INTRODUCTION

Toxoplasmosis, refers to the clinical and/or pathological evidence of disease (Wong and Remington, 1994) caused by the ubiquitous, obligate intracellular protozoan, Toxoplasma gondii. Infection is usually acquired orally or transplacentally, rarely by inoculation in a laboratory accident, by blood or leukocyte transfusion, or from a transplanted organ. Toxoplasma infection is capable of causing a wide spectrum of disease, the preponderance of which is asymptomatic (chronic/latent infection). The infection in chronic form is estimated to vary from 10-50% of the population in Malaysia (Tan and Zaman, 1973; Nissapatorn et al, 2003a).

The prevalence of toxoplasmosis was estimated mainly by the detection of specific antibodies (IgG and/or IgM) to T. gondii. Various serological methods have been used in Malaysia, such as the indirect hemagglutination (IHA) test, Sabin Feldman dye test, indirect fluorescent antibody test (Yahaya, 1991), and the enzyme-linked immunosorbent assay (ELISA) (Nissapatorn et al, 2002). The indirect immunoperoxidase (IIP) technique has also been useful for the diagnosis of toxoplasmosis (Yahaya, 1991). An alternative approach for detection of toxoplasmosis, polymerase chain reaction (PCR), a molecular method is considered a new, noninvasive, rapid, sensitive and specific technique which has been developed to detect T. gondii in blood (Sumati et al, 1999; Nissapatorn et al, 2003e).

This paper aims to review the epidemiological data of human toxoplasmosis in terms of the prevalence and risk factors as well as the management in an attempt to eliminate this disease from Malaysia.

THE SEROPREVALENCE OF HUMAN TOXOPLASMOSIS

Acquired toxoplasmosis

Newborns (congenital toxoplasmosis). A literature review showed there was one study conducted on 1,061 congenitally defective Malaysian children of 0 to 4 month old revealing a 0.4% positivity for toxoplasmosis. Toxoplasmosis in these children was confirmed by the detection of specific Toxoplasma-IgM antibody. However, children of the same age with non-congenital abnormalities showed a higher prevalence of toxoplasmosis. A total of 8.2 intrauterine toxoplastic infections per 1,000 live births was detected, of which one-third (2.7 per 1,000 live births) was overt, manifesting symptoms more of liver damage than eye or brain damage (Tan and Mak, 1985). Since then, no new data of congenital toxoplasmosis has been docu-
Table 1

<table>
<thead>
<tr>
<th>References</th>
<th>Prevalences</th>
<th>Donors</th>
<th>Percent positive by ethnic groups</th>
<th>Test used</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td>Malays</td>
<td>Chinese</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1971-1980</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Tan and Zaman, 1973</td>
<td>13.9 (728)</td>
<td>Healthy persons</td>
<td>25.4</td>
<td>5.0</td>
</tr>
<tr>
<td>Bisseru and Lim, 1974</td>
<td>4.6 (44)</td>
<td>Clinically suspected cases</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Cheah <em>et al.</em>, 1975</td>
<td>27.4 (1,459)</td>
<td>Pregnant women</td>
<td>38.8</td>
<td>20.7</td>
</tr>
<tr>
<td>Leong <em>et al.</em>, 1976</td>
<td></td>
<td>Clinically suspected cases (2)</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td><em>Tan et al.</em>, 1976</td>
<td>23.0 (365)</td>
<td>Pregnant women</td>
<td>33.0</td>
<td>17.0</td>
</tr>
<tr>
<td>Dissanaik <em>et al.</em>, 1977</td>
<td>16.0 (226)</td>
<td>Healthy persons</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td><em>Tan et al.</em>, 1978</td>
<td>13.0 (161)</td>
<td>Clinically suspected cases</td>
<td>50.0</td>
<td>22.0</td>
</tr>
<tr>
<td>Thomas <em>et al.</em>, 1980</td>
<td>20.9 (736)</td>
<td>Healthy persons</td>
<td>33.9</td>
<td>14.6</td>
</tr>
<tr>
<td>1981-1990</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Lim and Tan, 1983</td>
<td></td>
<td>Clinically suspected cases (31)*</td>
<td>48.4</td>
<td>25.8</td>
</tr>
<tr>
<td>Sinniah <em>et al.</em>, 1984</td>
<td>30.2 (1,550)</td>
<td>Healthy persons</td>
<td>37.7</td>
<td>20.8</td>
</tr>
<tr>
<td>Tan and Mak, 1985</td>
<td>2.0 (405)</td>
<td>Children ≤ 4 months</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Zahedi <em>et al.</em>, 1985</td>
<td>25 (1,772)</td>
<td>Healthy persons</td>
<td>30.4</td>
<td>15.5</td>
</tr>
<tr>
<td>1991-2000</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Khairul Anuar <em>et al.</em>, 1991a</td>
<td>27.9 (1,035)</td>
<td>Pregnant women</td>
<td>29.8</td>
<td>21.4</td>
</tr>
<tr>
<td>Zainul <em>et al.</em>, 1992</td>
<td>45.8 (144)</td>
<td>Women with still births</td>
<td>47.5</td>
<td>58.3</td>
</tr>
<tr>
<td>Lokman <em>et al.</em>, 1994</td>
<td>10.6 (415)</td>
<td>Orang Asli patients</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Hamifah <em>et al.</em>, 1996</td>
<td></td>
<td>AIDS (TE), USM (case report)</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Ravichandran <em>et al.</em>, 1998</td>
<td>31.6 (209)</td>
<td>Pregnant women</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Zuraine <em>et al.</em>, 2000</td>
<td></td>
<td>Clinically suspected cases (134)*</td>
<td>36.4</td>
<td>24.6</td>
</tr>
<tr>
<td>2001 up to present</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Shamailah <em>et al.</em>, 2001</td>
<td>31.3 /24.3</td>
<td>HIV positive/HIV negative</td>
<td>42.1/27.0</td>
<td>22.0/21.4</td>
</tr>
<tr>
<td>Nissapatornorn <em>et al.</em>, 2002</td>
<td>21.0 /28.1</td>
<td>HIV-AIDS/HBD</td>
<td>75.0/34.5</td>
<td>22.2/44.8</td>
</tr>
<tr>
<td>Nissapatornorn <em>et al.</em>, 2003b</td>
<td>51.2 (406)</td>
<td>AIDS, HKL</td>
<td>47.5</td>
<td>34.6</td>
</tr>
<tr>
<td>Nissapatornorn <em>et al.</em>, 2003d</td>
<td>49.0 (200)</td>
<td>Pregnant women, UMMC</td>
<td>55.3</td>
<td>19.4</td>
</tr>
<tr>
<td>Nissapatornorn <em>et al.</em>, 2003a</td>
<td>41.2 (301)</td>
<td>HIV/AIDS, HKL</td>
<td>57.9</td>
<td>38.7</td>
</tr>
</tbody>
</table>

