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Rickettsioses as causes of CNS infection in southeast Asia

In *The Lancet Global Health*, Sabine Dittrich and colleagues\(^1\) report that scrub typhus caused by *Orientalia tsutsugamushi*, murine typhus caused by *Rickettsia typhi*, and leptospirosis caused by various *Leptospira* species account for more than a third of CNS infections diagnosed over 8 years in Vientiane Hospital in Laos. The study is one more great contribution from this team in their investigation of undocumented syndromes, as well as in the public health challenge of rickettsial diseases in southeast Asia. The same investigators have previously reported that scrub typhus was the second most common microbial cause of fever of unknown origin in rural Laos (122 [15%] of 799 diagnosed cases)\(^2\). In 2006, rickettsial infection was detected in 115 (27%) of 427 adults admitted to Vientiane Hospital for fever with negative blood culture.\(^3\) The most common rickettsial agent was *Otsutsugamushi* followed by *R typhi*. Fewer data are available about the prevalence of these diseases in other southeast Asian countries. In Thailand, scrub and murine typhus has been reported\(^4\) in 16% and 2%, respectively, of fever of unknown origin, with mortality of 3–17% for scrub typhus.\(^5\) The lack of local negative controls causes false positives because of the commonness of asymptomatic forms of infectious diseases; therefore, European controls cannot be used to evaluate the specificity of diagnostic techniques in tropical countries.

Collaborations of investigators in the tropics combined with powerful diagnostic methods have increased the recognition of neglected pathogens in patients with acute undifferentiated fever. However, when studying the causes of fever of unknown origin, inclusion of local negative controls is essential because the incidence of many pathogens in these regions is totally different from their incidence in Europe, changing the predictive value of diagnostic tests. The lack of local negative controls causes false positives because of the commonness of asymptomatic forms of infectious diseases; therefore, European controls cannot be used to evaluate the specificity of diagnostic techniques in tropical countries.

Rickettsioses are severe diseases that can be fatal, yet in Dittrich and colleagues’ study few patients with scrub and murine typhus received doxycycline (55% and 39%, respectively).\(^1\) As a consequence, the use of an empirical doxycycline treatment for patients with fever of unknown origin should be discussed, especially when empirical treatment with β-lactams has failed or in cases with severe clinical presentation. Doxycycline is used for malaria prophylaxis in travellers. Only two prospective randomised studies\(^10\) have shown the effectiveness of prophylactic doxycycline to prevent scrub typhus. Designing comparative studies to test the drug’s effectiveness for preventing scrub typhus would be difficult. However, we propose that doxycycline be given as a priority for chemoprophylaxis against malaria in travellers to the tropics to thereby protect against rickettsioses and leptospirosis.

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