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CASE REPORT

Eschars and estate fever: A case series from the Johorean oil palm heartland highlighting the changing face of scrub typhus in Malaysia

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ABSTRACT

Scrub typhus, a zoonotic bacterial infection caused by the arthropod-borne, Gram-negative, obligate intracellular bacillus *Orientia tsutsugamushi* and transmitted by larval chiggers, is an underdiagnosed cause of acute undifferentiated febrile illness. Its clinical spectrum ranges from a self-limited dengue-like illness to rapidly progressive multiorgan dysfunction driven by smallvessel vasculitis, including pneumonitis, acute kidney injury, hepatitis, encephalitis and circulatory shock. Early recognition is frequently missed because the characteristic eschar may be absent or easily overlooked in concealed or pigmented skin sites, and definitive diagnostics such as polymerase chain reaction (PCR) or indirect immunofluorescence assay (IFA) are often unavailable in resource-limited settings. Occupational and environmental exposures, particularly work in oil palm or rubber plantations and contact with forest–estate ecozones, remain key epidemiological clues that may be under-elicited in routine clinical practice. We report a case series of four patients with confirmed scrub typhus presenting to a hospital in Kluang district, Johor, Malaysia. All patients had acute fever and non-specific viral-like symptoms, including malaise, chills, headache and myalgia. Thrombocytopenia and acute kidney injury occurred in 50%, while 75% demonstrated transaminitis. Eschars were identified in all patients following comprehensive dermatological examination. Diagnosis was confirmed by PCR for *O. tsutsugamushi* DNA, a fourfold rise in IFA titres, or a single high-titre IgM or IgG in a compatible clinical syndrome. Three patients (75%) had clear domiciliary or occupational risk factors, including oil palm work or residence near secondary scrubland. One patient developed organ-threatening complications with acute kidney injury and severe hepatitis, illustrating the vasculitic end-organ involvement of severe scrub typhus. All patients achieved clinical defervescence and symptomatic improvement within 24–48 hours of doxycycline initiation, consistent with the characteristic brisk antimicrobial response. This series underscores the need for a low threshold of clinical suspicion and early empiric rickettsial coverage in undifferentiated febrile illness with relevant exposure in rural Malaysia and highlights the need for larger multicentre studies to define predictors of severity, guide triage and inform prevention in high-risk land-use settings.

Keywords: Scrub typhus; rickettsioses; eschar; zoonotic infections; acute febrile illness.

INTRODUCTION

Scrub typhus is an acute febrile illness caused by the obligate intracellular Gram-negative bacterium, *Orientia tsutsugamushi*, and is a zoonotic disease that was traditionally defined by a distribution within the 'Tsutsugamushi Triangle' (Xu *et al*., 2017) but has recently been reported outside this geographical region in South America. Globally, the public health burden of this neglected disease is substantial, with an estimated one million new cases occurring annually (Kala *et al*., 2020) and approximately one billion individuals residing in at-risk areas (Watt & Parola, 2003). Consequently, scrub typhus represents a significant etiology of acute febrile illness, particularly prevalent in the Global South, with a case fatality rate which ranging from as low as 1% in Japan (Yasunaga *et al*., 2011) to as high as 33% in India (Devasagayam *et al*., 2021). Despite its significant morbidity, there is currently no commercially available vaccine for scrub typhus, whereas development of novel anti-Orientia agents has stagnated since the introduction of chloramphenicol and doxycycline in the WWII era. Malaysia has a documented historical association with scrub typhus, with cases reported as early as 1926 by Fletcher and Field (Fletcher & Field, 1927). Despite its recognition as an endemic area for scrub typhus and the initial plethora of rickettsial research between 1960 to 1980, comprehensive current data regarding its precise incidence in the modern Malaysian context remains limited. Nevertheless, evidence from seroprevalence studies and various case reports compiled over the past three decades consistently confirms the

persistent endemicity of scrub typhus within the local community. Recent serological surveys and case series conducted in Sabah (Taylor *et al*., 1986), Perak (Yuhana *et al*., 2022), and Negeri Sembilan (Lee *et al*., 2025b) further highlight scrub typhus as the most frequently identified rickettsial infection among febrile hospitalized patients in Malaysia.

Despite scrub typhus being a cause of undifferentiated acute febrile illness in Asia, thorough understanding regarding the actual disease burden, incidence and epidemiology are limited. We report four cases of scrub typhus in a secondary hospital (Hospital Enche' Besar Hajjah Khalsom) in Kluang which presented with a wide range of clinical symptomology. This hospital services Kluang district in Johor state, which is part of Malaysia's palm-oil heartland, with over a third of the state's landmass is comprising of oil palm estates, with extensive areas of mixed oil palm and rubber smallholderships. This pattern is strongly reflected in the land use of Kluang district, where residents are involved in agricultural activities which center around shrub land. (Pakiam *et al*., 2020; Kang & Kanniah, 2022).

The cases discussed in this series highlight the wide range of clinical presentations, and highlight the shortfalls in management of such cases which could influence management outcomes in endemic areas.

Case 1

An 80-year-old lady with underlying hypertension and dyslipidemia with no history of previous hospitalization, presented with a festering left leg wound for 1 week associated with fever, for which she could not recall any preceding stings or bites. She stayed on the fringes of an oil palm estate. After visiting a primary healthcare facility and completing a course of oral cloxacillin, she visited the hospital emergency department in view of persistent malaise and fever despite therapy. She was then admitted with the provisional diagnosis of partially treated cellulitis. Upon examination, she was haemodynamically stable. However, an eschar was described on the anterior aspect of the left ankle, just above the sock line (Figure 1), which was not associated with regional lymphadenopathy. She had a maculopapular, non-blanching rash on her trunk. Blood investigations showed borderline anemia as reflected in hemoglobin (Hb) 10.9 g/dl, as well as white blood cell (WBC) 4.56 x 10^9 /L, platelet 186 x 10^9 /L, urea 3.6mmol/L, creatinine 85umol/L, and mild transaminitis as demonstrated by aspartate transaminase (AST) 81U/L and alanine transaminase (ALT) 66 U/L. A clinical diagnosis of rickettsial infection (scrub typhus) was made in view of the eschar which was associated with both occupational and geographical risk factors, and she was treated with oral doxycycline, to which she responded and was subsequently discharged well. Both eschar swab and serum were sent for Rickettsial Polymerase Chain Reaction (PCR) and were positive for Orientia tsutsugamushi DNA. Serum indirect immunoperoxidase (IIP) showed Scrub Typhus IgM 1:100, IgG 1:100.

Case 2

A 50-year-old gentleman with no significant cardiometabolic risk factors presented with a 10-day history of fever with intermittent chills and rigors, headache, myalgia and night sweats. After visiting the local general practitioner on Day 7 of illness and completing two days of oral amoxicillin-clavulanate, the fever failed to defervesce leading him to present to the local emergency department where he was managed as a case of occult sepsis since preliminary examination failed to reveal a nidus of infection. However, on detailed skin survey in the ward, an eschar was found on the medial aspect of right arm (Figure 2) which was associated with right axillary lymphadenopathy. Blood investigations revealed significant transaminitis (AST of 375 U/L and ALT 640 U/L), mild acute kidney injury (urea 7.9 mmol/L, creatinine 131.2 umol/L) and a normal CBC profile (WBC 8.22 x 10^9 /L, Hb 13.1g/dl, platelet 140 x 10^9 /L).

Serum and eschar swab for Rickettsial PCR were both positive for *Orientia tsutsugamushi* DNA, whereas serum IIP Scrub Typhus IgM paired titres revealed a significant increase (1:100, followed by 1:3200 at 2 weeks).

He responded to oral doxycycline which was followed by gradual improvement in both renal and liver function.

