

A REVIEW OF HUMAN LEPTOSPIROSIS IN MALAYSIA

¹El Jalii, I. M. and ²Bahaman, A. R.

¹Department of Preventive Medicine and Public Health

Faculty of Veterinary Medicine

University of Khartoum, Sudan

²Faculty of Veterinary Medicine

Universiti Putra Malaysia

43400, Serdang, Selangor

Abstract: This paper reviews the literature on human leptospirosis in Malaysia from its first description in 1925 until the present day. Fletcher diagnosed the first case of human leptospirosis in Malaysia in 1925. Following Fletcher, many investigations on human leptospirosis in Malaysia disclosed a high prevalence of infection (Tan, 1970a; Supramaniam, 1979; El Jalii, 2002). These investigations indicated that the disease was endemic in the country. Tan (1970) examined 1993 suspected human cases of leptospirosis and found 28 % of the cases were positive. In a recent survey, 2190 serum samples from patients with different clinical manifestations in the country disclosed 12.6% were positive for antibodies to leptospire. The risk to leptospiral infection with respect to occupation, location, sex, race and age groups was demonstrated. Both civilians and military personnel were affected. Thirty-eight serovars from thirteen serogroups have been identified in the country. Recent studies on animal leptospirosis showed that the disease was highly endemic in the animal population. It is considered that the majority of leptospirosis cases in man were due to association of man with animals and disease-infected environment.

Introduction

Leptospirosis is an important zoonotic disease world-wide (Gussenhoven *et al.*, 1997). It is evident that the epidemiology of leptospirosis involves domestic animals and wildlife. Rodents are the important maintenance hosts and the main source of leptospiral infection to livestock and humans. Most of the cases of human leptospirosis worldwide have been attributed to rodents (Miller *et al.*, 1991). Human leptospiral infection primarily resulted from direct or indirect exposure to the urine of infected animals (Faine, 1982). Serological or bacteriological evidence of leptospiral infection has been reported in a wide variety of animal species in Malaysia (Bahaman *et al.*, 1987; Bahaman *et al.*, 1988). There are now 11 recognised species of *Leptospira* (Faine *et al.*, 1999) and out of the more than 200 serovars, thirty-seven serovars have been isolated from animals and humans in Malaysia (Bahaman *et al.*, 1988). The wet and warm climate in the Southeast Asia region is a favorable condition for leptospire to be in the environment and pathogenic leptospire have frequently been isolated from Malaysian waters and soils (Fletcher, 1928; Baker & Baker, 1970; Alexander *et al.*, 1975; Khairani and Bahaman, 1997). The high prevalence of leptospirosis in humans in this region is of great public health concern. This paper reviewed the historical aspects of human leptospirosis in Malaysia.

Human Leptospirosis in Malaysia

Fletcher (1928) was the first person who began working on human leptospirosis in Malaysia. He reported the first fatal case of human leptospirosis in 1925 due to

Leptospira icterohemorrhagiae and during this early period he was able to identify serovars *icterohemorrhagiae*, *hebdomadis* and *pyrogenes* from 21 patients. Galloway (1926) detected four cases of human leptospirosis in Singapore, which at that time was a state in Malaysia. In 1927, Fletcher and Kanagarayer were able to demonstrate leptospire in four patients from Kuala Lumpur General Hospital. Following these early studies, more investigations of leptospirosis were made (Ryrie, 1930). Typical cases with jaundice were well recognized in Malaysia (Danaraj, 1950). Cases of febrile illness appeared frequently among military personnel and civilians in Malaysia. These cases drawn attention to leptospirosis as an emerging disease in the country (Broom, 1953). Cox *et al.* (1955) examined sera of 190 leptospirosis patients from Malaya and leptospire were isolated from 79 patients. The results revealed infections due to at least 24 different serovars. Robinson and Kennedy (1956) detected 31 cases of leptospirosis among British army personnel in Malaysia. Twenty-nine of these cases were proven to be leptospirosis, either by culture or serology. McCrumb *et al.* (1957) studied febrile illness in 614 military personnel operating in the jungle during the Malayan emergency. In their investigation, leptospirosis was shown to be the most common cause of fever in soldiers, accounting for 35% cases admitted for fever to a military hospital. Simultaneous investigations of 238 civilian adult males admitted to an urban hospital yielded a diagnosis of leptospirosis in only 13% of the cases. From 1953 to 1955, 30 pathogenic leptospiral serovars have been identified by Alexander *et al.* (1957) from both military personnel and civilians. Studies by Broom (1953), Robinson & Kennedy (1956) and McCrumb *et al.* (1957) showed the importance of leptospirosis as a febrile disease in military personnel and civilians in Malaysia.

