to 63% in 1964 to 1980 (De Roever-Bonnet *et al.*, 1964; Yamamoto *et al.*, 1970; Clarke *et al.*, 1973a-b, 1975; Cross *et al.*, 1975a-d, 1976; Partono and Cross, 1975; Durfee *et al.*, 1976; Srisari, 1978; Srisari and Endardjo, 1980), 3.1 to 60% from 1981 to 1994 (Chomel *et al.*, 1993) and 58 to 70% during 1995 till 2003 (Uga *et al.*, 1996; Konishi *et al.*, 2000; Terazawa *et al.*, 2003). This largest country clearly showed the highest *Toxoplasma* prevalence in this region. Furthermore, only one study was reported in Laos PDR, where 15.3% of *Toxoplasma* seroprevalence was shown in a group of inhabitants with a prevalence increasing with age (Catat *et al.*, 1992). However, in Malaysia, the seroprevalence of toxoplasmosis varied from 13.9 to 30.2% in healthy persons. The Malays showed the highest prevalence when compared to other ethnic groups, signifying that *Toxoplasma* seropositivity tends to increase with age. Moreover, a higher prevalence was found in males and unemployed individuals, whereas a lower rate was observed in people with higher incomes. The risk behaviors such as contact with cat and consumption of uncooked meat were found to be the main sources of *Toxoplasma* infection (Tan and Zaman, 1973; Dissanaik *et al.*, 1977; Thomas *et al.*, 1980; Sinniah *et al.*, 1984; Zahedi *et al.*, 1985; Hakim *et al.*, 1994; Nissapatorn *et al.*, 2002). Two cases of human acquired toxoplasmosis were reported in the early period (Leong *et al.*, 1976) and thereby toxoplasmosis was also suggested to be given priority in the investigation of pyrexia of unknown origin (PUO) cases (Tan *et al.*, 1978). Similarly, from 1975 to 2000, studies in the Philippines showed varying results of *Toxoplasma* seroprevalence from < 2 to 61.2% in different settings. The prevalence tended to increase with age and a significantly higher rate was found in rural than urban areas (Cross *et al.*, 1997; Eduardo, 1991; Kawashima *et al.*, 2000). Subsequently in Singapore, the first report on *Toxoplasma* seroprevalence was 41.3% in the sera of clinically suspected cases and 17.2% in healthy individuals (Singh *et al.*, 1968). Taking into account the comparison between different regions, the highest *Toxoplasma* seropositivity was found among the Malays, with their living habits and sanitary conditions greatly attributing to this finding (Zaman and Goh, 1969).

During the period of 80s, *Toxoplasma* seroprevalence was 42.5% in clinically suspected cases (Lim *et al.*, 1982). From 1991 to date, 18.8% of *Toxoplasma* seroprevalence was shown in healthy individuals and the epidemiology and clinical profiles of patients presenting with acute toxoplasmosis were indicative of asymptomatic cervical lymphadenopathy (Mohan *et al.*, 1991a, b). The first

Table 1: The prevalence of *Toxoplasma* infection and clinical evidence of toxoplasmosis in different groups of the Southeast Asian population

Country origin	Year	<i>Toxoplasma</i> seroprevalence			Clinical toxoplasmosis (year)
		Healthy persons	Pregnant women	Children	
Cambodia-	-	-	-	-	-
Indonesia	1964-1980	2-63%	-	-	Congenital toxoplasmosis (1976)
	1981-1994	3.1-60%	-	-	Congenital toxoplasmosis (1989)
	1995-2003	58-70%	-	-	-
Lao PDR	1992	5.3%	-	-	-
Malaysia	1973-2005	13.9-30.2%	23-49%	2-33.3%	Acquired toxolasmosis (1976)
					Congenital toxoplasmosis (2005)
Myanmar	1977	-	-	28.4-43.8%	-
Philippines	1977-2000	<2-61.2%	-	-	-
Singapore	1968-1990	17.2%	-	-	Congenital toxoplasmosis (1967, 1971, 1982 and 1989)
	1991-2003	18.8%	upto 17.2%	-	Acute toxoplasmosis (lymphadenopathy) (1991a and b)
Thailand	1967-2003	2.8-18.5%	1.4-21.7%	-	Fatal human toxoplasmosis (1978)
Viet Nam	1959-2003	7.7-24.3%	11.2%	-	-

Table 2: The prevalence of *Toxoplasma* infection and clinical evidence of toxoplasmosis in patients with ocular diseases and other immunosuppressed

Country origin	Year	<i>Toxoplasma</i> (IgG/IgM) seroprevalence		Clinically diagnosed of ocular toxoplasmosis
		Ocular	Immunosuppressed ¹	
Cambodia	-	-	-	-
Indonesia	1976-2003	-	-	Present(1976, 1982, 1988, 1991 and 2003)
Lao PDR	-	-	-	-
Malaysia	1974-2005-	31.1%/19.3%	-	Present (1974, 1983, 2000 and 2005)
Myanmar	-	-	-	-
Philippines	-	-	-	-
Singapore	1991	-	-	Present (1991a and b)
Thailand	1995-2001	12.5%/3.1%	11%	-
Vietnam	-	-	-	-

