(L) LEST WE FORGET TROPICAL TYPHUS ST 1983

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Thank you Mr. Chairman. In some febrile diseases, such as malaria, the diagnosis can usually be made quickly and simply, even in a rural clinic. Other infections, such as typhoid, leptospirosis, viral and rickettsial infections are frequently difficult to distinguish from one another, clinically. They often require a relatively sophisticated laboratory investigation. There seems to be considerable confusion among health professionals in T.A.P.A. as to the incidence of rickettsial diseases.

Such diseases often go undiagnosed, appear to be grossly under reported, and are in fact responsible for a substantial loss of efficient productivity within each of the Asiatic-Pacific nations. Thus, the necessity for a review of murine and scrub typhus.

May I have the First Slide.

Here, in Malaysia, a disease syndrome once known as "Tropical Typhus", was first recognized in the 1920's. "Tropical Typhus" was described as mild or moderate illness, with a low mortality, and was diagnosed mostly in Asians. The disease was more severe among foreign plantation managers.

Fletcher, Lesslar and Lewthwaite, while working at the Institute for Medical Research here in KL, soon recognized that "Tropical Typhus" could be divided into two distinct epidemiological, and serological entities, which they called urban and rural typhus.

The OX-19 and OX-K proteus antigens were used in the Weil Felix reaction to identify and distinguish serum agglutins in patients having urban typhus or rural typhus, and in 1936 Lewthwaite and Savoor clearly demonstrated that rural typhus was a separate entity from urban typhus. Epidemiologically rural typhus occurred in the countryside with a high incidence among plantation workers and urban typhus occurred, in town and city environs.

Throughout the years, urban typhus has been known as shops typhus, flea-borne typhus, endemic typhus and murine typhus -- the now preferred nomenclature is murine typhus.

Likewise rural typhus -- now known as scrub typhus -- has been labeled as mite fever, mite borne typhus, and tsutsugamushi disease.

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Today, throughout this region of the world, the Weil-Felix reaction remains the most commonly used laboratory test for the diagnosis of selected rickettsial diseases.

However, please be reminded by this table, that the OX-19 proteus antigen reacts not only with the serum agglutinins of murine typhus patients, but, with the agglutinins of epidemic typhus as well. A point, if forgotten, that can lead to erroneous reporting of epidemic typhus, a disease not endemic to the Asiatic-Pacific region.

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To better appreciate the distribution, and determinates, of murine and scrub typhus, allow me to draw from the many works of Traub, Audy and Markette, to review and compare the determinant factors of etiologic agent, reservoir, natural host, vector, man, exposure and distribution, as they relate to murine and scrub typhus. But first, let me draw your attention to a serious typographic error on this and following slides. The House Rat and not the Forest Rat is both the reservoir and natural host for murine typhus. The Forest Rat and not the House Rat is the natural host of scrub typhus.

The etiologic agents of both diseases is a rickettsia, Rickettsia typhi for murine typhus and that of scrub typhus being Rickettsia tsutsugamushi.

In Malaysia, the house rat (Rattus rattus) is the most notable reservoir of R. typhi while certain trombiculid mites serve as the reservoir of R. tsutsugamushi.

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The house rat (Rattus rattus) reservoir of R. typhi.

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The adult stage of the trombiculid mite Leptotrombidium arenicola, the reservoir of Rickettsia tsutsugamushi.

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The natural host for the agent of murine typhus in Malaysia is, again, the House Rat, not the Forest Rat as is mistakenly listed in this table.

The sylvatic forest rat (Rattus raja), in the next slide, is a natural host of scrub typhus as well as is the plantation rat.

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Zenopcilla keyopis, the common rat flea, serves as the vector of murine typhus.

The chigger, or larval stage, of the scrub typhus reservoir trombiculid mite, is also the vector of R. tsutsugamushi.

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A rat flea, the murine typhus vector, and

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The chigger vectors of scrub typhus.

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Man serves only as a chance or incidental and terminal host for the etiologic agent of both murine and scrub typhus.

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Please be reminded that the life-cycle of both murine typhus and

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Plague are very similar, involving the same reservoir, the same vector, and the same chance host. From a view point of disease incidence monitoring, and early warning sentinel animal monitoring, a sudden increase in the incidence of murine typhus can signal an increase in the rat flea population, and its interaction with man -- this is the same rat flea population that serves as a vector for Yersinia pestis, plague.

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Again man is only an incidental, or chance host, of the scrub typhus rickettsia.

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As is indicated by the descriptive names of the past, exposure to R. typhi most often occur indoors in urban. Rat and rat flea infested home and shop environments. Conversely, rural or scrub typhus is always contracted in outdoor settings.

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Traub has very simply listed for us, those 4 features, or determinant characteristic if you wish, of all scrub typhus endemic foci.

Chiggers, wild rats, scrubby vegetation and ecological changes.

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The final determinant factor, is distribution.

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Plainly stated the etiologic agent of murine typhus has been identified on 7 continents, thus global, while that of scrub typhus is limited to a rather triangle in shape Asiatic Pacific region.

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At least 5 of the determinant factors I have reviewed contribute to the unsimilar distributions of murine and scrub typhus.