Tan (1964) pointed out that many cases of leptospirosis escaped recognition either because the actual clinical features of the leptospirosis did not always conform with the generally accepted picture of Weil's disease or because clinicians failed to consider it in the differential diagnosis of febrile illnesses. In her study, she emphasized that leptospirosis is much more common in Malaysia than is generally realized and the disease can be mild and may even be subclinical and deceptive. Tan (1964) studied 584 cases of pyrexia of unknown origin (PUO) over a period of 4 ½ years (June 1958 to December 1962). The cases were from different states of Malaysia. One hundred and seventy-three (29.6%) were found to be positive. The diagnosis was based on blood cultures, significant serological titres, or both. Leptospire were isolated from blood specimens of 14 patients in this study. The serovars of the 14 isolates obtained were *pyrogenes* (5), *canicola* (3), unidentified (3), *autumnalis* (2) and *pomona* (1). Her results indicated that an overall proportion of nearly 1 in 3 PUO cases in Malaysia could possibly be due to leptospirosis. According to Tan (1964) rubber estate workers were the highly infected group followed by labourers who worked with sewage, draining, town cleaning, forestry and anti-malarial work. Army and police personnel have high seropositive rate of infection. With respect to sex, the occurrence in males is not significantly different than in females and this is because females formed a considerable proportion of the labour force in rubber estates and mines. The differences noted in the results for different racial groups have no statistical significance, and the incidence may be regarded as having no racial bias. Although a fair proportion of the patients investigated for leptospirosis by Tan (1964) had signs and symptoms indicative of

leptospirosis. The majority of the cases investigated for leptospirosis might well have been influenza, acute respiratory disease, gastritis, dengue, malaria, typhoid or hepatitis.

Ungku Omar (1967) stated that leptospirosis is endemic in Malaysia. His survey in humans showed that a high incidence of antibodies to leptospire was observed throughout Malaysia. The highest distribution was shown among labourers working in rubber estates and those dealing with sewage, drainage, forestry, town cleaning and anti-malaria work. Veterinarians, farmers, abattoir workers and people handling livestock and animals did not appear to be frequently affected which was very surprising. Important serovars isolated from human cases were *canicola*, *icterohemorrhagiae*, *pyrogenes*, *hebdomadis* and *autumnalis* (Bahaman & Ibrahim, 1987). In West Malaysia, a serological survey of 4819 febrile individuals throughout the country during the period of 1960-1961, revealed an overall prevalence of 11.8% (Tan, 1969).

Tan (1970a) carried out a study on leptospirosis in rural West Malaysia and out of 1993 suspected cases of leptospirosis examined, 559 (28%) were confirmed positive. The highest number of cases occurred among males, 20-40 years old, and of the three main racial groups, Malays, Chinese and Indians, the Indian community was the most frequently affected based on estimated population. Tan's findings bore a direct relationship to the distribution of cases by occupation, where the general labourers (they dealt with sewage, drainage, forestry, town cleaning or anti-malaria work) and rubber estate workers, who were mainly of Indian origin, headed the list in the order of case frequency. Padi planters, tin miners, farmers and veterinary workers were comparatively free of clinical leptospirosis.