¹Immunosuppressed includes patients with organ transplant

study in Thailand showed that 4 out of 265 slaughter workers were *Toxoplasma* seropositivities (Sungkasuwan, 1967), while, a report of three fatal cases on human toxoplasmosis was found in the late 70s (Bunyaratvej *et al.*, 1978). *Toxoplasma* seroprevalence was between 2.8 to 18.5% in healthy persons and consumption of raw meat and contact with cats were among the risk factors contributing to *Toxoplasma* infection (Tanphaichitra *et al.*, 1976; Nabnien, 1979; Morakote *et al.*, 1984; Bunnag *et al.*, 1988; Maleewong *et al.*, 1989; Wongkamchai *et al.*, 1995; Maruyama *et al.*, 2000; Tantivanich *et al.*, 2001; Sukthana *et al.*, 2003). Viet Nam, the first Southeast Asian country, was also actively involved with epidemiological study on toxoplasmosis, with an incidence of 2.9% using toxoplasmin skin test as shown in the earliest study (Sery *et al.*, 1959). 15.7 and 24.3% of *Toxoplasma* seroprevalence were found in two different groups of population (Sery *et al.*, 1988); while 7.7% in intravenous drug users in one recent study (Buchy *et al.*, 2003).

In pregnant women, 23 to 49% of *Toxoplasma* prevalence was found in Malaysia (Cheah *et al.*, 1975; Tan *et al.*, 1976; Khairul Anuar *et al.*, 1991; Ravichandran *et al.*, 1998; Nissapatom *et al.*, 2003a),

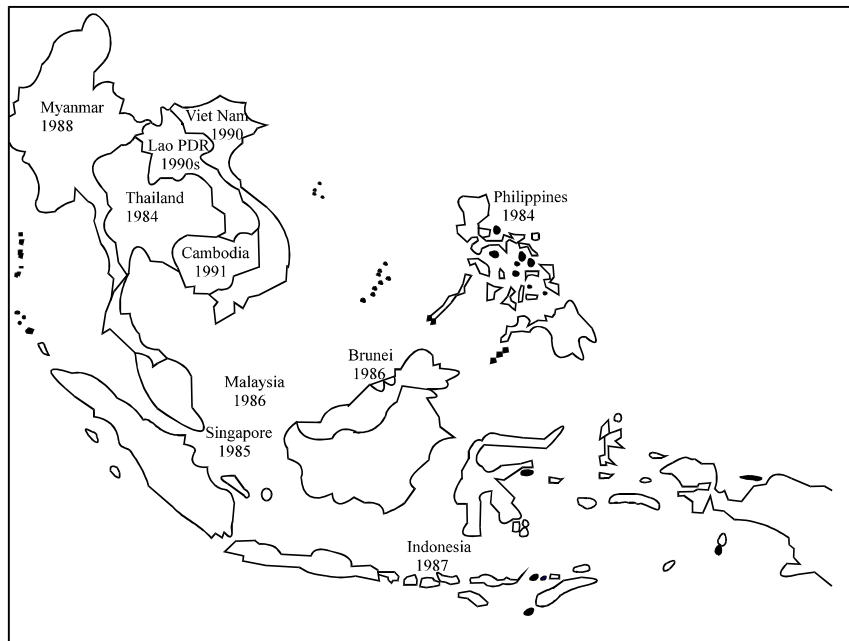


Fig. 1: The first case reported of HIV/AIDS in Southeast Asia

Table 3: The Prevalence of *Toxoplasma* infection and clinical evidence of toxoplasmosis in HIV/AIDS patients

Country origin	No. of HIV/AIDS ¹	<i>Toxoplasma</i> (+) ²	TE ³
Cambodia	170,000	No report	Rare
Indonesia	110,000	No report	No report
Lao PDR	1,700	No report	No report
Malaysia	51,000	21-44.8%	Yes/relapse
Myanmar	320,000	No report	No report
Philippines	8,900	No report	No report
Singapore	4,100	No report	Yes
Thailand	560,000	22.4-53.6%	Yes/relapse
Viet Nam	200,000	No report	No report

¹4th report on the global AIDS epidemic, UNAIDS, 2004. ²*Toxoplasma* (IgG) seroprevalence. ³TE: Toxoplasmic Encephalitis

and it was shown to be the highest *Toxoplasma* rate found in this region as compared to 1.4 to 21.7% in Thailand (Nabnien, 1979; Tantivanich *et al.*, 1980, 2001; Maleewong *et al.*, 1989; Chintana *et al.*, 1991, 1998; Daenseekaew *et al.*, 1992; Taechowisan *et al.*, 1997; Sukthana, 1999; Wanachiwanawin *et al.*, 2001), up to 17.2% in Singapore (Mohan *et al.*, 1991a; Wong *et al.*, 2000) and 11.2% in Viet Nam (Buchy *et al.*, 2003). Surprisingly, few studies have been reported on *Toxoplasma* seroprevalence in children, newborn or still births in this region. In Malaysia, 33.3% (Bisseru and Chong, 1974) and 2% (Tan and Mak, 1985) of *Toxoplasma* prevalence in children and 45.8% in women with still births (Zainul Rashid *et al.*, 1992) were reported. 43.8 and 28.4% *Toxoplasma* prevalence were found in 2 different groups of school children in Myanmar (Tin, 1977). In addition, 7.18 to 13.14% were found in the cord blood (Chintana, 1991; Taechowisan *et al.*, 1997) and up to 21.05% in the new born (Tantivanich *et al.*, 2001) were shown in Thailand. Interestingly, the clinically evident cases of congenital toxoplasmosis have been reported in two neighboring countries; Malaysia and Singapore (Lim, 1967; Paul, 1967, 1971, 1982; Nissapatorn *et al.*, 2005) and have focused their attention on its importance and associated problems (Singh *et al.*, 1972; Singh, 1987; Wong, 1987).

