

SCRUB TYPHUS — A PROBLEM IN MALAYSIA?

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Summary

Scrub typhus is a febrile illness caused by infection with *Rickettsia tsutsugamushi*, the vector of which is the larval stage of trombiculid mites, commonly referred to as chiggers. Although the disease was first recognized in Japan, it is now known to have a widespread distribution in the Asiatic/Pacific region. The disease assumed military importance during World War II when scrub typhus accounted for a large number of casualties among both Allied and Japanese forces throughout the endemic area. With the advent of broad spectrum antibiotics, which are effective in treating the disease, interest in scrub typhus waned, and the disease was no longer considered a medical problem. Recent studies have shown, however, that scrub typhus is a common cause of febrile illness in rural Malaysia.

The name "typhus" is derived from the Greek word *typhos* which means stupor. Savor and Audy¹ in their introduction to the Chapter on Typhus in the Jubilee volume, *The Institute for Medical Research 1900-1950*, state, "this is a doubly appropriate name, for not only is stupor a striking and characteristic feature of the intoxication of both typhus and the typhoid or enteric fevers, but the Greek word *typhos* also means smoke or haze — and until fairly recent times the complex of diseases related to typhus was but darkly seen through the smoky clouds of our ignorance." Although many advances have been made in treating and controlling the typhus group of diseases, the assessment made by these 2 learned workers over 25 years ago remains appropriate. Clouds of ignorance still blur our vision.

Interest in rickettsial diseases has generally waned. Undoubtedly this is due, in large part, to the reluctance of anyone to accept the fact that a disease, for which there is adequate treatment, could still be a problem. With development of adequate therapy most people felt that rickettsial diseases could be laid to rest. Fortunately, the broad spectrum antibiotics have markedly reduced mortality, but unfortunately, they have masked the problem in many instances.

The problem is not confined to typhus or scrub typhus. In the United States, Rocky Mountain spotted fever has been increasing since 1960 with 1115 cases being reported to

the Center for Disease Control in 1977.² This represents an increase of 19% over the 937 cases reported in 1976 and is the largest number of cases of this illness ever reported in the United States. Most of these cases were confined to the southeastern and south central states. The overall reported case — fatality rate was 4.9%, a decrease from 5.9% in 1976. However, in individuals over age 40 the case — fatality rate was 12.3%. A delay in diagnosis which leads to a delay in initiation of specific therapy is probably the single most important factor contributing to the unacceptable fatality rate. The lack of means to establish an early definitive diagnosis remains a serious problem in the management of rickettsial diseases.

In the context of modern medicine little is known about the pathophysiology of most rickettsial diseases. A tentative diagnosis of scrub typhus results in initiation of specific therapy, and the disease is aborted or altered before complete laboratory data can be acquired using modern clinical laboratory methods. Thus, most descriptions of the disease date from before or during World War II when clinical laboratory medicine, as we know it today, was still in its infancy.

This paper is intended to serve as an introduction and an overview to the scrub typhus problem, particularly as it exists in Malaysia.

GENERAL

Scrub typhus, or tsutsugamushi disease, is a

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febrile illness caused by infection with *Rickettsia tsutsugamushi*, the vector of which is the larval stage of trombiculid mites, frequently referred to as chiggers.

The earliest description of the disease was a report in the Japanese literature by Hashimoto in 1810.³ He described it as the "tsutsuga" found along the banks of the upper tributaries of the Shinano River. The first English report was made by Dr Theobald Palm, a medical missionary in Niigata Prefecture, Japan.⁴ The report, contained in a letter to the Rev John Lowe and published in the Edinburgh Medical Journal of 1878, provided a description of a disease which the natives called "Shima-mushi" or "island insect" disease. There is some evidence to suggest that the same disease was known in south China even before its recognition in Japan. In a Chinese writing of the 16th century, a "sand mite" is described as a fever carrier.⁵

In Japan the disease has been associated for generations with narrow strips of weeds and grass along banks of rivers as well as lowlands which are sometimes flooded. The infection, which caused high mortality among Japanese farmers, has been studied intensively in Japan by medical scientists for nearly a century. The disease has become part of the lore of Japan where its association with the red mite, "akamushi", has apparently been recognized for many years.