Tan (1970b) examined sera from afebrile padi planters in five rice fields in the State of Kelantan during the dry and wet seasons. The overall prevalence rate was 14.2%. The sera collected during the wet season showed a prevalence rate of 24.2% while those obtained during the dry season was 7.2%. There was no cumulative increase in incidence with age. Persons under 20 years old had 23.1% compared to 12.3% in persons aged 21 to 40 years and 14.2% in those aged 40 years and above. Seven serovars were disclosed by the microscopic agglutination test (MAT). They were *hebdomadis*, *javanica*, *icterohemorrhagiae*, *autumnalis*, *pyrogenes*, *australis* and *bataviae*.

Tan (1970c) examined suspected cases of leptospirosis in clinics and hospitals all over West Malaysia. Leptospire were isolated in 34 cases from blood specimens. Twenty-eight of the isolates have been identified: nine were identified as serovar *pyrogenes*, five each as serovars *autumnalis* and *canicola*, three as serovar *hebdomadis*, two each as serovars *icterohemorrhagiae*, *pomona* and *grippotyphosa*

Tan & Lopes (1972) conducted a survey for leptospirosis on two categories of afebrile Malaysian soldiers. Those in service for six months to 20 years and new recruits of only 2 to 3 weeks service undergoing basic military training. The total percentage of the antibody prevalence was 17.2%. Contrary to expectation, the newly recruited soldiers have a much higher antibody rate (22.0%) than those who have been longer in service (12.1%).

According to Tan (1973), a total of 4646 sera were tested of which 12.7% were positive. High antibody rates (23.2% to 32.6%) were found among oil palm estate, rubber estate workers and hospital staff. Moderately high rates (13.0% to 17.9%) were observed in labourers, the army soldiers, tin miners, farmers and padi planters. Moderate rates

(11.6% to 12.2%) were found among shopowners, policemen and veterinary staff. Low rates (1.5% to 9.4%) were detected in school teachers, housewives, office workers. In another study, Tan (1974) examined 197 suspected cases of leptospirosis and 38% were found to be positive.

Brown *et al.* (1976) collected acute and convalescent serum samples from unselected febrile in-patients at two district hospitals and from outpatients at a rural health center in Central West Malaysia. Leptospirosis was diagnosed in 6.0% of the cases. The clinical symptoms were mild to moderate in all cases. According to sex and age, leptospirosis was mainly a disease of the youngs (from school age through to the working period) and males.

In a 10 years study by Tan (1979), 1,738 suspected cases were examined. Three hundred and forty (19.6%) were positive for leptospirosis with males (93.3%) markedly predominating over females (6.7%). Malay (66.5%) cases were more common than Indian and /or Chinese. Most of the cases occurred between age 20-50 years.

Supramaniam (1979) reviewed the status of leptospirosis among the Malaysian army personnel. He stated that two cases have been reported from 1969 to 1978 and two deaths have been certified as due to leptospirosis. Serological studies revealed a 12% to 22% prevalence of antibodies indicating past infection. Study of febrile cases showed that only 4.6% of fever in Malaysian soldiers were due to leptospirosis. Brown *et al.*, (1984) studied 1629 patients with febrile illness from Pahang in Central Malaysia. Leptospirosis was accounted for 6.8% of five diseases diagnosed.

In 1984 a group of British cave explorers undertook an exploration of the caves of Mulu in the Guong Mulu National Park, Malaysia. After their return to Britain the 16

explorers showed PUO, hepatomegaly but no renal failure. Leptospirosis was suspected and was confirmed by serology. The serological evidence suggested that the infecting serogroup was Hebdomadis. In 1985 a group of British tourists visited the Sarawak Chamber and 2 people subsequently developed leptospirosis (Sheena and Buchan, 1987).