The reservoir, natural host and the vector of murine typhus are by their domestic association with man and his commercial endeavors found worldwide. A considerable portion of the murine typhus vector fleas' life is spent on, and thus in, the moist, humid, warm and mobile environment of both the reservoir and the natural host, that of the domestic rat. Thus, environmental stresses of low humidity, severe cold and extreme heat must in theory be severe enough to effect the rat reservoir, before they are severe enough to affect the flea vector.

Secondly, man often by his commercial endeavors, provides a sheltered environment for the domesticated rat and is vector mites, while providing free global transport.

Conversely, the reservoir and vector mites of scrub typhus spend only a few days of their long life on a forest rat host and thereafter must find suitable, and by nature non-mobile, shelter from environmental extremes.

Likewise, the forest rat is not a common traveller with man and thus even the natural host of scrub typhus must rely upon itself, and not man or his vessels, to cross natural barriers such as arid mountain and deserts, or vast oceans.

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On a closer look at the Asiatic-Pacific one notes an endemic area bound by high cold and arid land barriers, and vast ocean expands.

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Lastly, I wish to share with you a situational analysis of the 1976-1982 incidence of "Tropical Typhus" in Malaysia. The raw statistical data was kindly provided by the Ministry of Health.

Over the past 7 year period, 821 cases of rickettsial typhus have been reported. 633 of which were scrub typhus. Other, represents those cases, hopefully erroneously reported to health officials, as epidemic typhus. Such reporting, most likely, has one of, or a combination of 3 sources.

1. A non confirmed clinical impression.

2. An unawareness that murine typhus, as well as epidemic typhus, agglutinins react indistinguishably with the OX-19 diagnostic antigen.

3. Recording or transcription errors of epidemic rather than endemic (murine) typhus.

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On a region $\overline{vs}$ year basis, the vast majority of typhus occurs in Peninsular Malaysia. Most likely a reflection of:

1. Population density

2. Regional physician awareness, or lack there of

3. Quality and distribution of health services.

4. And availability of diagnostic facilities.

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Murine typhus represents only 60, of the previous 821 cases of typhus, in all of Malaysia.

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Scrub typhus accounted for 633 of 821 cases of typhus reported during the past 7 years, an annual average of only 90 cases, for the 7 year period.

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When the typhus data is broken down into incidence of type $\overline{vs}$ state, Negri Sembilan, Pahang, and Johore each reported over 100 cases of scrub typhus for the 7 year period. These 7 peninsular states accounted for 722 of the 821 typhus cases reported. Thus, the 7 year incidence of reported typhus is unalarming and rather low.

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The 1972 work of Cadigan & coworkers demonstrated a prevalence of scrub typhus specific antibody of up to 64% in some rural populations. Yet an annual average of only 55 cases of scrub typhus was reported throughout Malaysia during 1967-74. Thus, indicating that a large number of infections were, either not being correctly diagnosed, or were not producing the text book clinical symptoms, or fever, rash, eschar and adenopathy.

In true importance of scrub typhus was not recognized until the Halmark work of Brown, Robinson, Huxsoll and coworkers reported that scrub typhus accounted for almost 80% of the febrile illnesses observed in oil palm workers at three rural Malaysian health facilities.

As illustrated in a previous slide, the annual incidence of scrub typhus has risen from 55 to 90 cases, from the 1967-74 time frame, to the 1976-82 period.

The slide you are now viewing also illustrates the point that the incidence of scrub typhus is considerably greater than is reported.

Data from 3 rural hospitals in Peninsular Malaysia, collected over a 3 year period, indicates a 15 to 46% incidence of scrub typhus among patients admitted with a pyrexia of unknown origin (PUO). Here alone, there are 326 cases of scrub typhus, for a yearly incidence of 109 cases -- from only 4 hospitals.

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The reasons for the under reporting of tropical typhus are most likely:

1. A lack of recognition of both scrub and murine typhus, for example the classical rash is difficult to detect on dark skinned people.

2. Physician awareness is most likely low, and

Thirdly, our diagnostic capabilities are not only limited, but are often not available, and when available, as illustrated in this table are as best only 75-85% accurate for known cases of scrub typhus.

The two serological methods for the laboratory diagnosis on scrub typhus, that are available within the Asiatic Pacific region, are the IFA, available at the IMR/USAMRU and at (AFRIMS/USAMRU Bangkok). And the classical Weil-Felix OX-19 and OX-K antigens.

I have compiled the serological data from 138 PUO patients, from which R. tsutsugamushi was isolated. For sera collected during the first week of clinical disease, the incidence of false negatives was, as would be expected, quite high, almost 40%. Thus pointing out the necessity of evaluating paired sera. The accuracy, however, rapidly improved with time, to the point where both the IFA and OXK techniques were 100% accurate (for positive isolate patients) when used to evaluate sera collected beyond 3 weeks after the initial illness was reported.

Over all, the incidence of any single sera being reported as a false negative was 25% for the OXK test and 16% for the IFA technique.

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Lastly, we need to be reminded of the characteristics of all scrub typhus outbreaks.

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Unfortunately, Dr. Traub's list is in harmony, if you wish, with a rapidly developing and modern Malaysia. Lest we not forget Tropical Typhus.

Last Slide

Thank you!