# MURINE TYPHUS IN A MALAYSIAN VILLAGE

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#### INTRODUCTION

Fletcher and Lesslar (1926) first recognised the existence of typhus in Malaysia, and in 1936, Lewthwaite and Savoor (1936a, c, d) demonstrated that murine, or urban (fleaborne) typhus was a separate entity from scrub, or rural (mite-borne) typhus. These workers also demonstrated rat to rat transmission by fleas of the causative organism of murine typhus (Lewthwaite and Savoor, 1936b).

Murine typhus is still recognised as a sporadic and uncommon cause of illness in the country. The reported annual incidence of typhus (including both murine and scrub typhus) varied from 36-155 (mean 100) during the 7 years, 1968-1974 (Monthly Statistical Bulletin of West Malaysia, 1976). Although the clinical syndrome may be difficult to recognise, a diagnosis can be made by the Weil-Felix (WF) (Fletcher and Lesslar, 1926), complement fixation (CF) (Hersey et al., 1957a, b) or indirect fluorescent antibody (IFA) (Elisberg and Bozeman, 1966) tests.

In a study of rickettsioses in Malaysia, Marchette (1966) found murine typhus CF antibody in 10% of rats (*Rattus rattus diardi*) trapped from urban areas and in only one of

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218 human sera obtained from a variety of sources.

In the course of an investigation of the causes of febrile illnesses in rural Malaysia (Brown et al., 1977), several cases of murine typhus were recognised in patients of Kuala Pilah hospital, Negri Sembilan. Two cases, in close succession, occurred in individuals who lived only 3 houses apart in Senaling, a small village 2 miles south of Kuala Pilah. The first patient (H 6259), a 16 year old girl, was admitted to hospital on 20 May 1976 and the second, a 5 year old boy (H 6278), on 3 June 1976. Both diagnoses were confirmed by the WF and IFA tests.

In order to investigate the prevalence of the infection in Senaling, a serological survey was conducted of the residents, and of rats trapped in the village.

## MATERIALS AND METHODS

Sera were collected from 53 human volunteers, by house to house visiting, on 28 and 29 June 1976. A special effort was made to sample relatives and close neighbors of the two patients, though some of the sera were collected from residents of houses 100-200 meters away.

Rats were trapped using locally constructed basket traps (Harrison, 1960). One hundred traps were given to 20 homeowners in the late afternoon on each of 2 days. They were to be set at night and collected early the next morning. Shortly after collection of the traps, the rats were anaesthetized with ether,

combed for fleas and bled by cardiac puncture. The fleas were transported to the laboratory for identification.

All sera were examined for antibody to murine typhus by a micro-IFA test (Philip et al., 1976; Robinson et al., 1976), in which the Wilmington strain of Rickettsia typhi (obtained from the Rickettsial Disease Section, Walter Reed Army Institute of Research, Washington, D.C. 20012) was used as antigen. The sera were diluted 2-fold from an initial dilution of 1/25. In addition, the human sera were examined for Proteus OX19 agglutinins (Wellcome Reagents, Beckenham, U.K.) by a microtiter technique (Gaultney et al., 1971). Sera obtained from a control group of 265 normal Malaysian soldiers were examined for antibody by the IFA test. No attempt was made to isolate the organism from humans, rats or fleas.

# **RESULTS**

Human: The serological results of the 2 index cases are shown in Table 1. The diagnosis was confirmed by a high IFA titer and a 4-fold rise in WF titer in H 6259. There was a significant rise in both IFA and WF titers in patient H 6278.

Table 1
Serological results in patients
H 6259 and H 6278.

	Date	FA	WF
H 6259	20 May	1/200	1/160
	25 May	1/400	1/640
	28 June	1/400	1/80
H 6278	3 June	1/25	<1/40
	5 June	1/1600	1/320
	28 June	1/400	1/80

FA = Fluorescent antibody titer to R. typhi. WF = Weil-Felix Proteus OX19 titer.