Case 3

45 years old lady with no known co-morbid, who lives on the fringe of an oil palm estate, presented with 9 days history of fever associated with vomitting, loss of appetite and frothy urine. She completed two days of oral antibiotics and presented

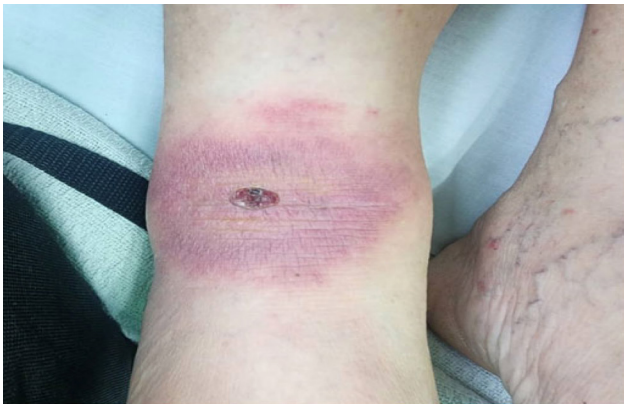

Figure 1. Eschar with surrounding maculopapular rash on the anterior aspect of the patient's left ankle as described in Case 1.

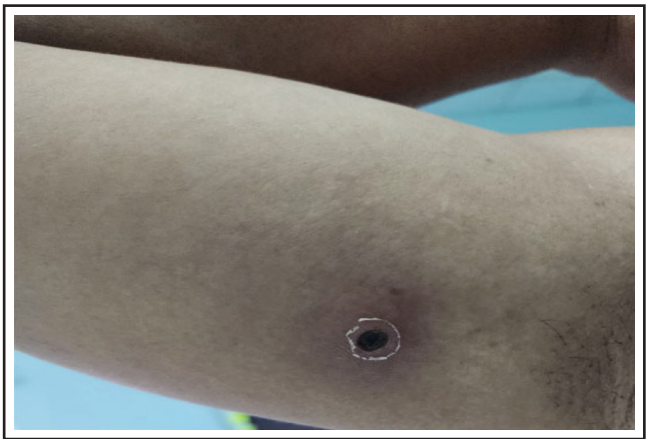

Figure 2. Eschar on the medial aspect of the right arm of the patient in Case 2.

to the emergency services with intractable fever with vague abdominal pain, for which hepatic pyogenic abscess was initially suspected. Upon examination, there was an eschar noted on the medial aspect of the left calf (Figure 3). Blood investigations revealed transaminitis ALT 178 U/L, AST 190 U/L, ALP 509 U/L, leucocytosis (WBC 15.7 x 10^9 /L), normochromic normocytic anemia (Hb 10.9g/dl) and normal platelet counts (platelet 161 x 10^9). Of note, there was gross albuminuria with microscopic hematuria. Ultrasound abdomen revealed no obvious hepatic or renal pathology.

Her eschar swab and serum samples PCR sent and *Orientia tsutsugamushi* DNA detected while non-paired scrub typhus IgM and IgG are 1:400 and 1:200 respectively.

She responded to a course of oral doxycycline and was discharged well.

Case 4

49 years old gentleman with underlying hypertension and dyslipidemia presented with fever for 5 days associated with profuse diarrhea, vague abdominal pain and tea-colored urine. He developed hemodynamic instability reflective of fulminant septic shock, complicated by pulmonary hemorrhage and persistent metabolic acidosis, for which he required mechanical ventilation and intensive care management for multiorgan failure. On examination, an eschar was found on the anterior aspect of right thigh (Figure 4).

Blood investigations demonstrated thrombocytopenia (71 x 10^9 /L), normochromic normocytic anemia (10.8g/dl) and significant leukocytosis (23.88 x 10^9 /L). He also experienced oliguric acute kidney injury with creatinine (264.8 umol/L), as well as transaminitis (ALT 136 U/L, and ALT 130 U/L) with a liver function profile which was not in keeping with obstructive hyperbilirubinemia.

Eschar swab for Rickettsial PCR was positive for *Orientia tsutsugamushi* DNA, whereas nonpaired serum IIP Scrub Typhus revealed IgM titre of 1:3200 and IgG titre of 1:3200. Of note, serum Leptospira IgM was also positive, and this was confirmed by a positive Leptospirosis Microscopic Agglutination Test (MAT) (with a titre of 1:800).

This gentleman responded to a combination of intravenous methylprednisolone (for the pulmonary hemorrhage), intravenous ceftriaxone for severe leptospirosis and oral doxycycline, after which he gradually recovered and was subsequently discharged well from the intensive care unit.

A summary of the salient clinical presentation, investigations and outcomes of the cases discussed in this series are delineated in Table 1.

DISCUSSION

Between the years 1970 to 2025, we have identified twelve published case reports and case series regarding scrub typhus in the Malaysian context (see Table 2 and Figure 5). Whilst Malaysia has historically been the cradle of scrub typhus research,

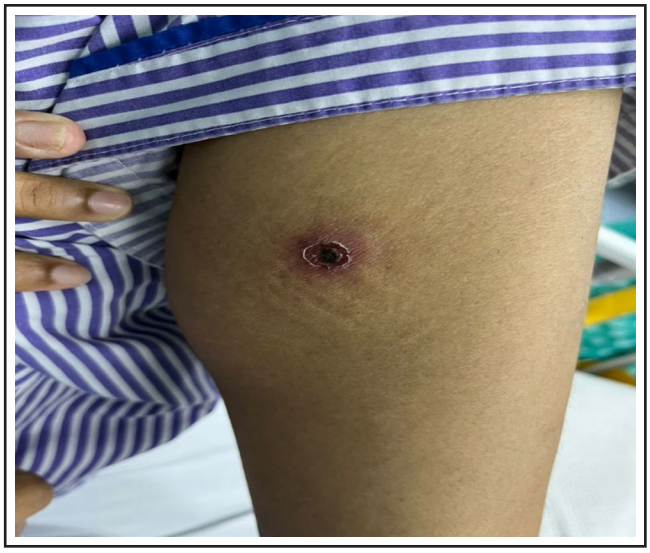

Figure 3. Eschar on the medial aspect of the left calf of the patient in Case 3.

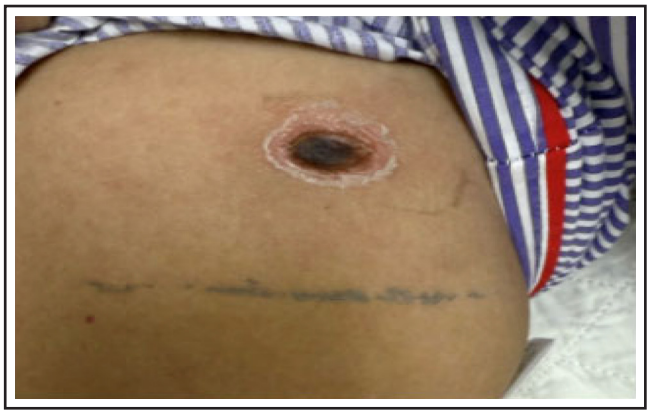

Figure 4. Eschar on the anterior aspect of the patient's thigh in Case 4.

Table 1. Summary of clinical presentation, investigations and clinical outcomes in 4 cases of scrub typhus reported in this case series

Case	Age and Gender	Symptomology	Day of illness at time of presentation	Domiciliary or occupational risk factor present	Cardio metabolic risk factors	Eschar	Thrombo-cytopenia	Trans-aminitis	Acute kidney injury	Initial clinical diagnosis	Rickettsial PCR (*Orientia tsutsugamushi* DNA)	Rickettsial IIP Test (Serology)	ICU Admission
1	80, F	Fever, ankle wound with cellulitis	Day 7	Yes	Yes	Yes	No	No	No	Cellulitis	Detected	IgM 1:100 IgG 1:100	No
2	50, M	Fever, chills and rigors, headache, night sweats.	Day 10	No	No	Yes	Yes	Yes	Yes	Occult sepsis	Detected	Paired IgM 1:100 and 1:3200	No
3	45, F	Fever, vomiting, loss of appetite and frothy urine	Day 9	Yes	No	Yes	No	Yes	No	Suspected pyogenic liver abscess	Detected	IgM 1:400 IgG 1:200	No
4	49, M	Fever, diarrhea, abdominal pain and tea-colored urine	Day 5	No	Yes	Yes	Yes	Yes	Yes	Septic shock secondary to leptospirosis with pulmonary haemorrhage	Detected	IgM 1:3200 IgG 1:3200	Yes