In patient with ocular diseases, few studies showed that 12.5 to 31.1% (IgG) and 3.1 to 19.3% (IgM) of *Toxoplasma* prevalence were found in Malaysia and Thailand (Wongkamchai *et al.*, 1995; Nissapatom *et al.*, 2005). Interestingly, the evident cases of congenitally acquired ocular toxoplasmosis, which is a common vision-threatening disease and the most common of primary retinochoroiditis were mainly reported from Indonesia (Partono and Cross, 1976; Srisari, 1982; Kadarisman *et al.*, 1991; Suhardjo *et al.*, 2003). The critical stage of the disease was also found to be the most common occurrence in these patients (Lim and Tan, 1983). Patients with ocular manifestations of congenital toxoplasmosis where the incidence of congenital infection was high, belonged to the number of cases presenting with fetal wastage and the prevalence of ocular toxoplasmosis (Mohan *et al.*, 1991a, b). In addition, ocular manifestations and *Toxoplasma* serodiagnosis were the main useful tools of investigation (Chee *et al.*, 1992; Zurainee *et al.*, 2000; Nissapatom *et al.*, 2005). Among the immunosuppressed, 11% of *Toxoplasma* seroprevalence was found in patients with kidney transplants (Sukthana *et al.*, 2001) as shown in Table 2.

The first case of HIV/AIDS was reported in 1984. Since then, the epidemiological and clinical relevance of toxoplasmosis has been studied in a few dominant countries, although no study regarding this has been conducted in Indonesia, Laos PDR, Myanmar, Philippines and Viet Nam. The first report on seroprevalence of toxoplasmosis was conducted in Thailand (Wongkamchai *et al.*, 1995). Since then, the varying *Toxoplasma* prevalence from 21 to 53.7% has been consistently reported from different settings in Malaysia (Shamilah *et al.*, 2001; Nissapatom *et al.*, 2001, 2002, 2003b-d, 2004, 2005) and Thailand (Wongkamchai *et al.*, 1995, 1999; Sukthana *et al.*, 2000; Wanachiwanawin *et al.*, 2001). In Viet Nam, a screening of toxoplasmosis was subjected for recommendation in HIV/AIDS patients (Buchy, 2003). After HIV/AIDS epidemic, toxoplasmic encephalitis (TE) was first reported in clinical practice found in Thailand (Thongchareon, 1992). The incidence of this opportunistic infection varied from place to place and mostly occurred at a time when the patient had a very low CD4 cell count (<100 cells/mm³). Reactivation of latent *Toxoplasma* infection and relapse of TE cases have been subsequently reported in AIDS patients (Swasdisevi, 1994; Haniffah *et al.*, 1996; Ruxrungtham *et al.*, 1996; Chariyalertsak *et al.*, 2001; Pichit *et al.*, 2001; Iverarity *et al.*, 2002; Senya *et al.*, 2003; Nissapatom *et al.*, 2003b-d, 2004, 2005; Subsai *et al.*, 2004; Anekthananon *et al.*, 2004) as shown in Fig. 1 and Table 3, respectively.

Toxoplasmosis: From Source to Outbreaks

No ever-reported study of clinically evident of toxoplasmosis outbreak on food and water issue has been documented in the Southeast Asian subcontinent.

DISCUSSION

Toxoplasmosis is one of the most important infectious diseases, which causes epidemiological and clinical impacts in humans. This review confirms that these surveys have been successfully conducted over the past years and have greatly helped in the better understanding of this existing parasitic infection in this region. However, there were certain predisposing factors that play an important role in the acquisition of *Toxoplasma* infection. Indonesia and Philippines are good examples of countries sharing striking similarities in their geographical distributions based on over a thousand islands and Volcanic Mountains; moreover, both the countries show high *Toxoplasma* seroprevalence (upto 70%). In this context, geographical variations (mountainous or volcanic vs plain areas) could be one of the hypotheses to explain the contribution to the spreading of *Toxoplasma* infection. On a broader aspect, most countries have shown no difference in their life styles, particularly in the consumption of raw or half cooked meat, which is most probably and accidentally infected by *Toxoplasma* cyst; however, these studies are mainly conducted in the cities or the urban areas.

Therefore, it would be more interesting if future studies are carried out in the suburbs or rural places, including tribal areas and certain groups of inhabitants in the remote areas. Besides, health education particularly eating habits should be wisely practiced, since it is the most common route of *Toxoplasma* transmission. It was evident from the living conditions of different regions that certain groups were more exposed to *Toxoplasma* infection than others. Many studies found that Malays had the highest prevalent rate, which was due to the fact of their close contact with cats kept as pets particularly in these two neighboring countries of Malaysia and Singapore. Toxoplasmosis is considered as one of the blood borne diseases either via blood products or organ transplant, however, there were very few data on epidemiological aspects and none was documented on clinical evidence of toxoplasmosis. The importance of *Toxoplasma* screening is very much in need to promote the awareness among blood donation, which would further prevent passive seroconversion particularly during the post-transfusional period. So far, this factor has not posed a major public health problem in this region.