The IFA titers of the control and Senaling sera are shown in Table 2. Only 13 (5%) of 265 control sera titered 1/50 or more compared with 24/53 (45%) of the Senaling sera. Three (6%) of the Senaling sera titered 1/200or more, and all 3 also had WF titers of 1/160 or more. One subject having an IFA titer of 1/800 and a WF titer of 1/160, was the 7 year old brother of patient H 6278, and lived in the same house. The father recalled no recent illnesses in the child. It is known from our records that this subject had been admitted to Kuala Pilah hospital a year previously (5 June 1975) with a febrile illness, and that paired sera collected at that time had IFA titers of < 1/25 and WF titers of 1/40. Sera collected from the other 4 residents of the same house also had demonstrable antibody, including a 13 year old girl, whose IFA titer was 1/200 and WF 1/640. She denied any recent illnesses. The remaining subject with an IFA titer of 1/200, and WF of 1/320, was a 34 year old man, who admitted having had a short febrile illness, with headache, about one month prior to the survey.

Three relatives of patient H 6259, all of whom lived in the same house with the index case, had IFA titers of < 1/25, 1/25 and 1/100 (all WF titers < 1/160); and none admitted any illness.

Rodents: Seventy-nine rats were collected from a total of 200 traps set during the 2 nights (40% trap rate). Of the trapped rats, 77 were Rattus exulans and 2 were Rattus rattus diardi. Sera were obtained from 69 of the 79 rats. The results of the IFA test on these sera are shown in Table 2. Altogether, 24 (35%) had titers of 1/50 or more, including 15/22 (68%) sera from rats trapped in three adjacent houses.

Fleas: Forty of the 79 trapped rats were infested with a total of 102 *Xenopsylla cheopis* (flea index 1.3), with the number of fleas per infested rat varying from 1 to 8.

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Table 2	
Murine typhus antibody in humans and	rodents.

FA titer	Number (Per cent)		
	Malaysian soldiers	Senaling residents	Senaling rats
< 1/25	186 (70)	11* (21)	37 (53)
1/25	66 (25)	18 (34)	8 (12)
1/50	11 (4)	14 (26)	6 (9)
1/100	2(1)	7 (13)	7 (10)
1/200	0	2** (4)	5 (7)
1/400	0	0	6 (9)
1/800	0	1***(2)	0
Total	265 (100)	53 (100)	69(100)

<sup>\*</sup> WF titer of 1/160 in 1 subject. \*\* WF titers 1/320 and 1/640. \*\*\* WF titers 1/160.

### DISCUSSION

Senaling is a typical small village of West Malaysia with mostly ethnic Chinese inhabitants. The town itself consists of approximately 70 shophouses: coffeeshops, provision shops, rubber storage buildings and general ware shops. These shops are often connected in groups of 4 or 5, allowing for easy movement of rodents from one shop to another through the roofs and walls. The shophouses are usually constructed in such a manner that the shop area is in the front of the building and the living area is at the rear or upstairs.

Within the provision shops, food items are usually stored in sacks at the rear of the shop (Fig. 1) and items for sale are placed in bins or open containers within the shop (Fig. 2). Such practices provide sources of food and harborage for rodents, resulting in a large buildup of rodent numbers. This was noted in some of the provision shops. The traps were dispensed from 3:30 p.m. on the first day, with some shopowners setting their traps at this time. Before all the traps had been distributed (at 5:30 p.m.), 9 rats had been trapped. Most of these were from provision shops located adjacent to or near the two shophouses from which the first two cases of typhus

were reported. The fact that such daytime trapping occurred indicated that there was a large, active population of rats.

The prevalence of antibody in the Senaling rats (35% at titers of 1/50 or more in the IFA test) was very high. Marchette (1966) reported a prevalence of CF antibody in 10% of rats trapped from urban areas in West Malaysia.

Among the humans there was also evidence of a high prevalence of infection. In addition to the 2 index cases, 24 (45%) of the subjects studied had IFA titers  $\geq 1/50$ . The 3 subjects with IFA  $\geq 1/200$  also had significant WF titers, indicative of recent infections. Two of the 3 lived with one of the index cases, while the other lived in a house approximately 100 meters away. One of the 3 had had a febrile illness possibly attributable to murine typhus, though not clinically diagnosed as such. Forty five percent of the subjects with IFA titers of 1/50 or greater contrasts sharply with 5% of the controls. It is usual for ill people in communities such as Senaling to treat themselves, or to see general practitioners, who may prescribe antibiotics without a definitive diagnosis. Also, murine typhus is often relatively mild and self-limiting, and

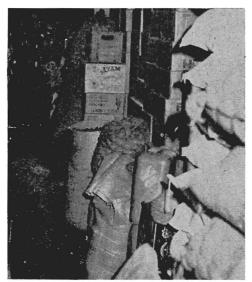


Fig. 1—Food storage area at rear of a typical provision shop in Senaling, West Malaysia.