Tan *et al.* (1986a) examined 36 cases of acute renal failure admitted to Kuala Lumpur General Hospital from 1980-1983. Sixteen (44.4%) of these cases were due to leptospirosis. The findings showed that cases from males (93.8%) predominated over cases from females and the Malays (75%) were over the other two races, Indians (18.8%) and Chinese (6.2%). All cases had acute onset of fever. Jaundice and headache occurred in more than half of the cases. The infecting serovars in 16 cases were due to either serovars *celledoni* or *pomona*. One positive culture was obtained and was identified as belonging to the *Sejroe* serogroup. Tan (1986b) investigated icteric patients with clinical evidence of liver disease from various hospitals in Malaysia. Leptospirosis was detected in 17.2% of the total 64 patients examined.

Since 1986 no investigations were made on human leptospirosis in Malaysia. Institute for Medical Research (IMR) is the main institute that carried out routine work on the diagnosis of human cases based on serum samples submitted from clinics and hospitals throughout the country. Recent studies on the disease were carried out by the Universiti Putra Malaysia (Bahaman and Ibrahim, 1987; Bahaman *et al.*, 1988; Bahaman and Chumponbunchorn 1993; Khairani, 1997). El Jalii *et al.* (2000) did a retrospective study on the incidence of human leptospirosis in Malaysia from 1983 to 1998. The overall incidence of leptospirosis was 13%, with the Indians showing the highest incidence (16.7%) followed by the Malays (11.5%) whilst the Chinese (5.9%) were the

least affected by the disease. The percentage of males (81.1%) affected were higher than females (18.9%) in a male female ratio of 4:1. The 20-29 years age group (17.1%) showed the highest prevalence whilst the young (less than 10 years), and old (above 60 years) groups showed low prevalence. This study indicated that human leptospirosis is probably an endemic infection in Malaysia. In another study, 2190 samples collected from general hospitals in eight states in West Malaysia were examined for evidence of leptospiral infection. The overall prevalence of leptospiral infection from this study was 12.6%. Kuala Lumpur had the highest number of positive sera (57/300 or 19%) followed by Selangor (51/300 or 17%) whilst, Penang recorded the lowest prevalence (20/300 or 6.7%). From a small sample of cattle farmers and veterinary staff, serological examination revealed a large number of positive reactors, 56.8% (89/220) and 70% (21/30) respectively (El Jalii *et al.*, 2002).

References

- Alexander, A. D., Evans, L. B. Baker, M. F., Baker, H. J. Ellison, D. and Marriapan, M. (1975). Pathogenic leptospires isolated from Malaysian surface waters. *Applied Microbiology*. **29**: 3033.
- Alexander, A. D., Evans, L. B., Toussant, A. J., Marchwicki, R. H. and McCrumb. F. R. (1957). Leptospirosis in Malaya. 11. Antigenic analysis of 110 leptospiral strains and other serologic studies. *American Journal of Tropical Medicine and Hygiene*. **6**: 871-879.
- Bahaman, A. R. (1988). A serological and bacteriological study of leptospiral infection in domestic animals in Peninsular Malaysia. Ph.D. thesis, Universiti Pertanian Malaysia.
- Bahaman, A. R. and Ibrahim, A.L (1986). A serological and bacteriological study of leptospiral infection in a cattle herd in Malaysia. *Veterinary Record*. **119**: 325-326.