In pregnant women, the clinical implications of *Toxoplasma* infection during pregnancy are tremendously dangerous such as spontaneous abortion, still births or premature delivery with various fetal malformations. The studies in Malaysia showed the highest rate of *Toxoplasma* infection than other parts in this subcontinent, but the incidence of congenital toxoplasmosis was surprisingly scare or at very low rate. Overall, the evidence of congenital toxoplasmosis is not well documented in this region either due generally to the fact that no study has been properly conducted or it actually shows low incidence. Even though toxoplasmosis is relatively low in certain countries; however, a large proportion of antenatal women are still susceptible to this infection. This aspect strongly necessitates imparting health education, including general guidelines of primary prevention to childbearing seronegative women and pregnant women from preventing primary *Toxoplasma* infection during pregnancy. Mass or routine antenatal toxoplasmosis screening is cost effective and not appropriate to practice particularly in limited resource settings or low incidence of congenital toxoplasmosis, however, it could be justified in the area where high prevalence of *Toxoplasma* infection affects mothers, congenital toxoplasmosis and in countries where TORCHs screening is an applicable tool in that setting. In addition, women with bad obstetric history such as abortion (spontaneous or repeated), still birth or fetal malformations should be tested for *Toxoplasma* serological status, which can reduce the possibility of congenital toxoplasmosis.

The existence of clinically diagnosed toxoplasmosis in patients with ocular diseases has been periodically reported in different studies from Indonesia, Malaysia and Singapore. Whether ocular toxoplasmosis is either congenital or acquired, is still controversial, nonetheless, toxoplasmosis is not only the most common cause of posterior uveitis in majority of cases, but it should also be primarily considered in the differential diagnosis in any suspected patients with ocular diseases. Ocular presentations and *Toxoplasma* serodiagnosis are the primary sources of investigation; in addition, improvement of clinical and funduscopy conditions after the introduction of anti-*Toxoplasma* therapy should be the clue for the confirmation of toxoplasmosis.

HIV/AIDS is the subject of great interest and of utmost concern particularly in Southeast Asia, being a region of the fastest growing HIV epidemic in the world. Toxoplasmosis is still reported in clinical practices in co-existence with HIV/AIDS patients. *Toxoplasma* parasite is the most common cause of intracerebral lesions and one of the leading opportunistic pathogens and causes of death in AIDS patients. Due to its noteworthy significance, toxoplasmosis has been included in the centers for Disease Control and Prevention (CDC), Atlanta for AIDS defining illness till date. The incidence of toxoplasmic encephalitis (TE) is directly proportionate to the prevalence of *Toxoplasma* infection and the number of AIDS patients. The empirical diagnosis of TE is based on few criteria. The neurological presentations mimic other brain diseases and make the diagnosis difficult. Results from the brain involvement in either neuroimaging finding, which is widely used, or stereotactic brain biopsy (Yeo *et al.*, 2000), are useful in AIDS patients with cerebral lesions to confirm the etiology in majority

of cases. Serology (IgG and/or IgM antibodies), is shown as a sensitive investigation to determine whether TE is primary, which is less common, or secondary (reactivation), which occurs in more than 95% of these patients. However, other techniques are also used to detect the presence of organism, but the sensitivity and specificity are quite varied and depend on its availability or unavailability in the laboratory. Responding to anti-*Toxoplasma* therapy is the key to confirm the diagnosis of TE. Moreover, the occurrence of TE was significantly related to very low level of CD4 count and one study suggested that the correlation of imaging findings with CD4 counts is especially useful in obtaining a working diagnosis (Corr, 2003). Primary chemoprophylaxis should be compulsorily given to all new HIV infected patients particularly in poor resource settings, where they might not be able to access HAART. However, this is not an absolute hypothesis to explain the relationship between the occurrence of TE and its chemoprophylaxis in these patients. In due course, one study found that the mounting medical care cost for adult AIDS patients has become critical (Suwanagool *et al.*, 1997) in certain countries where the number of HIV/AIDS patients is still increasing. In the era of HAART, it should be considered as the most effective approach in reducing the incidence of TE, however, it is still questionable whether it is the ideal option in case management regarding this parasite in times to come.

CONCLUSIONS

Toxoplasmosis is still shown to be highly prevalent in Southeast Asia. A few recognized, known and accepted risk behaviors to *Toxoplasma* infection have consistently been identified. Clinical toxoplasmosis in different groups of population has been periodically reported in this region. However, few recommendations could be conducive to the completeness of this literature review: firstly, more studies should be carried out in the area of Mae-Khong region (Cambodia, Lao PDR and Viet Nam) and with the epidemic of HIV/AIDS, toxoplasmosis should be more importantly given an attention due to the fact that suspected cases might be misdiagnosed and subsequently led to life-threatening or fatal condition. This is also an opportunity for researchers to focus on this pathogen in these patients and extend more works in other vulnerable groups; secondly, there are many other risk factors involved which are undiscovered and need to be investigated to further clarify the pathogenesis of this parasite; thirdly, the novel drugs including herbal medicine, should be given serious consideration in clinical trials, particularly in tackling the cystic stage of this parasite and reducing the treatment burden through new effective medicines of both private and government hospitals; and lastly, multi centers for studying toxoplasmosis should be established, which could serve as smart partnerships to strengthen the regional collaborations and also enhance the existing activities in terms of prevention and control measures, thereby logically conducting assessments according to their own feasibilities for the benefit of the affected individuals. It is therefore hoped that a new chapter of managing health issues regarding toxoplasmosis would be thoroughly successful in the future.