The numerous synonyms for scrub typhus include: tsutsugamushi (disease mite) disease; kedani (hairy mite) fever; akamushi (red mite) fever; flood fever; Japanese river fever; tropical typhus; rural typhus; mite-borne typhus and chigger-borne typhus. The name "scrub typhus", which was coined by Fletcher in 1927 to stress the association of the disease with wasteland,¹ was easy to pronounce and carried some meaning in English. The name gained widespread usage during World War II when military forces operating in the Asiatic/Pacific region encountered outbreaks of the disease which they associated with exposure to a "scrub" environment.

Although the disease was originally reported only from restricted areas in Japan, it is now known to have a widespread distribution within a large triangular area bounded by Siberia in the north, Australia in the south and Pakistan in the west. The distribution of the disease

parallels that of known vector mites.

Scrub typhus gained military importance among both Allied and Japanese Forces during World War II. Records are incomplete on casualties suffered from the disease by Japanese Forces, but estimates approaching 30,000 have been made.¹ Among Allied Forces, available statistics indicate that approximately 18,000 cases occurred. Of 11,000 cases for which adequate data are available there were nearly 650 deaths. In American troops case-fatality rates in different epidemics varied from less than 1% to greater than 35%.⁶ Scrub typhus not only seriously affected morale but often jeopardized the operational efficiency of military units in which the sudden outbreaks occurred. In Vietnam scrub typhus was a leading cause of fever of unknown origin in US soldiers.^{7,8}

EARLY STUDIES IN MALAYSIA

In the early 1900's Schuffner⁹ observed and studied a disease on the east coast of Sumatra to which he gave the name "pseudo-typhoid". On the basis of extensive clinical and epidemiological observations he concluded that "pseudo-typhoid" was a variety of Japanese "kedani fever". A primary lesion (eschar) was always present in Europeans. In the natives it was not always present, but Schuffner attributed the failure in part to the fact that it was more difficult to distinguish on the skin of the natives than on the healthy skin of Europeans. The disease seemed much milder than it was in Japan, since the case-fatality rate was much lower.

With the recognition of tsutsugamushi or kedani fever on the east coast of Sumatra interest in the disease arose in Malaya, only a few miles distant across the Straits of Malacca.

In 1915 Dowden¹⁰ described a suspected case of "kedani river fever" in Malaya. With the exception of this one probable case, tsutsugamushi disease was not recognized in Malaya until 1926 when Fletcher and Field¹¹ observed and studied 4 cases of the disease in European planters, 3 of whom were from the same oil palm estate and were apparently infected in a 15 acre block which had become overgrown and was being cleared. The 4 cases were severe, one being fatal.

In 1925 Fletcher and Lesslar,¹² working at the Institute for Medical Research, reported their observations on cases of fever which they

diagnosed as typhus. The first cases were from the small mining village of Kepong near Kuala Lumpur. They felt that the disease was common in Malaya and predicted that it extended beyond the borders of the peninsula. Since the disease was unlike the epidemic form of typhus, they called it "tropical typhus". Although many cases diagnosed as tropical typhus had signs and symptoms very similar to those of tsutsugamushi, the latter was distinguished from tropical typhus by the presence of an eschar and associated lymphadenopathy or bubo.

Following these early observations, intensified studies on typhus fevers were initiated at the Institute for Medical Research and continued throughout the late 1920's and 1930's. This resulted in a series of comprehensive publications¹³⁻²⁷ which added immeasurably to the knowledge of this disease complex. It soon became evident that under the designation of tropical typhus were 2 distinct diseases which had similar clinical features but differed sharply in epidemiology and serology. The "urban" type was mainly a disease of indoor workers in shops or stores in towns and villages, and the cases were generally scattered. On the other hand the "rural" form, which was commonly known as "scrub typhus", was a disease of the countryside or rural areas and was usually found in people whose occupations brought them into contact with vegetation near jungles. The cases of "scrub typhus" tended to be more focal in distribution. Reactions in the Weil-Felix test also proved helpful in separating the 2 forms. Sera from patients with the "urban" form reacted with strains of *Proteus* X19, such as the "Warsaw" strain. Thus, the "urban" form was accordingly called the "W" form. In contrast, sera from patients with the "rural" form, or "scrub typhus", did not react with strains of *Proteus* X19, but did react with strains of *Proteus* known as "Kingsbury". The "rural" form, or "scrub typhus", was frequently referred to as the "K" form.