*a*Aborigines population; *b*Foreigners; *c*Ocular toxoplasmosis report
mented in Malaysia. The Department of Parasitology, Faculty of Medicine has recorded about a 2% positive rate for congenital toxoplasmosis (personal communication, 2002).

General healthy population
The first report of toxoplasmosis in Malaysia showed 13.9% of 728 sera collected from healthy persons of different age groups, races and occupations from various parts of West Malaysia, to be IHA positive (Tan and Zaman, 1973). The Sabin-Feldman dye test was used to detect Toxoplasma-specific IgG from 44 in-patients, who were admitted for various medical conditions, showing a rate of 4.6% (Bisseru and Lim, 1974). From 1975 to 1984, the main diagnostic test for Toxoplasma infection was the indirect fluorescent antibody (IFA) test. The seroprevalence of toxoplasmosis in the population has been increasing over the years (16% to 30%). From 1985 to present, the trend of toxoplasmosis prevalence has shown a similar figure (20% to 30%) (Zahedi et al, 1985; Shamilah et al, 2001; Nissapatorn et al, 2002).

Pregnant women
The earlier studies of the seroprevalence of toxoplasmosis in pregnant women was estimated to be 27.4% and 23.0% (Cheah et al, 1975; Tan et al, 1976). It is noted that from 1990 to now the percentage of Toxoplasma infection in this group of the population has significantly increased (Khairul Anuar et al, 1991; Ravichandran et al, 1998; Nissapatorn et al, 2003d).

Ocular toxoplasmosis
Ocular toxoplasmosis has been recorded in Malaysia (Lim and Tan, 1983). They reviewed 31 clinically suspected cases diagnosed as congenital ocular toxoplasmosis. Nineteen (63.3%) out of 31 patients presented with the cicatrical stage of the disease which is the most common presentation of ocular toxoplasmosis. Acute recurrences of chronic congenital ocular toxoplasmosis was seen in 12 patients. This usually occurs below the age of 40, as is the case in this series, and the number of recurrent attacks may vary from 1-13. In a recent study, a total of 134 patients suspected of having toxoplasmosis with clinical presentations ranging from blurred vision to severe retinal detachment. Of these patients, 72% were seropositive for Toxoplasma infection. Chorioretinitis and vitritis were found to be the most apparent symptoms, both having 100% correlation with serological positivity (Zurainee et al, 2000).

Immunocompromised individuals (HIV/AIDS)
Toxoplasmosis has been implicated as one of the most common opportunistic infections and has posed many diagnostic and therapeutic challenges for clinicians treating HIV/AIDS patients. In spite of this, there are few reports of the seroprevalence of toxoplasmosis in immunocompromised individuals in Malaysia. Recent studies have shown 21%, 51.2%, and 41.2% rates of Toxoplasma prevalence in this group of the population (Nissapatorn et al, 2002; 2003a,b,c).