REFERENCES

- Anekthananon, T. and W. Ratanasuwan *et al.*, 2004. HIV infection/acquired immunodeficiency syndrome at Siriraj Hospital, 2002: Time for secondary prevention. *J. Med. Assoc. Thailand*, 87: 173-179.
- Bisseru, B. and L.K. Chong, Letter, 1974. *Toxoplasma* antibody in West Malaysia (Peninsular Malaya). *Tran. R. Soc. Trop. Med. Hyg.*, 68: 172-173.
- Buchy, P. and J.Y. Follezou *et al.*, 2003. Serological study of toxoplasmosis in Vietnam in a population of drug users (Ho Chi Minh City) and pregnant woman (Nha Trang). *Bull. de la Societe de Pathologie Exotique de ses Filiales*, 96: 46-47.
- Bunnag, T. and K. Klongkammuanakarn *et al.*, 1988. Seroepidemiology of toxoplasmosis in rural villagers, Phayao province. *J. Med. Assoc. Thailand*, 71: 96-99.

- Bunyaratvej, S. and S. Chaimuanggrai *et al.*, 1978. Human adult toxoplasmosis: Report of three fatal cases. Southeast Asian J. Trop. Med. Public Health, 9: 288.
- Catar, G. and M. Giboda *et al.*, 1992. Seroepidemiological study of toxoplasmosis in Laos. Southeast Asian J. Trop. Med. Public Health, 23: 491-492.
- Chariyalertsak, S. and T. Sirisanthana *et al.*, 2001. Clinical presentation and risk behaviors of patients with acquired immunodeficiency syndrome in Thailand, 1994-1998: Regional variation and temporal trends. Clin. Infect. Dis., 32: 955-962.
- Cheah, W.C. and C.S. Fah *et al.*, 1975. Pattern of *Toxoplasma* antibodies in Malaysian pregnant women. Med. J. Malaysia, 29: 275-279.
- Chee, S.P. and S. Seah *et al.*, 1992. Anti-*Toxoplasma* serotitres in uveitis and ocular toxoplasmosis. Anna. Acad. Med. Singapore, 21: 226-229.
- Chintana, T., 1991. Pattern of antibodies in toxoplasmosis of pregnant women and their children in Thailand. Southeast Asian J. Trop. Med. Public Health, 22: 107-110.
- Chintana, T. and Y. Sukthana *et al.*, 1998. *Toxoplasma gondii* antibody in pregnant women with and without HIV infection. Southeast Asian J. Trop. Med. Public Health, 29: 383-386.
- Chomel, B.B. and R. Kasten *et al.*, 1993. Serosurvey of some major zoonotic infections in children and teenagers in Bali, Indonesia. Southeast Asian J. Trop. Med. Public Health, 24: 321-326.
- Clarke, M.D. and J.H. Cross *et al.*, 1973a. A parasitological survey in the Jogjakarta area of Central Java, Indonesia. Southeast Asian J. Trop. Med. Public Health, 4: 195-201.
- Clarke, M.D. and J.H. Cross *et al.*, 1973b. Human malarias and intestinal parasites in Kresek, West Java, Indonesia, with a cursory serological survey for toxoplasmosis and amoebiasis. Southeast Asian J. Trop. Med. Public Health, 4: 32-36.
- Clarke, M.D. and J.H. Cross *et al.*, 1975. Serological study of amebiasis and toxoplasmosis in the Lindu Valley, Central Sulawesi, Indonesia. Trop. Geograph. Med., 27: 274-278.
- Corr, P., 2003. Imaging of Acquired Immunodeficiency Syndrome (AIDS). Ann. Acad. Med. Singapore, 32: 477-482.
- Cross, J.H. and G.S. Irving *et al.*, 1975a. The prevalence of *Entamoeba histolytica* and *Toxoplasma gondii* antibodies in Central Java, Indonesia. Southeast Asian J. Trop. Med. Public Health, 6: 467-471.
- Cross, J.H. and M.D. Clarke *et al.*, 1975b. Parasitology survey in the Palu Valley, central Sulawesi (Celebes), Indonesia. Southeast Asian J. Trop. Med. Public Health, 6: 366-375.
- Cross, J.H. and M.D. Clarke *et al.*, 1975c. Parasitology survey in Northern Sumatra, Indonesia. Am. J. Trop. Med. Hygiene, 79: 123-126.
- Cross, J.H. and M.D. Clarke *et al.*, 1975d. Parasitic infections in humans in West Kalimantan (Borneo), Indonesia. Trop. Geograph. Med., 28: 121-130.
- Cross, J.H. and M.D. Clarke *et al.*, 1976. Parasitic infections in humans in West Kalimantan (Borneo), Indonesia. Trop. Geograph. Med., 28: 121-130.
- Cross, J.H. and T. Banzon *et al.*, 1997. Biomedical survey in North Samar Province, Philippine Islands. Southeast Asian J. Trop. Med. Public Health, 8: 464-475.
- Daenseekaew, W. and W. Maleewong *et al.*, 1992. Seroprevalence of *Toxoplasma gondii* in pregnant women in Ubon Ratchathani province. J. Med. Assoc. Thailand, 75: 609-610.
- De Roever-Bonnet, H. and J.C. Molenaar *et al.*, 1964. Toxoplasmosis in West New Guinea. Trop. Geograph. Med., 16: 82-87.
- Dissanaike, A.S. and S.P. Kan *et al.*, 1977. Studies on parasitic infections in Orang Asli (Aborigines) in Peninsular Malaysia. Med. J. Malaysia, 32: 48-55.
- Durfee, P.T. and J.H. Cross *et al.*, 1976. Toxoplasmosis in man and animals in South Kalimantan (Borneo), Indonesia. Am. J. Trop. Med. Hygiene, 25: 42-47.
- Eduardo, S.L., 1991. Food-borne parasitic zoonoses in the Philippines. Southeast Asian J. Trop. Med. Public Health, 22: 16-22.