In summary, by the late 1920's 2 types of tropical typhus were known to exist in Malaya – the "scrub", "rural" or "K" type and the "urban" or "W" type. Later it was shown, primarily through animal inoculations, that the "urban" or "W" form of tropical typhus was in fact "murine" or "fleaborne" typhus known to exist in many parts of the world.

In 1930 Lewthwaite²⁸ reported the investigation of an outbreak of scrub typhus among the labour force on a young oil palm plantation where the European manager and 2 European assistants had contracted tsutsugamushi disease in 1926.¹¹ The trees were being "brought into bearing", and due to an "industrial depression", little weeding had been done since the trees were planted. The observations were made between January 1927 and April 1929. During this period 121 cases of scrub typhus were diagnosed of which 11 were fatal. The highest incidence occurred among "pruners and harvesters" who had the responsibility of pruning the trees, clearing debris from the base of the trees and harvesting the ripe fruit. The daily number of pruners and harvesters ranged from 15–30 during the 28 month observation period. Among this group, 51 cases of scrub typhus were diagnosed.

The report of this outbreak contains not only valuable clinical and epidemiological information but illustrates the importance of scrub typhus at that time and place.

In 1929 Fletcher, Lesslar and Lewthwaite¹⁵ suggested that the tsutsugamushi disease and scrub typhus had a similar etiology and that scrub typhus, like the tsutsugamushi disease, was carried by trombiculidae. It was subsequently demonstrated primarily through animal inoculations, that scrub typhus and tsutsugamushi disease were indeed caused by the same organism.²⁴ The earlier confusion had been due to the wide variation in clinical manifestations of the infection.

Numerous sudden outbreaks of the disease have been reported throughout the endemic region including Malaysia. The outbreaks, wherein a large proportion of a susceptible population is infected almost simultaneously, occur upon exposure to hyperendemic areas. Such outbreaks were common among military forces during World War II.²⁹

Evidence of the existence of hyperendemic areas in Malaysia also arose in chemoprophylactic studies on scrub typhus in 1948–1949.³⁰⁻³² In these tests volunteers were exposed for 6–10 days in areas where a large number of cases had previously occurred among labourers. During the course of these trials as many as 72% of the unprotected volunteers (controls) contracted the disease.

RECENT STUDIES IN MALAYSIA

Immediately prior to 1975, available information indicated that scrub typhus was not a problem in Malaysia. During the period 1967–1974 an average of only 55 cases of scrub typhus was reported per annum.^{3,3} Serological surveys,^{3,4–3,6} however, demonstrated a high prevalence of antibody in some rural areas, indicating a high rate of transmission among the population.

In early 1975 studies were initiated to determine the true incidence of scrub typhus in selected populations. Studies on febrile patients in the district hospitals at Mentakab and Kuala Pilah, and at the Bukit Mendi (Pahang) health sub-center demonstrated that scrub typhus is a very common cause of febrile illness in that area, accounting for as high as 23% of the fevers at Mentakab Hospital.^{3,3} In the same study it was shown that of the oil palm workers admitted to Mentakab Hospital with fever, approximately 80% (19/24) were suffering from scrub typhus.

In a recently completed study^{3,7} wherein the efficacy of a single oral dose of 200 mg. of doxycycline was compared to a 7 day course of tetracycline for treatment of scrub typhus, it was clearly shown that scrub typhus is a major cause of fevers of unknown origin in rural Malaysia.

CONCLUSION

Scrub typhus has a widespread distribution in the vast Asiatic/Pacific region which contains over half of the human race. Although the importance of the disease before and during World War II is well documented, the significance of scrub typhus as a medical problem has not been recognized in recent years. This undoubtedly resulted from several factors: an indifferent attitude toward febrile illnesses on the part of many clinicians, laboratory personnel, and administrators; the unavailability of appropriate diagnostic tests for febrile illnesses in most hospital laboratories; and the widespread use of broad spectrum antibiotics, which fortunately are effective in treating the disease but often may have masked the magnitude of the problem. Recent studies in central Peninsular Malaysia have shown that scrub typhus is a common cause of febrile illness in that area, accounting for a very significant proportion of hospitalized fever cases.

Thus, in terms of numbers of cases, scrub typhus may be the most important febrile illness in rural Malaysia.

The impact of fevers on economic development is quite clear. While the treatment of fevers adds considerably to the cost of government medical services, the child with a fever cannot attend school, and the rural worker cannot be productive.

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