Table 2. A summary of the published case reports, case series and notable prospective studies pertaining to scrub typus in Malaysia from 1975-2025

Publication	Location and Population Studied	Number	Eschar	Main clinical features, signs and biochemical derangements at presentation	Comment
(Brown *et al*., 1976)	Rural Peninsular Malaysia involving indigenous communities and oil palm plantation workers in Mentakab, Kuala Pilah and Bukit Mendi	137 confirmed or suggestive cases	Absent in all 44 cases reported in Mentakab; not documented in the other 2 cohorts	Fever (96-100%) Chills (62-89%) Headache (50-93%) Cough (36-64%) Splenomegaly (14%) Lymphadenopathy (14%)	This was a major Malaysian-based survey which quantified very high febrile burden in plantation settings. Established scrub typhus as a common cause of undifferentiated fever in Malaysia's plantation belt and indigenous settings, reframing it as a local public health problem, not a historical curiosity.
(Ramanathan *et al*., 1987)	Melaka General Hospital; inpatients with suspected scrub typhus (1983–April 1986).	25 confirmed cases	Eschars found in 40%	Fever (100%) Chills (84%) Headache (56%) Vomiting (28%) Arthralgia (16%) Rash (28%) Hepatomegaly and splenomegaly (36%) Lymphadenopathy (60%).	Evaluated real-world diagnostic practice (Weil–Felix, rising titres) and showed how often scrub typhus was initially misclassified, emphasising the limits of routine diagnostics in Malaysian hospitals of that era. This paper marked a shift from descriptive outbreak reports toward hospital-based clinical recognition and diagnostic critique within Malaysia, arguing for better, earlier suspicion in febrile admissions.
(Chua *et al*., 1999)	Kuala Lumpur patient returning after exposure in Taman Negara in Pahang rainforest (camping).	1	Present	Fever Vomiting Cough Altered mental status (drowsiness) Transaminitis Acute kidney injury **CT-MRI demonstrated multifocal cerebral white matter lesions and ring-enhancing lesions suggestive of small-vessel vasculitis which regressed after treatment with doxycycline*	First Malaysian case report to clearly link scrub typhus to CNS involvement with radiological correlation, expanding the phenotype beyond "fever with eschar" to include encephalopathy.
(Pau & Tan, 2008)	Seremban, involving paediatric patients with acute febrile illness	2	Present	Fever Rash Abdominal pain Thrombocytopenia	Highlights that scrub typhus presents with non-specific symptoms which may be mistaken for either dengue or viral illness especially in the paediatric age group, and rapidly resolve with doxycycline
(Lim, 2014)	Remote primary care clinic along the Batang Rejang, Sarawak (Iban patient from riverine interior).	1	Present (though not clearly obvious at first presentation; authors emphasised eschars in darker skin can be subtle)	Fever Generalized rash Lymphadenopathy Myalgia Headache	Highlighted that scrub typhus is endemic in interior Sarawak communities, and that clinical recognition in indigenous patients is hampered by subtle skin findings and limited diagnostics.
(Tai & D Gupta, 2018)	Selangor; Malaysian woman after trekking through oil palm plantation	1	Present	Fever Headache Myalgia Localized lymphadenopathy Malaise	Underscored "recreational exposure" in semi-urban Malaysians entering plantation or shrubland margins, not just occupational or indigenous exposure, hence broadening the at-risk population beyond estate workers.

(Awang *et al.*, 2020)	Tumpat; non-aboriginal Malay male labourer following presumed mite bite to neck.	1	Present	Fever Rapidly progressive quadriplegia Encephalomyelitis Myalgia Headache	Showed that scrub typhus in Malaysia can mimic acute myelitis or severe CNS inflammation, including near-paralysis, even in non-indigenous patients.
(Zaini & Ibrahim, 2020)	Bentong; National Park exposure	1	Present	Fever Headache Diarrhoea Anorexia Transaminitis	Demonstrated that scrub typhus may present as fulminant septic shock which is reversible with early doxycycline if recognised.
(Yuhana *et al.*, 2022)	Teluk Intan	24	1 (4.1%)	Fever (100%) Cough (46%) Headache (42%) Vomiting (42%) Diarrhea (38%) Arthralgia (25%).	Rickettsioses in general contributed significantly to overall mortality from acute febrile illness, second to leptospirosis, causing 4 deaths (11% of all deaths), of which scrub typhus formed 25%. Despite this, empiric management rarely targeted rickettsiae directly. In this cohort, three-quarters of patients received broad-spectrum antibiotics such as ceftriaxone or ampicillin–sulbactam, often combined with azithromycin or doxycycline, but of note, none in the rickettsial group were started on a focused anti-rickettsial agent alone.
(Tan *et al.*, 2024)	Negeri Sembilan; semi-rural Malaysian patients including an indigenous farmer from forested Jelebu district.	4	Present in 2 cases (50%).	Prolonged fever (100%) GI symptoms including nausea or abdominal pain (100%) Thrombocytopenia (50%); Hepatitis (75%) Severe acute renal injury (25%) Leucocytosis (75%)	Most recent published clinical case series involving Malaysian scrub typhus adult patients since the Malaccan series in 1987
(Eltanahy *et al.,* 2024)	Batu Pahat; paediatric patient residing near oil palm estate	1	Present	Fever Chills and rigors Maculopapular rash on palms and trunk Anorexia Malaise Rhinitis Tonsillar hypertrophy with cervical lymphadenopathy	Paediatric cases of scrub typhus may present in a manner mimicking non-specific viral fever
(Khor *et al.,* 2024)	Segamat; adult patient working at a durian orchard	1	Absent	Fever Chills Diarrhea Arthralgia Myalgia Dry cough Malaise	First published Malaysian case of scrub typhus resembling severe dengue (Dengue IgM positive, NS1 Antigen negative, positive Orientia tsutsugamushi IgG serology >1:800)
(Ramli *et al.,* 2025)	Pekan district, Pahang involving a cluster of oil palm estate workers.	5	Eschar found only in Index case (20%)	Fever (100%) Headache (80%) Myalgia (60%) Cough (60%) Lymphadenopathy (20%) Thrombocytopenia (20%) Transaminitis in 2 of 3 cases where liver function was documented *Index case developed:* *Acute kidney injury* *Acute respiratory distress with bilateral pleural effusions*	First Malaysian cluster to demonstrate molecular confirmation not only via blood PCR and serology but also via urine PCR, which was proposed as a practical diagnostic specimen in severe disease, as well as directly tying occupational land use to severe multiorgan scrub typhus requiring ICU-level care.