- Hakim, S.L. and T. Radzan *et al.*, 1994. Distribution of anti-*Toxoplasma gondii* antibodies among Orang Asli (Aborigines) in peninsular Malaysia. Southeast Asian J. Trop. Med. Public Health, 25: 485-489.
- Haniffah, A.G. and A. Khairul Anuar *et al.*, 1996. Cerebral toxoplasmosis in an AIDS patient. Trop. Biomed., 13: 29-33.
- Inverarity, D. and Q. Bradshaw *et al.*, 2002. The spectrum of HIV-related disease in rural Central Thailand. Southeast Asian J. Trop. Med. Public Health, 33: 822-831.
- Kadarisman, R.S. and M. Marsetio *et al.*, 1991. Visual impairment and blindness in ocular toxoplasmosis cases. Southeast Asian J. Trop. Med. Public Health, 22: 99-101.
- Kawashima, T. and Khin-Sane-Win *et al.*, 2000. Prevalence of antibodies to *Toxoplasma gondii* among urban and rural residents in the Philippines. Southeast Asian J. Trop. Med. Public Health, 31: 742-746.
- Khairul Anuar, A. and A.B. Afifi *et al.*, 1991. *Toxoplasma* antibody in pregnant women in Northern peninsular Malaysia. Diagnosis, 5: 18-23.
- Konishi Houki Y. *et al.*, 2000. High prevalence of antibody to *Toxoplasma gondii* among humans in Surabaya, Indonesia. Japanese J. Infect. Dis., 53: 238-241.
- Leong, A.S.Y. and F. Wangm *et al.*, 1976. Acquired toxoplasmosis in Malaysia. Southeast Asian J. Trop. Med. Public Health, 7: 10-15.
- Lim, A.S.M., 1967. Adult ocular manifestation of congenital toxoplasmosis. Singapore Med. J., 8: 241-245.
- Lim, K.C. and R. Pillai *et al.*, 1982. A study on the prevalence of antibodies to *Toxoplasma gondii* in Singapore. Southeast Asian J. Trop. Med. Public Health, 13: 547-550.
- Lim, V.K.E. and P.L. Tan, 1983. Ocular toxoplasmosis in Malaysia. Med. J. Malaysia, 38: 185-187.
- Maleewong, W. and V. Lulitanond *et al.*, 1989. Prevalence of *Toxoplasma* antibodies in blood donors and pregnant women in Khon Kaen Province. J. Med. Assoc. Thailand, 72: 256-259.
- Maruyama, S. and S. Boonmar *et al.*, 2000. Seroprevalence of *Bartonella henselae* and *Toxoplasma gondii* among healthy individuals in Thailand. J. Vet. Med. Sci., 62: 635-637.
- Mohan, T.C. and H. Abdul Jalil *et al.*, 1991a. Anti-*Toxoplasma* antibodies in healthy adults and in different patient categories. Singapore Med. J., 32: 344-347.
- Mohan, T.C. and M. Nadarajah *et al.*, 1991b. A Review of 58 patients in Singapore with significantly high anti-*Toxoplasma* serotitres. Ann. Acad. Med. Singapore, 20: 374-378.
- Morakote, N. and W. Thamasonthi *et al.*, 1984. Prevalence of *Toxoplasma* antibodies in Chiang Mai population. Southeast Asian J. Trop. Med. Public Health, 15: 80-85.
- Nabnien, K., 1979. Seroepidemiological study of toxoplasmosis in the central part of Thailand. Mahidol University. MS Thesis, pp: 89.
- Nissapatorn, V. and Y. Wattanagoon *et al.*, 2001. Seroprevalence of toxoplasmosis in HIV infected patients in Chonburi Regional Hospital, Thailand. Trop. Biomed., 18: 123-129.
- Nissapatorn, V. and A. Kamarulzaman *et al.*, 2002. Seroepidemiology of toxoplasmosis among HIV infected patients and healthy blood donors. Med. J. Malaysia, 57: 304-310.
- Nissapatorn, V. and M.A. Nor Azmi *et al.*, 2003a. Toxoplasmosis-prevalence and risk factors. J. Obstet. Gynaecol., 23: 618-624.
- Nissapatorn, V. and C.K.C. Lee *et al.*, 2003b. Seroprevalence of toxoplasmosis among AIDS patients in Hospital Kuala Lumpur, 2001. Singapore Med. J., 44: 194-196.
- Nissapatorn, V. and C.K.C. Lee *et al.*, 2003c. Toxoplasmosis in HIV/AIDS patients in Malaysia. Southeast Asian J. Trop. Med. Public Health, 34: 80-85.
- Nissapatorn, V. and C. Lee *et al.*, 2003d. AIDS-related opportunistic infections in Hospital Kuala Lumpur. Japanese J. Infect. Dis., 56: 187-192.
- Nissapatorn, V. and C. Lee *et al.*, 2004. Toxoplasmosis in HIV/AIDS patients: a current situation. Japanese J. Infect. Dis., 57: 160-165.