DEMOGRAPHIC PROFILE, RISK FACTORS, CD4 + T CELL COUNT AND ANTIBODY PREVALENCE

Ethnic group and antibody prevalence
Table 1 summarizes the major ethnic groups of Malaysia, namely Malay, Chinese, Indians and Aborigines. The data of various studies showed that the prevalence rate was highest among the Malays, followed by the Indians in the early studies (from 1973 to 1984) and the Chinese in later years (from 1991 to present).

Association of age, sex and antibody prevalence
The sera samples were collected from all age groups as well as from cord blood. The prevalence of Toxoplasma infection was considered to be acquired in early life and tended to increase with age (up to middle age) and then decline in later life (Tan and Zaman, 1973; Nissapatorn et al, 2003a). It is interesting to view the majority of studies showing that the prevalence of toxoplasmosis was higher in males than females (Tan and Zaman, 1973; Lim and Tan, 1983; Zurainee et al, 2000; Shamilah et al, 2001; Nissapatorn et al, 2002).

Socioeconomic status and antibody prevalence
A study showed the prevalence of toxoplasmosis was higher in lower income groups (71.8%) than higher (28.2%) income groups (Cheah et al,
1975). It also revealed that *Toxoplasma* seropositivity was higher among rural than in suburban dwellers (Thomas *et al*., 1980). One recent study showed a higher prevalence rate among individuals living in Kuala Lumpur than those outside Kuala Lumpur (Nissapatorn *et al*., 2003a).

**Occupation and antibody prevalence**

Studies on different occupations showed that the highest antibody prevalence rate (22.2%) in padi planters, followed by veterinarians (20.2%), workers in oil palm and rubber estates (13.5%), antimalarial laborers (10.1%) and underground tin miners (3.7%) (Tan and Zaman, 1973). In another study, it was found that zoo workers had the highest antibody prevalence rate (51.25%), followed by medical students (41.7%), vegetarian Hindu priests (29.4%) and housewives (25.0%) (Zahedi *et al*., 1985). In recent studies, investigations on three different occupational groups, found that unemployed persons had the highest prevalence rate (36.7% and 44.8%) followed by non-laborers (26.3% and 40.3%) and laborers (19.1% and 37.3%), respectively (Nissapatorn *et al*., 2002; 2003a).

**Association between risk factors (contact with cat, consumption of undercooked meat and history of blood transfusion) and antibody prevalence**

Very few studies have focused on the association between cat ownership and *Toxoplasma* seropositivity (p < 0.02) (Zahedi *et al*., 1985; Zainul *et al*., 1992). In contrary, a recent study found that there was no significant association between a single or combination of risk factors (contact with cat, consumption of undercooked meat and history of blood transfusion) and *Toxoplasma* seropositivity (p > 0.05) (Nissapatorn *et al*., 2002). The latest study also found no significant association between possible risk factors and disease transmission (Nissapatorn *et al*., 2003a).

**Association between CD4 counts and antibody prevalence in HIV/AIDS**

As we know, a CD4 count is a prognostic marker of AIDS-defining illness according to the communicable diseases control (CDC) in 1993 which is related to the progressiveness of HIV infection to full blown AIDS with opportunistic infections involved. A recent study showed no significant association between CD4 counts and *Toxoplasma* seropositivity (p > 0.05) (Nissapatorn *et al*., 2003a).

**Association between CD4 count and toxoplasmic encephalitis (TE) in AIDS**

The first reported case of toxoplasmic encephalitis occurred in an AIDS patient with a CD4 count < 200 cell/mm³ (Haniffah *et al*., 1996). Similar findings have also been noted by other investigators (Nissapatorn *et al*., 2003a,d).

**Toxoplasmosis and its complication in AIDS**

Some studies have documented 1 (4.8%) of 21 *Toxoplasma* seropositive immunocompromised patients developed TE as studied at the University Hospital (Nissapatorn *et al*., 2002). They also discovered that 14.9% of AIDS–related toxoplasmosis patients developed TE and relapsing TE was detected in 9.7% of previous TE patients at the Hospital Kuala Lumpur (Nissapatorn *et al*., 2003b). The latest study showed only 1 (0.8%) of 124 *Toxoplasma* seropositive patients developed active TE (Nissapatorn *et al*., 2003a).

**Toxoplasmosis in transplant recipients**

At present, no data has been reported in Malaysia.