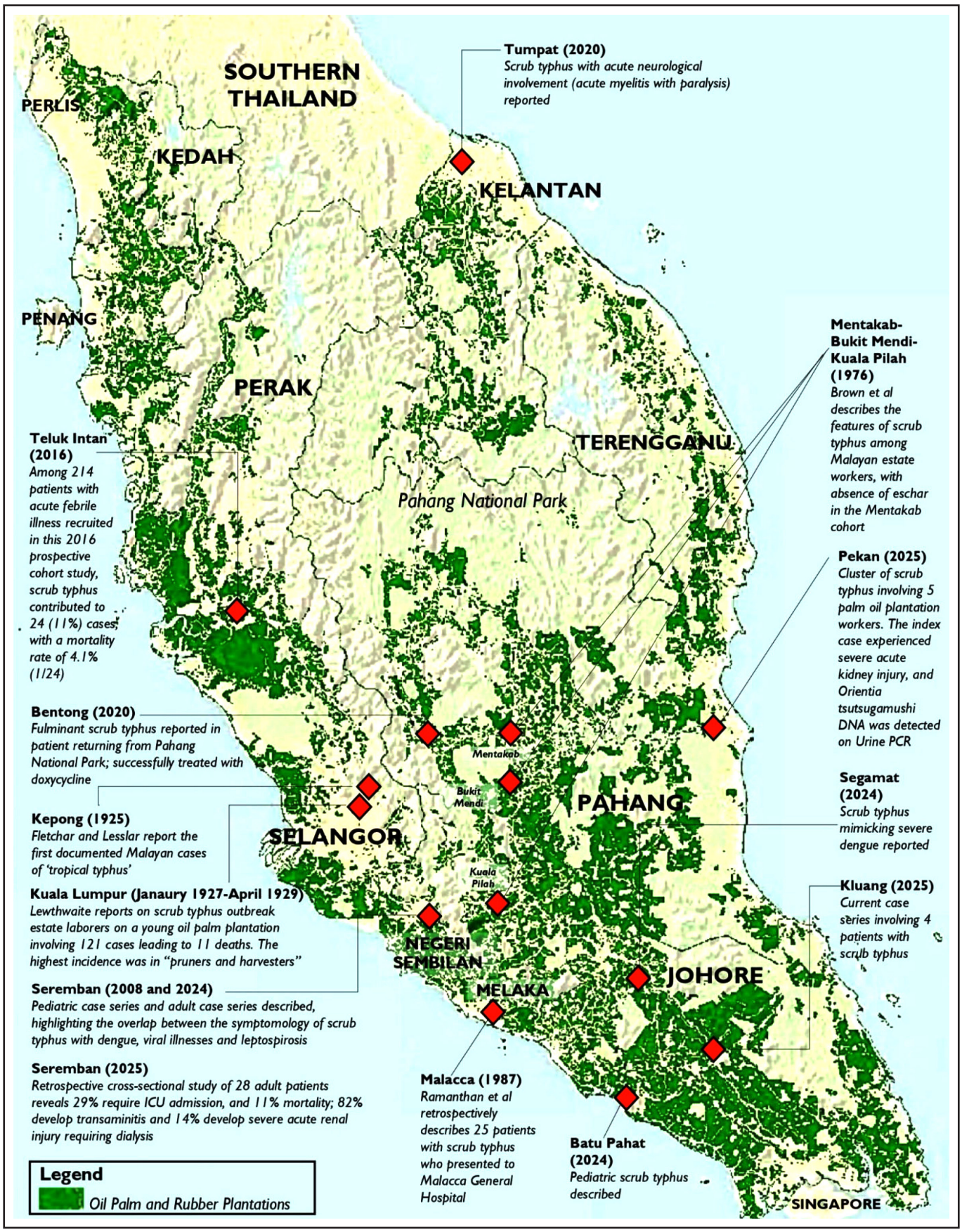

Figure 5. Location of the various published case reports, case series and selected cross sectional studies on scrub typhus in Malaysia (Sarawak and Sabah have not been depicted in this map). Distribution of palm oil and rubber plantations, adapted from Roda *et al*. (2015).

the limited availability of case reports and case series on this otherwise potentially fatal disease, highlights the numerous significant research opportunities in this area. The initial proliferation of epidemiological studies and seroprevalence studies in peri-World War II era in Malaya, has significantly slumped, and this is reflected also in research surrounding anti-rickettsial vaccines and antimicrobial agents as shown in Figure 6.

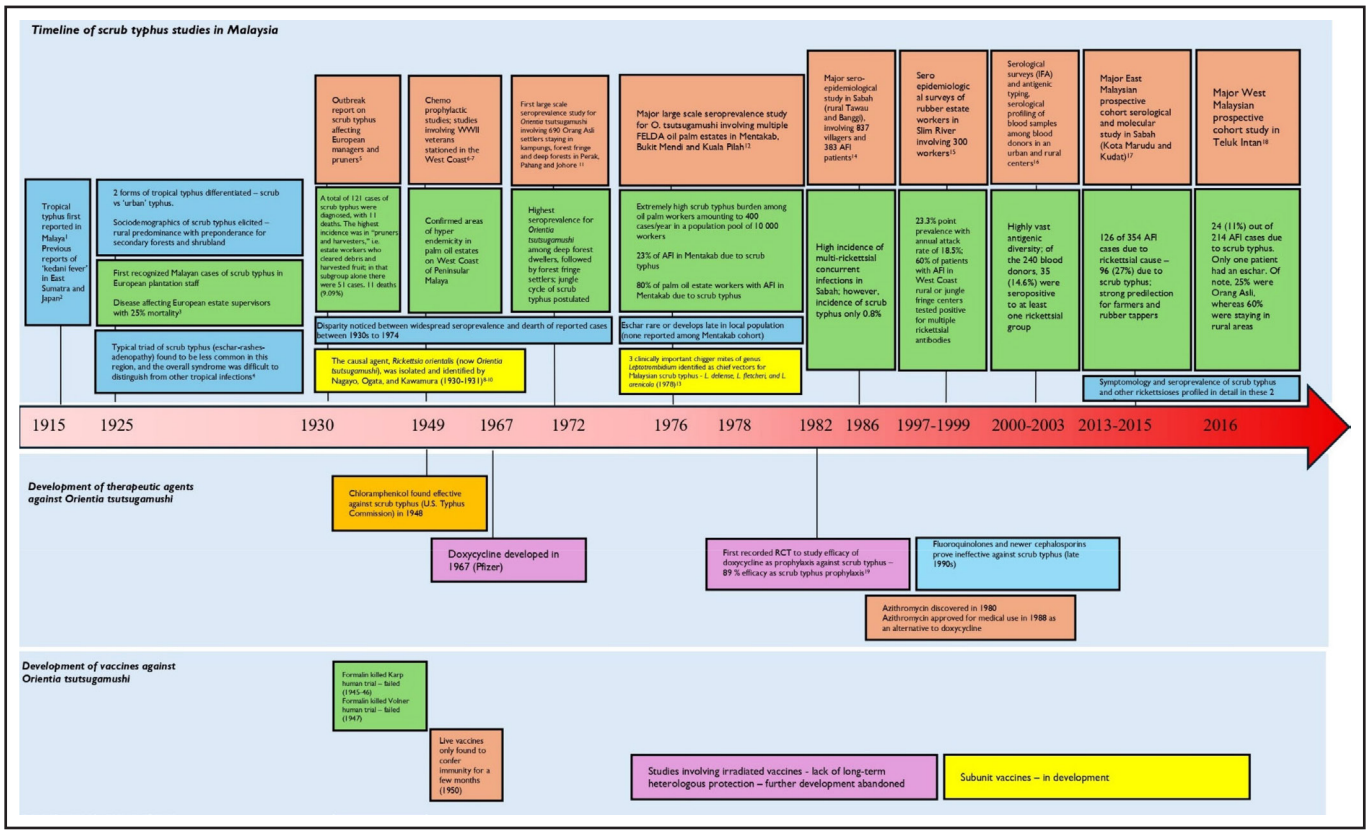

Figure 6. Timeline of key scrub typhus studies in Malaysia, alongside milestones in development of anti-rickettsial agents and vaccines.

References for this figure:

[1]Dowden, R. (1915). Kedani River Fever in the Federated Malay States. *The Indian Medical Gazette* **50**: 208-211.

[2]Schüffner, W. (1915). Pseudotyphoid Fever In Deli, Sumatra (A Variety Of Japanese Kedani Fever). *The Philippine Journal of Science* **10**: 345.

[3]Fletcher, W. & Field, J.W. (1927). The Tsutsugamushi disease in the Federated Malay States. *Bulletin of the Institute for Medical Research, Federated Malay States* No. **1**: 1-26.

[4]Brown, G.W., Robinson, D.M., Huxsoll, D.L., Ng, T.S., Lim, K.J. & Sannasey, G. (1976). Scrub typhus: a common cause of illness in indigenous populations. *Transactions of the Royal Society of Tropical Medicine and Hygiene* **70**: 444-448.

[5]Lewthwaite, R. (1930). Clinical and epidemiological observations on tropical typhus in the Federated Malay States. *Bulletin from the Institute for Medical Research, Federated Malay States* No. 1. Institute for Medical Research, Kuala Lumpur.