- Nissapatorn, V. and Y.A.L. Lim *et al.*, 2005. Parasitic infections in Malaysia: changing and challenges. Southeast Asian J. Trop. Med. Public Health, 36: 50-59.
- Partono, F. and J.H. Cross, 1975. *Toxoplasma* antibodies in Indonesian and Chinese medical students in Jakarta. Southeast Asian J. Trop. Med. Public Health, 6: 472-476.
- Partono, F. and J.H. Cross, 1976. Congenital toxoplasmosis in Indonesia. Trop. Geographical Med., 28: 63-64.
- Paul, F.M., 1967. A case of congenital toxoplasmosis. J. Singapore Paedia. Soc., 9: 46-49.
- Paul, F.M., 1971. A survey of mental abnormality in Singapore children. MD Thesis, University of Singapore.
- Paul, F.M., 1982. Experiences in the diagnosis and prevention of mental retardation of environmental origin in Singapore. Med. J. Malaysia, 37: 357-361.
- Pichith, K. and H. Charroen *et al.*, 2001. Clinical aspects of AIDS at the Calmette hospital in Phnom Penh, Kingdom of Cambodia A report on 356 patients hospitalized in the Medicine B Department of the Calmette Hospital. Santé, 11: 17-23. (In French).
- Ravichandran, J. and N. Rahmah *et al.*, 1998. *Toxoplasma gondii* antibodies among Malaysian pregnant women: A hospital-based study. Biomed. Res., 1: 25-28.
- Ruxrungtham, K. and O. Muller *et al.*, 1996. AIDS at a University Hospital in Bangkok, Thailand. AIDS., 10: 1047-1049.
- Senya, C. and A. Mehta *et al.*, 2003. Spectrum of opportunistic infections in hospitalized HIV-infected patients in Phnom Penh, Cambodia. Int. J. STD AIDS., 14: 411-416.
- Sery, V. and J. Sauer *et al.*, 1959. Study on Toxoplasmosis in Vietnam. J. Hyg. Epidemiol. Microbiol. Immunol., 3: 214.
- Sery, V. and M. Zastera *et al.*, 1988. To the problem of toxoplasmosis in Vietnam. Bull. Inst. Maritime Trop. Med. Gdynia, 39: 181-185.
- Shamilah, H. and L.S. Hakim *et al.*, 2001. Seroprevalence of *Toxoplasma gondii* antibodies in HIV positive and negative patients using the Immunofluorescence Antibody Test (IFAT) methods. Trop. Biomed., 18: 137-141.
- Singh, M. and V. Zaman *et al.*, 1968. A report on the prevalence of toxoplasmic antibodies in Singapore. Singapore Med. J., 9: 108-110.
- Singh, M. and K.L. Tan *et al.*, 1972. Toxoplasmic antibodies in newborn infants. Asian Federation J. Obstet. Gynaecol., 3: 58-61.
- Singh, M., 1987. Parasitic infections in Singapore. Ann. Acad. Med. Singapore, 16: 689-695.
- Sinniah, B. and V. Thomas *et al.*, 1984. Toxoplasmosis in West Malaysian population. Trop. Med., 1: 81.
- Srisasi, G., 1978. Serological study for antibodies to *Toxoplasma gondii* in Jakarta, Indonesia. Southeast Asian J. Trop. Med. Public Health, 9: 308-311.
- Srisasi, G. and S. Endardjo, 1980. *Toxoplasma* antibodies in Obano, Irian Jaya, Indonesia. Southeast Asian J. Trop. Med. Public Health, 11: 276-279.
- Srisari, G., 1982. *Toxoplasma* antibodies in ocular diseases in Jakarta, Indonesia. Proceeding of the 25th SEAMEO TROPED Seminar, pp: 133-138.
- Subsai, K. and S. Kanoksri *et al.*, 2004. Neurological complications in AIDS patients: the 1-year retrospective study in Chiang Mai University, Thailand. Eur. J. Neurol., 11: 755-759.
- Suhardjo, H. and P.T. Utomo *et al.*, 2003. Clinical manifestations of ocular toxoplasmosis in Yogyakarta, Indonesia: A clinical review of 173 cases. Southeast Asian J. Trop. Med. Public Health, 34: 291-297.
- Sukthana, Y., 1999. Difference of *Toxoplasma gondii* antibodies between Thai and Austrian pregnant women. Southeast Asian J. Trop. Med. Public Health, 30: 38-41.
- Sukthana, Y. and T. Chintana *et al.*, 2000. *Toxoplasma gondii* antibody in HIV-infected persons. J. Med. Assoc. Thailand, 83: 681-684.