**DISCUSSION**

Toxoplasmosis is common and has a high prevalence among the Malaysian population. It is interesting to note that the highest seroprevalence of toxoplasmosis in most of the studies was in Malays, when compared with other races (Chinese and Indians). This finding is in agreement with other studies in this region (Partono and Cross, 1975, Gandahusada, 1978; Wong *et al*., 2000). This could be explained by the fact that Malays have a habit of keeping cats in their house which leads to close contact where they will be more likely exposed to contaminated cat feces, which was noted by other investigators (Tan and Zaman, 1973; Thomas *et al*., 1980).

As we know, predisposing factors (contact with cats, consumption of undercooked meat and blood transfusion) play a crucial role in *Toxoplasma* infection. In Malaysia, very few studies try to verify these associations either in healthy or immunocompromised, particularly HIV-posi-
tive, persons. One of the earliest studies showed a significant association between cat ownership and *Toxoplasma* seropositivity in healthy persons (Zahedi et al, 1985) which is contrary to other previous studies (Ganley and Comstock, 1980; DiGiacomo et al, 1990; Bobic et al, 1998). A recent study showed no significant association between contact with cats and *Toxoplasma* seropositivity in HIV-positive patients (Nissapatorn et al, 2002). This finding is in agreement with other investigators (Wallace et al, 1993; Glaser et al, 1994). This could be explained by the possibility that contact with cats may not pose a risk for *Toxoplasma* infection. Further study should be made in order to ascertain this association. So far, only two studies in Malaysia have shown that the role of consumption of undercooked meat had no impact on *Toxoplasma* seropositivity (Thomas et al, 1980; Nissapatorn et al, 2003a). This suggests that eating habits among Malaysians must continue to be wisely practiced in order to prevent the transmission of the *Toxoplasma* parasite and achieve a healthy lifestyle. Other studies showed a strongly significant association between the consumption of undercooked meat and *Toxoplasma* seropositivity (Knaus, 1991; Arias et al, 1996; Fan et al, 2001). Only one study in Malaysia has documented no significant association between history of a blood transfusion and *Toxoplasma* seropositivity (Nissapatorn et al, 2002). This observation is contrary to various earlier studies (Beauvais et al, 1976; Nelson et al, 1989; Evans, 1992). This indicates the importance of *Toxoplasma* screening among different population groups in order to prevent passive seroconversion, particularly in the post-transfusion period even though this risk factor has not so far posed a significant health problem.

Since the pandemic of HIV infection has spread throughout the world, toxoplasmosis has been implicated as one of the most important opportunistic infections in AIDS patients of which toxoplasmic encephalitis is the most common clinical disease, most frequently causing focal intracerebral lesions in these patients (Wong and Remington, 1994). The CD4 cell count is a prognostic marker which is related to the progression of HIV infection to full blown AIDS with the occurrence of other opportunistic infections (AIDS-defining illness). Recent studies in Malaysia showed that CD4 cell count plays no role in association with *Toxoplasma* seropositivity (Nissapatorn et al, 2002). Whereas, patients have CD4 cell count of less than 200 cells/mm³ show significantly developed toxoplasmic encephalitis (Nissapatorn et al, 2003b). This observation is supported by other recorded studies (Renold et al, 1992; Mariuz et al, 1997; Nascimento et al, 2001). Therefore, it is still recommended to monitor CD4 cell counts, *Toxoplasma* serodiagnostic status, as well as the implementation of life-long anti-*Toxoplasma* therapy in this treatable condition.

In view of the national prenatal screening program for toxoplasmosis and the controversy over its cost effectiveness, we need to find an appropriate strategy to combat this silent disease. Simple preventive measures, particularly in pregnant women, as part of a health education system in order to increase maternal awareness of the disease and to reduce risk of infection as outlined by investigators (Zainul et al, 1992) has been implemented and practiced in the nationwide medical care centers in Malaysia. There is a growing interest in toxoplasmosis among the scientific and the medical community in this country. The disease has been recognized as an important cause of morbidity among immunocompromised individuals and in congenital infection. Though there are many treatment modalities that are available the proper diagnosis of infection still poses a major problem in the management of patients. Current research is focused on the characterization of molecular markers and DNA amplification. More work needs to be done to ease patients of this treacherous infection that continues to inflict a major toll on the Malaysian population.

In conclusion, toxoplasmosis continues to be an important infection in Malaysia. Various factors contribute to the acquisition of *Toxoplasma* infection and worsen its condition. We should increase our awareness in terms of prevention and control measures in order to decrease the incidence of toxoplasmosis in this country.

**REFERENCES**


Knaus BU. Epidemiological findings of *Toxoplasma gondii* infections of humans in the area of Cottbus. *Angew Parasitol* 1991; 32: 159-64.


Nissapatorn V, Kamarulzaman A, Init I, Chan LL, Fong MY, Khairul Anuar A. The sensitivity of PCR for detection of *Toxoplasma gondii* DNA from HIV-infected patients. *J University Malaya Med Centre* 2003e (Inpress).