[6]Philip, C.B., Traub, R. & Smadel, J.E. (1949). Chloramphenicol in the chemoprophylaxis of scrub typhus; epidemiological observations on hyperendemic areas of scrub typhus in Malaya. *American Journal of Hygiene* **50**: 63-74.

[7]Smadel, J.E., Ley, H.L., Jr, Diercks, F.H., Paterson, P.Y., Wisseman, C.L., Jr & Traub, R. (1952). Immunization against scrub typhus: duration of immunity in volunteers following combined living vaccine and chemoprophylaxis. *American Journal of Tropical Medicine and Hygiene* **1**: 87-99.

[8]Nagayo, M., Tamiya, T., Mitamura, T. & Sato, K. (1930). On the virus of Tsutsugamushi disease and its demonstration by a new method. *Japanese Journal of Experimental Medicine* **8**: 309-318.

[9]Ogata, N. (1931). Aetiologie der Tsutsugamushi-krankheit: Rickettsia tsutsugamushi. *Zentralblatt für Bakteriologie, Parasitenkunde, Infektionskrankheiten und Hygiene, Erste Abteilung Originale* **122**: 249-253.

[10]Kawamura, R. & Imagawa, Y. (1931). Die Feststellung des Erregers bei der Tsutsugamushikrankheit. *Zentralblatt für Bakteriologie, Parasitenkunde, Infektionskrankheiten und Hygiene, Erste Abteilung Originale* **122**: 253-261.

[11]Cadigan, F.C., Jr, Andre, R.G., Bolton, M., Gan, E. & Walker, J.S. (1972). The effect of habitat on the prevalence of human scrub typhus in Malaysia. *Transactions of the Royal Society of Tropical Medicine and Hygiene* **66**: 582-587.

[12]Brown, G.W., Robinson, D.M., Huxsoll, D.L., Ng, T.S. & Lim, K.J. (1976). Scrub typhus: a common cause of illness in indigenous populations. *Transactions of the Royal Society of Tropical Medicine and Hygiene* **70**: 444-448. https://doi.org/10.1016/0035-9203(76)90127-9

[13]Dohany, A.L. (1978). Vector transmission of scrub typhus and control of vector mites. *Malaysian Journal of Pathology* **1**: 15-18.

[14]Taylor, A.C., Hii, J., Kelly, D.J., Davis, D.R. & Lewis Jr, G.E. (1986). A serological survey of scrub, tick, and endemic typhus in Sabah, East Malaysia. *The Southeast Asian Journal of Tropical Medicine and Public Health* **17**: 613-619.

[15]Tee, T.S., Kamalanathan, M., Suan, K.A., Chun, S.S., Ming, H.T., Yasin, R.M. & Devi, S. (1999). Seroepidemiologic survey of Orientia tsutsugamushi, Rickettsia typhi, and TT118 spotted fever group rickettsiae in rubber estate workers in Malaysia. *The American Journal of Tropical Medicine and Hygiene* **61**: 73-77.

[16]Tay, S.T., Kamalanathan, M. & Rohani, M.Y. (2003). Antibody prevalence of Orientia tsutsugamushi, Rickettsia typhi and TT118 spotted fever group rickettsiae among Malaysian blood donors and febrile patients in the urban areas. Southeast *Asian Journal of Tropical Medicine and Public Health* **34**:165-170.

[17]Grigg, M.J., William, T., Clemens, E.G., Patel, K., Chandna, A., Wilkes, C.S., Barber, B.E., Anstey, N.M., Dumler, J.S., Yeo, T.W. *et al*. (2020). Rickettsioses as Major Etiologies of Unrecognized Acute Febrile Illness, Sabah, East Malaysia. *Emerging Infectious Diseases* **26**: 1409-1419. https://doi.org/10.3201/eid2607.191722

[18]Yuhana, M.Y., Hanboonkunupakarn, B., Tanganuchitcharnchai, A., Sujariyakul, P., Sonthayanon, P., Chotivanich, K., Pukrittayakamee, S., Blacksell, S.D. & Paris, D.H. (2022). Rickettsial infections are neglected causes of acute febrile illness in Teluk Intan, Peninsular Malaysia. Tropical Medicine and Infectious Disease **7**: 77. https://doi.org/10.3390/tropicalmed7050077

[19]Twartz, J.C., Shirai, A., Selvaraju, G., Saunders, J.P., Huxsoll, D.L. & Groves, M.G. (1982). Doxycycline propylaxis for human scrub typhus. The Journal of Infectious Diseases **146**: 811-818. https://doi.org/10.1093/infdis/146.6.811

Scrub typhus remains a major and often under-recognized cause of acute undifferentiated febrile illness in the Asia–Pacific arena. Its clinical course reflects a spectrum that ranges from selflimiting febrile illness to rapidly progressive multiorgan failure. Understanding its natural history is central to timely recognition, particularly in endemic settings where it overlaps clinically with other tropical infections such as dengue, leptospirosis, and malaria.

Transmission occurs through the bite of infected larval trombiculid mites ("chiggers"), typically in areas of disturbed vegetation such as plantation margins, forest fringes, and secondary scrub. The bite is painless and often unnoticed, as was the case in all four of the cases presented in this series. The incubation period for scrub typhus is approximately 6–21 days, and this is reflected in our case series, where the median incubation period was 8 days. During this period, *Orientia tsutsugamushi* replicates locally and spreads via the lymphatic and vascular systems. Patients are asymptomatic at this stage, however a characteristic lesion, the eschar, may develop at the inoculation site. This is classically described as a necrotic black or brown crust with an erythematous halo. The eschar is typically non-tender and may be mistaken for a minor abrasion especially in manual labourers. It is frequently located in warm, sheltered areas such as the axilla, groin, inframammary folds, belt lines, or scalp. The presence of an eschar in a febrile patient in an endemic region such as hilly, palm oil estates is highly suggestive of scrub typhus. However, eschars are not universally present, and even when present they may be overlooked, particularly in individuals with darker skin or when located in areas not routinely examined. This contributes to diagnostic delay. The variation in the incidence of eschar among confirmed scrub typhus cases has been documented even in the early days of bush fever research in Malaya, where despite scrub typhus being a cause of up to 23% of acute febrile illness in rural healthcare centres in 1970s Malaya, eschar was noticeably absent in nearly all the cases documented in one of the constitutive cohorts in the groundbreaking study which first characterised scrub typhus as a major occupational health hazard among oil palm workers in rural Malaya (Brown *et al*., 1976). Regional lymphadenopathy draining the inoculation site may also be observed in this early phase, and this is reflected in the inguinal lymphadenopathy seen in Case 4.

The clinical utility of the trombiculid eschar has been the subject of research. Although the eschar is highly specific, it is limited by a wide variation in sensitivity, which ranges between 7% up to 97% (Saraswati *et al*., 2018). Of note, this dermatological stigmata of scrub typhus is frequently absent in Southeast Asian cases and in endemic areas with less severe illness (Silpapojakul, 1997). Nevertheless, this variation in rates of reported eschar may be due to the protean nature of this stigmata of chigger bites, where it may range from a non-descript macular or vesicular erythematous rash, to a sclerotic lesion (Lee *et al*., 2025a). Nevertheless, the eschar serves as a distinctive diagnostic indicator for scrub typhus, and has been associated with increased risk to develop acute respiratory distress syndrome, acute kidney injury and cardiovascular hemodynamic instability (Kim *et al*., 2010; Chauhan *et al*., 2017). Interestingly, the lack of an eschar in cases of confirmed scrub typhus has been associated with unfavorable patient prognoses (Lee *et al*., 2009). We postulate that this is because the absence of eschar (or the lack of documentation therefor) is either a sign that this feature has been missed, or that immunosuppression has prevented an adequate immune response leading to failure of eschar formation, since the scab is formed by an inflammatory immune response against the inoculated bacteria at the chigger bite site.

