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Review Article

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Rising Burden of Scrub Typhus: Transmission Dynamics, Clinical Manifestations, Diagnostic Challenges, and Preventive Strategies

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Abstract

Scrub typhus is an emerging and re-emerging vector-borne bacterial infection caused by *Orientia tsutsugamushi*, transmitted to humans through the bite of infected chiggers (larval mites) of the genus *Leptotrombidium*. In recent years, the incidence of scrub typhus has increased significantly in many tropical and subtropical regions, posing a serious public health concern, particularly in rural and peri-urban settings. The disease is closely associated with exposure to dense vegetation, scrublands, and forested areas, commonly referred to as "mite islands."

Clinically, scrub typhus presents with non-specific flu-like symptoms such as acute fever, chills, headache, myalgia, and fatigue, often leading to misdiagnosis. A characteristic eschar at the bite site, though pathognomonic, is not always present or easily detectable, further complicating clinical recognition. If diagnosis and treatment are delayed, the infection may progress to severe complications, including acute respiratory distress syndrome, meningoencephalitis, acute kidney injury, myocarditis, and multi-organ failure, resulting in increased morbidity and mortality.

Diagnosis remains challenging due to limited awareness, overlapping symptoms with other febrile illnesses, and restricted access to reliable laboratory tests in resource-limited settings. Early initiation of appropriate antibiotic therapy, particularly doxycycline or azithromycin, is crucial for favourable outcomes and rapid recovery.

This review highlights the rising burden of scrub typhus by examining its transmission dynamics, clinical manifestations, diagnostic challenges, and preventive strategies. Emphasis is placed on improving early detection, strengthening surveillance, promoting vector control measures, and enhancing public awareness to reduce disease burden and prevent severe outcomes.

Keywords: Scrub typhus; *Orientia tsutsugamushi*; chigger mites; transmission dynamics; clinical manifestations; eschar; diagnostic challenges; antibiotic therapy; preventive strategies; public health.

Objectives of the Review

1. To critically assess the growing public health significance of scrub typhus as a re-emerging vector-borne infectious disease.
2. To explain the mechanisms of transmission of *Orientia tsutsugamushi*, with particular reference to chigger ecology and environmental determinants.
3. To outline the spectrum of clinical manifestations of scrub typhus, from early non-specific symptoms to severe and life-threatening complications.
4. To evaluate the major challenges involved in the timely diagnosis of scrub typhus, including clinical ambiguity and diagnostic limitations in endemic regions.
5. To highlight the importance of early and appropriate antibiotic therapy in preventing disease progression and reducing fatal outcomes.
6. To review existing preventive strategies, focusing on vector control, personal protective practices, and community-level interventions.
7. To emphasise the need for strengthened surveillance systems, increased clinical awareness, and integrated preventive measures to curb the rising burden of scrub typhus.

1. Introduction

Scrub typhus is a vector-borne infectious disease caused by the obligate intracellular bacterium *Orientia tsutsugamushi*. The disease is endemic in a large geographical region of the Asia–Pacific, commonly known as the "tsutsugamushi triangle," encompassing South and Southeast Asia, parts of East Asia, and northern Australia (Watt & Parola, 2003; Kelly et al., 2009). In recent decades, scrub typhus has re-emerged as a significant public health concern, particularly in rural and semi-rural areas.

Transmission occurs through the bite of infected chiggers, which are the larval stage of trombiculid mites, mainly belonging to the genus Leptotrombidium (Kelly et al., 2009). These vectors inhabit areas with dense vegetation such as scrublands, grasslands, forest margins, and agricultural fields. Humans act as accidental hosts and are typically infected during occupational or outdoor activities that involve close contact with mite-infested environments, especially farming and forestry-related work (Watt & Parola, 2003).
Environmental and occupational factors play a key role in the transmission of scrub typhus. Seasonal agricultural activities, land-use changes, deforestation, and expansion of human settlements into previously uncultivated areas increase human exposure to infected chiggers (Taylor et al., 2015). Individuals engaged in agricultural labor are therefore at higher risk of infection. Understanding these exposure patterns is essential for identifying vulnerable populations and designing effective prevention strategies.

Despite the availability of effective antibiotic treatment, scrub typhus remains underdiagnosed due to its non-specific clinical presentation and limited access to diagnostic facilities in endemic regions (WHO, 2023). Improved awareness of transmission dynamics is critical for early clinical suspicion, timely treatment, and reduction of disease-related complications.