Fig. 2—Front view of a typical provision shop in Senaling, West Malaysia.

may often escape recognition. Unless Senaling was particularly unusual, it is likely that the infection is more common than is generally recognised.

In Senaling, there was a suggestion that a certain group of houses were particularly heavily infested with infected, flea-carrying rats, resulting in the several human infections. In the house where one index case occurred and in two adjacent houses, 68% of 22 rats had significant antibodies to murine typhus.

The district health authorities were notified of results of the survey within 10 days, and the villagers were given appropriate advice on the use of insecticides and traps.

## **SUMMARY**

A high prevalence of murine typhus was found in the human and rodent populations of Senaling, West Malaysia. In addition to 2 index cases which prompted the investigation, 45% of the humans and 35% of the rodents had IFA titers of 1/50 or greater. Serological studies provided evidence of recent infections in 3 human subjects. In a control group of Malaysian soldiers IFA titers of 1/50 or greater were found in only 13 (5%) of 265 sera tested.

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## **REFERENCES**

Brown, G.W., Robinson, D.M., Huxsoll, D.L., NG, T.S., Lim, K.J. and Sannasey, G., (1976). Scrub typhus: A common cause of illness in indigenous populations. *Trans. Roy. Soc. Trop. Med. Hyg.*, 70: 444.

ELISBERG, B.L. and BOZEMAN, F.M., (1966). Serological diagnosis of rickettsial diseases by indirect immunofluorescence. *Arch. Inst. Pasteur Tunis*, 43:193.

FLETCHER, W. and LESSLAR, J.E., (1926). The Weil-Felix reaction in sporadic tropical typhus. *Bull. Inst. Med. Res.*, No. 1.

GAULTNEY, J.B., WENDE, R.D. and WILLIAMS, R.P., (1971). Microagglutination procedures for febrile agglutination tests. *Appl. Microbiol.*, 22: 635.

- HARRISON, J.L., (1960). A simple trap for squirrels. J. Mammal., 41: 142.
- HERSEY, D.F., COLVIN, M.C. and SHEPARD, C.C., (1957a). Studies on the serological diagnosis of murine typhus and Rocky Mountain spotted fever. I. Experimental infections in guinea pigs and rabbits. J. Immun., 79:401.
- HERSEY, D.F., COLVIN, M.C. and SHEPARD, C.C., (1957b). Studies on the serological diagnosis of murine typhus and Rocky Mountain spotted fever. II. Human infections. *J. Immun.*, 79: 409.
- LEWTHWAITE, R. and SAVOOR, S.R., (1936a). The typhus group of diseases in Malaya. III. The study of the virus of urban typhus in laboratory animals. *Brit. J. Exp. Path.*, 17:23.
- LEWTHWAITE, R. and SAVOOR, S.R., (1936b). The typhus group of diseases in Malaya. VI. The search for carriers. *Brit. J. Exp. Path.*, 17: 309.
- LEWTHWAITE, R. and SAVOOR, S.R., (1936c). The typhus group of diseases in Malaya. VIII. The relation of the tsutsugamushi disease (including rural typhus) to urban typhus. *Brit. J. Exp. Path.*, 17:461.

- LEWTHWAITE, R. and SAVOOR, S.R., (1936d). The typhus group of diseases in Malaya. IX: The relation of the tsutsugamushi disease (including rural typhus) and urban typhus to Rocky Mountain spotted fever. (With special reference to cross-immunity tests). Brit. J. Exp. Path., 17: 466.
- MARCHETTE, N.J., (1966). Rickettsioses (tick typhus, Q-fever, urban typhus) in Malaya. J. Med. Entom., 2:339.
- Monthly Statistical Bulletin of West Malaysia, (1976). Department of Statistics, Kuala Lumpur, Malaysia, August, p. 237.
- PHILIP, R.N., CASPER, E.A., ORMSBEE, R.A., PEACOCK, M.G. and BURGDORFER, W., (1976). Microimmunofluorescence test for the serological study of Rocky Mountain spotted fever and typhus. *J. Clin. Microbiol.*, 3:51.
- ROBINSON, D.M., BROWN, G., GAN, E. and HUXSOLL, D.L., (1976). Adaptation of a microimmunofluorescence test to the study of human *Rickettsia tsutsugamushi* antibody. *Amer. J. Trop. Med. Hyg.*, 25:900.