Following incubation, patients typically develop an acute undifferentiated febrile illness. The onset of fever is often abrupt and persistent rather than relapsing or cyclical. Common systemic features include high-grade fever, severe headache, myalgia and generalized arthralgia or limb pain, marked fatigue and malaise, gastrointestinal symptoms such as nausea and abdominal discomfort, dry cough, and generalized or regional lymphadenopathy (Mahajan, 2005; Banerjee & Kulkarni, 2021). Based on the patient profiles of the Malaysian case reports, we surmise that fever and symptoms resembling viral illness such as headache, myalgia, arthralgia and malaise, alongside evidence of reticuloendothelial proliferation such as lymphadenopathy are the commonest presentations of scrub typhus in Malaysia.

As reflected in the biochemical profiles of the patients in this series, laboratory findings in particular in the acute stage of illness, are nonspecific, and include mild thrombocytopenia, elevated transaminases, elevated inflammatory markers, and sometimes leucocytosis or leukopenia (Behera & Mohanty, 2015; Shrestha *et al*., 2022). Of note, scrub typhus hepatopathy was observed in 3 out of 4 cases in this series (75%), and this prevalence is reflected in surveillance and observational studies in India and Japan, where scrub typhus hepatitis may affect between 69.7% up to 87% of patients (Ogawa *et al*., 2002; Chauhan *et al*., 2024). These patterns overlap substantially with other endemic infections, in particular dengue, leptospirosis, and enteric fever, which may also present with hepatopathy. As a result, scrub typhus is frequently misclassified early in its course, as seen in Case 4. This acute febrile phase, however, is a critical diagnostic window. This is because appropriate antimicrobial therapy (doxycycline or azithromycin) initiated at this stage is associated with rapid clinical defervescence and prevention of progression to severe disease.

In addition, coinfections with leptospirosis and dengue have been documented in the literature, and as illustrated by Case 4, may pose a clinical quandary since the treatment for severe leptospirosis does not provide antimicrobial coverage against *Orientia tsutsugamushi*. The presence of dual zoonotic infections has also been documented in the recent case cohort involving palm oil plantation workers in Pekan, where the index case was initially treated for serology-confirmed leptospirosis (Ramli *et al*., 2025).

The pathophysiology of severe scrub typhus is driven by the organism's tropism for endothelial cells and macrophage lineage cells. This results in small-vessel vasculitis and perivasculitis affecting multiple organ systems (Peter *et al*., 2015). If untreated, this vasculitic phase generally emerges during the second week of illness and underlies the multisystem complications that define severe scrub typhus.

These major complications include interstitial pneumonitis progressing to acute respiratory distress syndrome which is characterised by progressive tachypnoea, hypoxaemia, and bilateral infiltrates which may mimic other bacterial causes of atypical pneumonia, acute kidney injury which is driven by pre-renal hypotension, systemic inflammation, and direct endothelial injury, hepatitis and central nervous system involvement such as encephalitis, meningoencephalitis, acute confusional state, seizures, and focal neurological deficits. In rare cases, severe neurological involvement can mimic acute demyelinating or inflammatory myelopathies, transverse myelitis and polyneuropathies (Chen *et al*., 2006; Ryu *et al*., 2020; Sardana & Shringi, 2020).

The cardiovascular manifestations of severe scrub typhus include myocarditis leading to distributive shock consistent with a sepsis-like pathophysiology and hyperlactemia (Avasthi *et al*., 2018; Chin *et al*., 2018).

Haematological manifestations of severe scrub typhus are thrombocytopenia and coagulopathy which resemble disseminated intravascular coagulation (Ono *et al*., 2012; Pandey

et al., 2022). This haematological feature of complicated scrub typhus can confound bedside differentiation from both severe dengue or leptospirosis (Subedi *et al*., 2021; Nazeera *et al*., 2024).

Critically, none of these complications are individually specific to scrub typhus. The syndrome at this stage can be indistinguishable from severe sepsis of another cause. Without a high index of suspicion particularly in the presence of compatible exposure history (such as residing or working in a plantation, at the forest edge, near shrub land or overgrown vegetation, or even recreation near such areas), and without an exhaustive skin survey to identify eschars, the diagnosis may still be missed.

Untreated, this severe vasculitic phase can lead to multiorgan failure, ICU admission, and death. Historical mortality in untreated cases is significant but falls dramatically with timely diagnosis and antimicrobial therapy. This is because scrub typhus is notable for its brisk response to appropriate antimicrobial therapy. Tetracyclines (classically doxycycline) remain first-line in most non-pregnant adults. Alternatives such as azithromycin are recommended in pregnancy and in some critically ill patients.

When therapy is initiated during the acute febrile phase, defervescence often occurs within 24–48 hours. Fever, headache, myalgia, and malaise typically improve in parallel. This rapid response has historically served both as treatment and as a pragmatic diagnostic confirmation in resource-limited settings (Peter *et al*., 2015; Barnabas *et al*., 2021). However, in patients who present late with established complications such as ARDS, encephalitis, shock, or acute kidney injury, appropriate therapy can still be lifesaving, but the course is less predictable. Recovery in such cases is slower and incomplete early antimicrobial benefit may be obscured by ongoing organ dysfunction.

Following clinical improvement, long-term immunity does not develop. Immunity to *O. tsutsugamushi* is believed to be strain-specific and relatively short-lived. Reinfection in the same individual is therefore possible, and indeed documented, particularly in persons with ongoing occupational or environmental exposure especially amongst agricultural workers, forestry workers and military personnel (Paris *et al*., 2013; Elliott *et al*., 2021).

Although scrub typhus diagnosis should ideally begins at the bedside when physicians are faced with a combination of undifferentiated fever, severe headache, myalgia, raised transaminases, thrombocytopenia, and a necrotic eschar at a concealed site, the variability in occurrence of eschar which may be missed in darker skin or in intimate skin folds, and the generic presentation which is clinically indistinguishable from dengue, leptospirosis or malaria, hinders an accurate or timely clinical diagnosis. On the other hand, laboratory confirmation is technically possible but operationally difficult. The reference standard in most literature is indirect immunofluorescence assay (IFA) detecting IgM/IgG against *O. tsutsugamushi*, or a ≥4-fold rise in paired titres, but acute-phase IFA is often insensitive early in illness and paired serology requires convalescent sampling, which is time consuming and impractical for real-time management. Many district hospitals instead still rely on rapid immunochromatographic assays or even the historical Weil–Felix agglutination test; these are fast and cheap but have variable sensitivity and poor specificity, especially in the early phase of the disease. PCR (whole blood, buffy coat, eschar swab, and even urine in severe cases) can identify *O. tsutsugamushi* directly and is most useful in the first week of illness, before antibodies mature, but availability of PCR in rural endemic and resource-limited settings may be challenging (Prakash, 2017; Kala *et al*., 2020). The net effect is a diagnostic gap at exactly the point when intervention matters most which is in the acute phase of the illness. Clinicians in endemic regions are often forced to treat empirically with doxycycline or azithromycin on syndromic grounds and exposure history, then observe for rapid defervescence within 24–48 hours as both therapy and *de facto* diagnostic support. In this case series, we are fortunate that our facilities, under the auspices of the Malaysian Ministry of Health, are able to send both PCR and serological samples for testing at the Malaysian Institute for Medical Research (IMR) with a turnaround time of 2 weeks. However, the treatment of the patients in our series pivoted on the clinical picture and dermatological stigmata of scrub typhus, with seroconversion and *O. tsutsugamushi* DNA PCR playing a supportive role in the diagnosis.