- Bahaman, A. R. and Ibrahim, A.L (1987). A short review of animal leptospirosis with special reference to Malaysia. *Tropical Biomedicine*. **4**: 93-99.
- Bahaman, A. R. and Chumponbunchorn, K. (1993). Cattle as maintenance host of *Leptospira interrogans* serovar *pomona* infection in Malaysia. *Malaysian Veterinary Journal*.**5**: 57-58.
- Bahaman, A. R., Ibrahim, A. L. and Adam. H. (1987).Serological prevalence of leptospiral infection in domestic animals in West Malaysia. *Epidemiology and Infection*. **99**: 379-392.
- Bahaman, A. R., Ibrahim, A.L., Stallman, N. D. and Tinnisswood, R. D. (1988). The bacteriological prevalence of leptospiral infection in cattle and buffaloes in West Malaysia. *Epidemiology and Infection*. **100**: 239-246.
- Baker, M. F. and Baker, H. J. (1970). Pathogenic *Leptospira* in Malaysian surface waters. *American Journal of Tropical Medicine and Hygiene*.**19**: 485-492.
- Broom, J. C. (1953). Leptospirosis in tropical countries. A review. *Transaction of the Royal Society of Tropical Medicine and Hygiene*. **47**: 273-291.
- Brown, G. W., Lee, C. K., Huxsoll, D. L., NG, T. S., Lim, K. J., Wan, H. S., Eeran, J. D. and Sannasey, G. (1976). Leptospirosis in Malaysia: A common cause of short-term fever. *Southeast Asian Journal of Tropical Medicine and Public Health*. **7**: 380-383.
- Brown, G. W., Shirai, A., Jegathesan, M., Burke, D., Twartz, J. C., Saunders, P. J. and Huxsoll, D. L. (1984). Febrile illness in Malaysia- An analysis of 1629 hospitalized patients. *American Journal of Tropical Medicine and Hygiene*. **33**: 311-315.
- Cox, C. D, Alexander, A. D. and Murthy. L. C. (1955). Evaluation of the hemolytic test in the serodiagnosis of human leptospirosis. *Journal of Infectious Diseases*. **101**: 210-215
- Danaraj, T. J. (1950). Leptospirosis. *Proceeding of the Alumni Association of King Edward VII College of Medicine, Singapore*. **3**: 326-339.
- El Jalii, I. M., Bahaman, A. R., Mohd-Azmi, M. L. and Mutalib, A. R. (2000). Occurrence of human leptospirosis in Malaysia: A retrospective study. *Tropical Biomedicine*. **16**: 1-5.
- El Jalii, I. M., Bahaman, A. R., Mohd-Azmi, M. L. and Mutalib, A. R. (2002). Seroprevalence of human leptospirosis in representative population in Malaysia. *Tropical Biomedicine*. **19**: 97-101.

- Faine, S. (1982). Guidelines for the control of leptospirosis. WHO Offset Publication No. 67, World Health Organization, Geneva.
- Faine, S., Adler, B., Bolin, C. and perolat, P (1999). *Leptospira* and leptospirosis. MediSci, Melbourne, Australia.
- Fletcher, W. (1928). Recent work on leptospirosis, tustsugamushi disease and tropical typhus in the Federal Malay States. *Transaction of the Royal Society of Tropical Medicine and Hygiene*. **21**: 265-288.
- Galloway, D. J. (1926). Epidemic Jaundice (*Leptospira icterohemorrhagiae*). *Malayan Medical Journal*. **1**: 1-5.
- Gussenhoven, G. C., Hoorn, M. A., Goris.M.G., Terpstra, J. W., Hartskeerl, R. A., Mol, B. W., Ingen, C. W. and Smits, H. L. (1997). Lepto dipstick, a dipstick assay for detection of leptospira-specific immunoglobulin M antibodies in human sera. *Journal of Clinical Microbiology*. **35**: 92-97.
- Khairani, B. (1997). A study of the leptospiral isolates obtained from cattle in Malaysia. Master Thesis, Universiti Pertanian Malaysia.
- Khairani, B. and Bahaman, A. R. (1997). Isolation of leptospires from waters and soils in cattle farms. The 9th Veterinary Association Malaysia Scientific Congress. Pp 41-42.
- McCrum, F. R., Stockard, J. L., Robinson, C. R., Turner, L. H., Levis, G., Maisey, C. W., Kelleher, M. F., Gleiser, C. A. and Smadel, J. E. (1957). Leptospirosis in Malay. 1. Sporadic cases among military and civilian personnel. *American Journal of Tropical Medicine and Hygiene*. **6**: 238-256.
- Miller, D. A., Wilson, M. A. and Beran, G. W. (1991). Relationships between prevalence of *Leptospira interrogans* in cattle, and regional, climatic, and seasonal factors. *American Journal of Veterinary Research*. **52**: 1766-1768.
- Robinson, C. R. and Kennedy, H. F. (1956). An investigation into clinical and laboratory features Of outbreak of 31 cases of anicteric leptospirosis. *Journal of the Royal Army Medical Corps*. **102**: 196-206.
- Ryrie, C. A. (1930). Concurrent leptospirosis and schistosomiasis in Malaya. *Malayan Medical Journal*. **5**: 148-150.
- Sheena, A. and Buchan, J. (1987). Leptospirosis in British cavers in Malaysia- The Sarawak Experience. *Israel Journal of Veterinary Medicine*. **43**: 346.
- Supramaniam, V. (1979). Leptospirosis in the Malaysian army. *Malaysian Journal of Pathology*. **2**: 11-14.