- Sukthana, Y. and T. Chintana *et al.*, 2001. Serological study of *Toxoplasma gondii* in kidney recipients. J. Med. Assoc. Thailand, 84: 137-141.
- Sukthana, Y. and J. Kaewkungwal *et al.*, 2003. *Toxoplasma gondii* antibody in Thai cats and their owners. Southeast Asian J. Trop. Med. Public Health, 34: 733-738.
- Sungkasuwan, V., 1967. Preliminary survey of toxoplasmosis. J. Med. Assoc. Thailand, 50: 607.
- Suwanagool, S. and W. Ratanasuwan *et al.*, 1997. The mounting medical care cost for adult AIDS patients at the Faculty of Medicine, Siriraj Hospital: Consideration for management. J. Med. Assoc. Thailand, 80: 431-437.
- Swadisevi, A., 1994. Clinical study of HIV disease in the lower area of northern Thailand in 1994. J. Med. Assoc. Thailand, 77: 440-443.
- Taechowisan, T. and R. Suttent *et al.*, 1997. Immune status in congenital infections by TORCH agents in pregnant Thais. Asian Pacific J. Allergy Immunol., 15: 93-97.
- Tan, D.S.K. and V. Zaman, 1973. *Toxoplasma* antibody survey in West Malaysia. Med. J. Malaysia, 17: 188-191.
- Tan, S.D.K. and W. Cheah *et al.*, 1976. The TORCHES (congenital toxoplasmosis) programme 1. in women of child-bearing age. Singapore Med. J., 17: 207-210.
- Tan, D.S.K. and V. Zaman *et al.*, 1978. Infectious mononucleosis or toxoplasmosis? Med. J. Malaysia, 33: 23-55.
- Tan, D.S.K. and J.W. Mak, 1985. The role of toxoplasmosis in congenital disease in Malaysia. Southeast Asian J. Trop. Med. Public Health, 16: 88-92.
- Tanphaichitra, D. and A. Limsuwarn *et al.*, 1976. Toxoplasmosis, a not uncommon inapparent infectious disease in Thai community-risk of consuming raw meat. J. Med. Assoc. Thailand, 59: 431-432.
- Tantivanich, S. and T. Savanat *et al.*, 1980. Serological studies on possible causes of intra-uterine infections in Thai infants. Southeast Asian J. Trop. Med. Public Health, 11: 387-394.
- Tantivanich, S. and P. Amarapal *et al.*, 2001. Prevalence of congenital cytomegalovirus and *Toxoplasma* antibodies in Thailand. Southeast Asian J. Trop. Med. Public Health, 32: 466-469.
- Terazawa, A. and R. Muljono *et al.*, 2003. High *Toxoplasma* antibody prevalence among inhabitants in Jakarta, Indonesia. Japanese J. Infect. Dis., 56: 107-109.
- Thomas, V. and B. Sinniah *et al.*, 1980. Prevalence of antibodies including IgM to *Toxoplasma gondii* in Malaysia. Southeast Asian J. Trop. Med. Public Health, 11: 119-125.
- Thongcharoen, P., 1992. Opportunistic infections in AIDS/HIV infected patients in Thailand. Thai AIDS J., 4: 117-122.
- Tin, F., 1977. Serological responses to *Plasmodium* and *Toxoplasma* in school children from two areas in Burma. Southeast Asian J. Trop. Med. Public Health, 8: 552-557.
- Uga, S. and K. Ono *et al.*, 1996. Seroepidemiology of five major zoonotic parasite infections in inhabitants of Sidoarjo, East Java, Indonesia. Southeast Asian J. Trop. Med. Public Health, 27: 556-561.
- Wanachiwanawin, D. and R. Suttent *et al.*, 2001. *Toxoplasma gondii* antibodies in HIV and non-HIV infected Thai pregnant women. Asian Pacific J. Allergy Immunol., 19: 291-293.
- Wong, H.B., 1987. The problems of congenital toxoplasmosis in Singapore. J. Singapore Paediatric Soc., 29: 1-6.
- Wong, A. and K.H. Tan *et al.*, 2000. Seroprevalence of cytomegalovirus, *Toxoplasma* and parvovirus in pregnancy. Singapore Med. J., 41: 151-155.
- Wongkamchai, S. and B. Rungpitaransi *et al.*, 1995. *Toxoplasma* infection in healthy persons and in patients with HIV or ocular disease. Southeast Asian J. Trop. Med. Public Health, 26: 655-658.
- Wongkamchai, S. and V. Mahakittikun *et al.*, 1999. Immunoblotting and enzyme linked-immunosorbent assay for diagnosis of *Toxoplasma* infection in HIV Thai patients. Southeast Asian J. Trop. Med. Public Health, 30: 580-582.

- Yamamoto, M. and M. Tokuchi *et al.*, 1970. A survey of anti-*Toxoplasma* hemagglutinating antibodies in sera from residents and certain species of animals in Surabaya, Indonesia. *Kobe. J. Med. Sci.*, 16: 273-280.
- Yeo, K.K. and T.T. Yeo *et al.*, 2000. Stereotactic brain biopsies in AIDS patients-early local experience. *Singapore Med. J.*, 41: 161-166.
- Zahedi, M. and H. Idruss *et al.*, 1985. Toxoplasmosis in Malaysia: Some epidemiological consideration. *J. Malaysian Soc. Health*, 5: 19-23.
- Zainul Rashid, M.R. and A. Zamri *et al.*, 1992. Toxoplasmosis-the silent killer. *Malaysian J. Obstet. Gynecol.*, 1: 9-13.
- Zaman, V. and T.K. Goh, 1969. Toxoplasmic antibodies in various ethnic groups in Singapore. *Trans. R. Soc. Trop. Med. Hyg.*, 63: 884.
- Zurainee, M.N. and A. Khairul Anuar *et al.*, 2000. Ocular presentations and *Toxoplasma* serology. *J. University of Malaya Medical Centre*, 2: 98-102.