Scrub typhus in Malaysia sits at an uncomfortable intersection of ubiquity and invisibility. It is clearly entrenched in rural, plantation, and forest-edge ecosystems and has repeatedly been documented among oil palm and rubber estate workers in Peninsular Malaysia, in indigenous and riverine communities in Sarawak, and in recreational or peri-urban exposures where plantation fringe meets human movement. Yet, published literature is still dominated by individual case reports and small clusters, which paint an incomplete picture of the disease and tend to focus on the more severe manifestations of the disease. This causes clinicians to perceive scrub typhus as exotic neuroinflammation, fulminant organ failure, or textbook eschar-plusfever, while in practice the disease is just as likely to present first as undifferentiated fever without a visible eschar and with only nonspecific laboratory derangements in liver or renal function. This under-recognition delays timely treatment with doxycycline or azithromycin at the exact window when treatment can abort the evolution from uncomplicated febrile illness to systemic vasculitis with multiorgan dysfunction. This consequence is visible in available Malaysian reports of scrub typhus presenting late with respiratory failure, shock, CNS involvement, and severe kidney injury, all of which are preventable trajectories if the infection is suspected and treated early. At the same time, there are challenges in timely laboratory confirmation: access to PCR is uneven, rapid tests have variable accuracy, and serology requires convalescent sampling that district hospitals and estate-area clinics in developing nations may not possess. Although the empirical treatment approach was a historical yet pragmatic *de facto* indirect diagnostic tool, it is unacceptable for a pathogen that is now recognized as an endemic occupational and environmental hazard with dire public health consequences.

The understanding of the disease profile of scrub typhus in the Malaysian context may be better facilitated by a multi-center, prospective Malaysian case series of larger sample size, stratified by land use, exposure setting, occupational background, and clinical severity. Such a series should standardize exposure geography (such as exposure or residence at estate fringes or secondary scrubland), bedside phenotype at first medical contact (including presence or absence and anatomical location of eschars), early laboratory features, organ involvement over time, antimicrobial timing and response, and long-term outcomes such as post-scrub typhus asthenia. This would generate actionable triage heuristics for primary and district-level clinicians, who are the main line of defense against preventable severe occupational disease. By linking exposure setting to presentation, it would also directly support public health programs and worker protection policies in high-risk land-use zones such as oil palm replanting fronts and forest–estate ecotones.

In short, scrub typhus in Malaysia is probably under-reported, and clinically under-described. A coordinated large-scale case series would convert what is currently impressionistic into quantifiable clinical and public health interventional pathways. That shift is essential if scrub typhus is to move from being recognized retrospectively in the wards to being interrupted prospectively in district clinics and via targeted public health programs.

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REFERENCES

Avasthi, G.L., Patel, P., Kuka, R. & Mahajan, R. (2018). Acute fulminant myocarditis as a rare manifestation in complicated scrub typhus: A case report. *IHJ Cardiovascular Case Reports* **2**: S18-S20. https://doi.org/10.1016/j.ihjccr.2018.07.009

Awang, H. & Arif, M.H.M. (2020). A paralyzing bite: an unorthodox case of scrub typhus in a non-aboriginal Malaysian patient. *Journal of Health and Translational Medicine* **23**: 39-43. https://doi.org/10.1016/j.ihjccr.2018.07.009

Banerjee, A. & Kulkarni, S. (2021). Orientia tsutsugamushi: The dangerous yet neglected foe from the East. *International Journal of Medical Microbiology* **311**: 151467. https://doi.org/10.1016/j.ihjccr.2018.07.009

Barnabas, R., Abhilash, K.P.P., Varghese, G.M., Shubanker, M., Ramya, I. & Prakash, J.A.J. (2021). Prospective study to assess the treatment modalities and fever defervescence in patients with scrub typhus from a tertiary care centre in South India. *Journal of Vector Borne Diseases* **58**: 33-38. https://doi.org/10.4103/0972-9062.321748

Behera, B. & Mohanty, S. (2015). Scrub typhus: Clinical spectrum and outcome. *Indian Journal of Critical Care Medicine* **19**: 366-367. https://doi.org/10.4103/0972-5229.158292

Brown, G.W., Robinson, D.M., Huxsoll, D.L., Ng, T.S., Lim, K.J. & Sannasey, G. (1976). Scrub typhus: a common cause of illness in indigenous populations. *Transactions of the Royal Society of Tropical Medicine and Hygiene* **70**: 444-448. https://doi.org/10.1016/0035-9203(76)90127-9

Chauhan, R., Ahmad, S., Goyal, C. & Tewatia, P. (2024). Hepatopathy in scrub typhus: clinical presentation, association with morbidity and impact on outcome. *Cureus* **16**: e52316.

Chauhan, V., Thakur, A. & Thakur, S. (2017). Eschar is associated with poor prognosis in scrub typhus. *Indian Journal of Medical Research* **145**: 693-696. https://doi.org/10.7759/cureus.52316

Chen, P.H., Hung, K.H., Cheng, S.-J. & Hsu, K.N. (2006). Scrub typhus-associated acute disseminated encephalomyelitis. *Acta Neurologica Taiwanica* **15**: 251-254. https://doi.org/10.29819/ANT.200612.0005

Chin, J.Y., Kang, K.W., Moon, K.M., Kim, J. & Choi, Y.J. (2018). Predictors of acute myocarditis in complicated scrub typhus: an endemic province in the Republic of Korea. *Korean Journal of Internal Medicine* **33**: 323-330. https://doi.org/10.3904/kjim.2016.303

Chua, C.J., Tan, K.S., Ramli, N., Devi, S. & Tan, C.T. (1999). Scrub typhus with central nervous system involvement: a case report with CT and MR imaging features. *Neurology Journal of Southeast Asia* **4**: 53-57.

Devasagayam, E., Dayanand, D., Kundu, D., Kamath, M.S., Kirubakaran, R. & Varghese, G.M. (2021). The burden of scrub typhus in India: A systematic review. *PLoS Neglected Tropical Diseases* **15**: e0009619. https://doi.org/10.1371/journal.pntd.0009619

Elliott, I., Thangnimitchok, N., Chaisiri, K., Wangrangsimakul, T., Jaiboon, P., Day, N.P.J., Paris, D.H., Newton, P.N. & Morand, S. (2021). Orientia tsutsugamushi dynamics in vectors and hosts: ecology and risk factors for foci of scrub typhus transmission in northern Thailand. *Parasites & Vectors* **14**: 540. https://doi.org/10.1186/s13071-021-05042-4

Eltanahy, M.A.E., Shah, K.A., Ee, A.T.R., Hul, T.Y.C., Ling, T.J., Rajandram, K.A.L. & Elhariri, S. (2024). Scrub typhus as missed diagnosis for acute febrile illness in Malaysia, Southeast Asia. *Journal of the Egyptian Society of Parasitology* **54**: 235-240. https://doi.org/10.21608/jesp.2024.373523

Fletcher, W. & Field, J.W. (1927). The Tsutsugamushi disease in the Federated Malay States. *Bulletin from the Institute for Medical Research, Federated Malay States* **1**: 1-26.

Kala, D., Gupta, S., Nagraik, R., Verma, V., Thakur, A. & Kaushal, A. (2020). Diagnosis of scrub typhus: recent advancements and challenges. *3 Biotech* **10**: 396. https://doi.org/10.1007/s13205-020-02389-w

Kang, C.S. & Kanniah, K.D. (2022). Land use and land cover change and its impact on river morphology in Johor River Basin, Malaysia. *Journal of Hydrology: Regional Studies* **41**: 101072. https://doi.org/10.1016/j.ejrh.2022.101072

Khor, Z.X., Muthuraman, V. & Vishnu Prashad, B.S. (2024). Scrub typhus: A great mimic of severe dengue. *International Journal of Clinical Studies & Medical Case Reports* **38**: 003. https://doi.org/10.46998/IJCMCR.2024.38.000948

Kim, D.M., Kim, S.W., Choi, S.H. & Yun, N.R. (2010). Clinical and laboratory findings associated with severe scrub typhus. *BMC Infectious Diseases* **10**: 108. https://doi.org/10.1186/1471-2334-10-108

Lee, C.S., Hwang, J.H., Lee, H.B. & Kwon, K.S. (2009). Risk factors leading to fatal outcome in scrub typhus patients. *American Journal of Tropical Medicine and Hygiene* **81**: 484-488. https://doi.org/10.4269/ajtmh.2009.81.484

Lee, C.S., Kim, S., You, H., Song, J., Choi, S.H., Kang, T.-J., Yoo, H.-H. & Park, J. (2025). Classifying eschar morphologies: enhancing early diagnosis of scrub typhus. *Journal of Korean Medical Science* **40**: e234. https://doi.org/10.3346/jkms.2025.40.e234

Lee, K.S., Rashid, A., Tan, Y., Abidin, N., Ramli, S. & Ng, T. (2025). Scrub typhus in Negeri Sembilan, Malaysia: A cross-sectional study. CRC Research Day 2025. Negeri Sembilan, Malaysia.