- Tan, D. S. K. (1964). The importance of leptospirosis in Malaya. *The Medical Journal of Malaya*. **18**: 164-171.
- Tan, D. S. K. (1969) Sensitized erythrocytes lysis (SEL) test as an epidemiological tool for human leptospirosis serological surveys. *Bulletin of World Health Organization*. **24**: 5-21.
- Tan, D. S. K. (1970a). Leptospirosis in rural West Malaysia. *The Medical Journal of Malaya*. **24**: 261-265.
- Tan, D. S. K. (1970b). Leptospirosis in the ricefields of West Malaysia. *Southeast Asian Journal of Tropical Medicine and Public Health*. **1**: 483-491.
- Tan, D. S. K. (1970c). Clinical leptospirosis in West Malaysia (1958-1968). *Southeast Asian Journal of Tropical Medicine and Public Health*. **1**: 102-111.
- Tan, D. S. K. (1973). Occupational distribution of leptospiral (SEL) antibodies in West Malaysia. *The Medical Journal of Malaysia*. **27**: 253-257.
- Tan, D. S. K. (1974). Evaluation of *Leptospira biflexa* antigens for screening human sera by the microscopic agglutination (MA) test in comparison with the sensitized-erythrocyte-lysis (SEL) test. *Southeast Asian Journal of Tropical Medicine and Public Health*. **5**: 12-16.
- Tan, D. S. K. (1979). Leptospirosis in West Malaysia-epidemiology and laboratory diagnosis. *Malaysian Journal of Pathology*. **2**: 1-6.
- Tan, D. S. K. and Lopes, D. A. (1972). A preliminary study of the status of leptospirosis in the Malaysian armed forces. *Southeast Asian Journal of Tropical Medicine and Public Health*. **3**: 208-211.
- Tan, D. S. K., Suleiman, A. and Jeyaindran, S. (1986a). 16 cases of acute renal failure due to leptospirosis. *Medical Journal of Malaysia*. **41**: 152-155.
- Tan, D. S. K., Dimitrakakis, M., Rahman, Z. M., Fang, R., Collett, D., Geok, B, O. and Gust, I. D. (1986b). Etiology of acute hepatitis in Malaysia. *Southeast Asian Journal of Tropical Medicine and Public Health*. **17**: 205-208.
- Ungku Omer, A. (1967). Veterinary public health with particular reference to Malaysia. *Kajian Veterinier*. **1**: 54-62.
- Wisseman, C. L., Traub, C., Gochenour, W. S., Smadel, J. E. and Lancacter, W. E. (1955). Leptospirosis of man and animals in urban, rural and jungle areas of Southeast Asia. *American Journal of Tropical Medicine and Hygiene*. **4**: 29-40.