Lim, J.L. (2014). A Rejang River rash. *Malaysian Family Physician* **9**: 33-34.

Mahajan, S.K. (2005). Scrub typhus. *Journal of the Association of Physicians of India* **53**: 954-958.

Nazeera, N.N., Sreelakshmi, M., Mathew, A. & Basheer, A. (2024). Double blow in the tropics: A case of concurrent leptospirosis and scrub typhus. *Cureus* **16**: e60732. https://doi.org/10.7759/cureus.60732

Ogawa, M., Hagiwara, T., Kishimoto, T., Shiga, S., Yoshida, Y., Furuya, Y. & Masukawa, K. (2002). Scrub typhus in Japan: epidemiology and clinical features of cases reported in 1998. *American Journal of Tropical Medicine and Hygiene* **67**: 162-165. https://doi.org/10.4269/ajtmh.2002.67.162

Ono, Y., Ikegami, Y., Tasaki, K., Abe, M. & Tase, C. (2012). Case of scrub typhus complicated by severe disseminated intravascular coagulation and death. *Emergency Medicine Australasia* **24**: 577-580. https://doi.org/10.1111/j.1742-6723.2012.01600.x

Pakiam, G.K., Khor, Y. & Chia, J. (2020). Johor's oil palm economy: Past, present and future. In: Johor: Abode of Development?, Hutchinson, F.E. & Rahman, S. (editors). Singapore: ISEAS–Yusof Ishak Institute, pp. 73-106.

Pandey, M., Kamath, S., Upadhyay, A. & Dubey, K. (2022). Disseminated intravascular coagulation manifesting as diffuse alveolar hemorrhage in a scrub typhus patient: A rarely thought of complication. *Cureus* **14**: e32974. https://doi.org/10.7759/cureus.32974

Paris, D.H., Shelite, T.R., Day, N.P.J. & Walker, D.H. (2013). Unresolved problems related to scrub typhus: A seriously neglected life-threatening disease. *American Journal of Tropical Medicine and Hygiene* **89**: 301-307. https://doi.org/10.4269/ajtmh.13-0064

Pau, W.S.C. & Tan, K.K. (2008). Importance of a thorough examination. *Pediatric Infectious Disease Journal* **27**: 569-570. https://doi.org/10.1097/INF.0b013e318168db08

Peter, J.V., Sudarsan, T.I., Prakash, J.A.J. & Varghese, G.M. (2015). Severe scrub typhus infection: Clinical features, diagnostic challenges and management. *World Journal of Critical Care Medicine* **4**: 244-250.

Prakash, J.A.J. (2017). Scrub typhus: Risks, diagnostic issues, and management challenges. *Research and Reports in Tropical Medicine* **8**: 73-83. https://doi.org/10.2147/RRTM.S105602

Ramanathan, M., Zainal Abidin, M.N.B. & Balachand, V. (1987). The diagnosis of scrub typhus: An evaluation. *Medical Journal of Malaysia* **42**: 61-64.

Ramli, S.R., Arifin, N., Ismail, M.F., Hii, S.Y.F., Sulaiman, N.S., Lah, E.F.C. & Nik Abdul Aziz, N.A.H. (2025). Severe scrub typhus with acute kidney injury: Urine PCR evidence from an East Coast Malaysian cluster. *Tropical Medicine and Infectious Disease* **10**: 208. https://doi.org/10.3390/tropicalmed10080208

Roda, J.-M., Goralski, M., Benoist, A., Baptiste, A., Boudjema, V., Galanos, T., Georget, M., Hʉvin, J.-E., Lavergne, S., Eychenne, F. *et al*. (2015). Sustainability of bio-jetfuel in Malaysia, Roda, J.-M. (editor). Paris: CIRAD, pp. 28.

Ryu, H.S., Moon, B.J., Park, J.Y., Kim, S.D., Seo, S.K. & Lee, J.K. (2020). Acute transverse myelitis following scrub typhus: A case report and review of the literature. *Journal of Spinal Cord Medicine* **43**: 548-551. https://doi.org/10.1080/10790268.2017.1420538

Saraswati, K., Day, N.P.J., Mukaka, M. & Blacksell, S.D. (2018). Scrub typhus point-of-care testing: A systematic review and meta-analysis. *PLoS Neglected Tropical Diseases* **12**: e0006330. https://doi.org/10.1371/journal.pntd.0006330

Sardana, V. & Shringi, P. (2020). Neurological manifestations of scrub typhus: A case series from tertiary care hospital in southern East Rajasthan. *Annals of Indian Academy of Neurology* **23**: 808-811. https://doi.org/10.4103/aian.AIAN_97_19

Shrestha, S., Karn, M., Regmi, S.M., Pradhan, S., Nagila, A. & Prajapati, R. (2022). Clinical profile and biochemical abnormalities in scrub typhus: A cross-sectional study. *Annals of Medicine and Surgery* **84**: 104903. https://doi.org/10.1016/j.amsu.2022.104903

Silpapojakul, K. (1997). Scrub typhus in the Western Pacific region. *Annals of the Academy of Medicine, Singapore* **26**: 794-800.

Subedi, P., Ghimire, M., Shrestha, K., Ghimire, K., Adhikari, S. & Tiwari, B. (2021). Dengue and scrub typhus co-infection causing septic shock. *Oxford Medical Case Reports* **2021**: 450-452. https://doi.org/10.1093/omcr/omab115

Tai, K.S. & Gupta, E.D. (2018). A woman with persistent fever and a skin lesion. *Australian Journal of General Practice* **47**: 535-536. https://doi.org/10.31128/AJGP-01-18-4465

Tan, Y.A., Lee, K.S., Thangavelu, S. & Ng, T.K. (2024). Scrub typhus, the forgotten acute febrile illness: A case series from Negeri Sembilan, Malaysia. *MJM Case Reports Journal* **3**: 184-187. https://doi.org/10.13140/RG.2.2.20391.46245

Taylor, A.C., Hii, J., Kelly, D.J., Davis, D.R. & Lewis, G.E., Jr (1986). A serological survey of scrub, tick, and endemic typhus in Sabah, East Malaysia. *Southeast Asian Journal of Tropical Medicine and Public Health* **17**: 613-619.

Watt, G. & Parola, P. (2003). Scrub typhus and tropical rickettsioses. *Current Opinion in Infectious Diseases* **16**: 429-436. https://doi.org/10.1097/00001432-200310000-00009

Xu, G., Walker, D.H., Jupiter, D., Melby, P.C. & Arcari, C.M. (2017). A review of the global epidemiology of scrub typhus. *PLoS Neglected Tropical Diseases* **11**: e0006062. https://doi.org/10.1371/journal.pntd.0006062

Yasunaga, H., Horiguchi, H., Kuwabara, K., Hashimoto, H. & Matsuda, S. (2011). Delay in tetracycline treatment increases the risk of complications in Tsutsugamushi disease: Data from the Japanese Diagnosis Procedure Combination database. *Internal Medicine* **50**: 37-42. https://doi.org/10.2169/internalmedicine.50.4220

Yuhana, M.Y., Hanboonkunupakarn, B., Tanganuchitcharnchai, A., Sujariyakul, P., Sonthayanon, P., Chotivanich, K., Pukrittayakamee, S., Blacksell, S.D. & Paris, D.H. (2022). Rickettsial infections are neglected causes of acute febrile illness in Teluk Intan, Peninsular Malaysia. *Tropical Medicine and Infectious Disease* **7**: 77. https://doi.org/10.3390/tropicalmed7050077

Zaini, A.F.S.M. & Ibrahim, A. (2020). A case of successful treatment of septic shock secondary to scrub typhus. *Clinical Infectious Diseases: Open Access* **4**: 119. https://doi.org/10.37421/jid.2020.4.119