Background

Scrub typhus is a zoonotic, mite-borne infectious disease that has emerged as a major public health concern, particularly in Southeast Asia. The disease is caused by the obligate intracellular bacterium *Orientia tsutsugamushi* and is transmitted to humans through the bite of infected larval mites (chiggers) belonging to the genus *Leptotrombidium* (Watt & Parola, 2003). It is estimated that nearly one billion people are at risk of infection, with approximately one million cases occurring annually in endemic regions (Kelly et al., 2009).

Traditionally, scrub typhus was considered endemic to the "tsutsugamushi triangle," which includes much of Southeast Asia, East Asia, and northern Australia. However, recent studies have reported its occurrence beyond this region, including parts of Africa, South America, and the

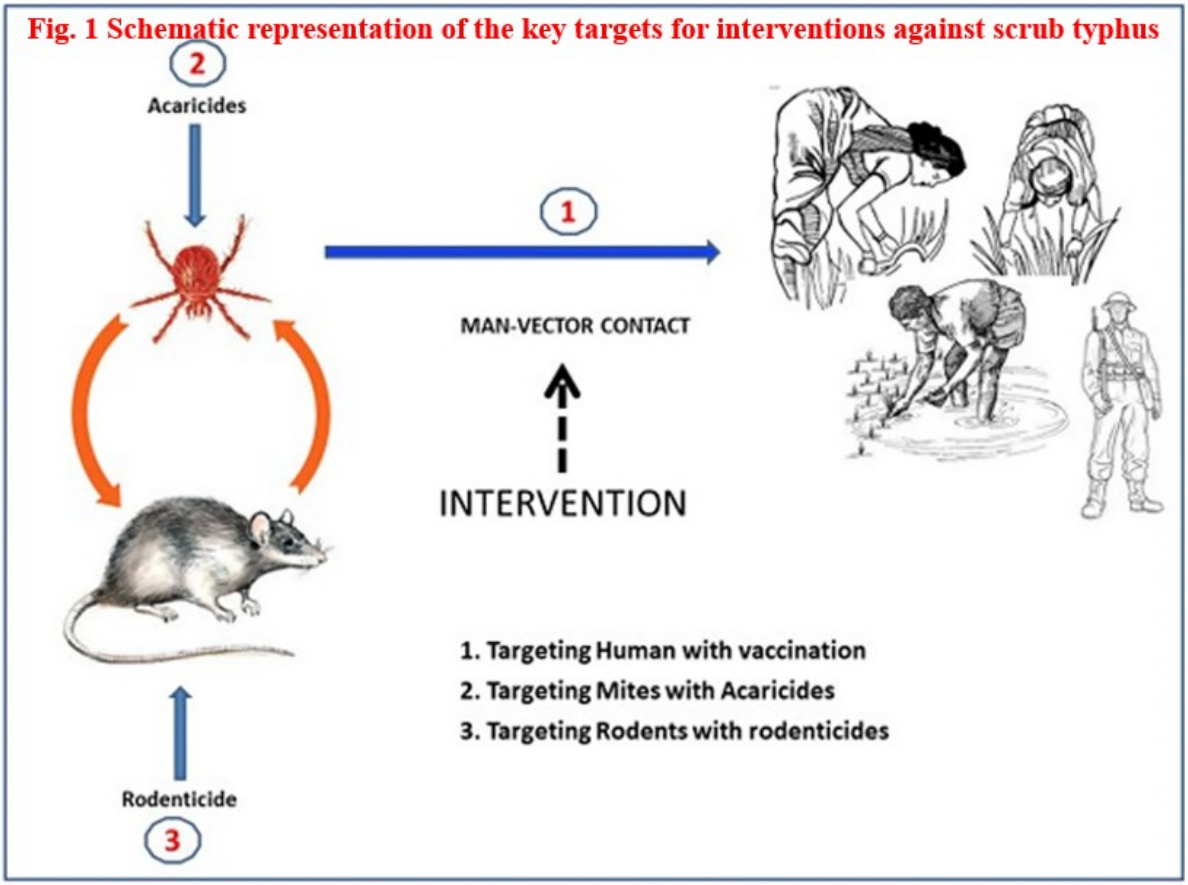
Middle East, indicating a wider global distribution than previously recognised (Izzard et al., 2010; Weitzel et al., 2016). The increasing incidence of scrub typhus in endemic areas has highlighted the urgent need for improved surveillance and effective control measures (Varghese et al., 2015).

In nature, *Orientia* species are maintained in a zoonotic cycle involving rodents and trombiculid mites. Humans are accidental hosts who become infected upon entering mite-infested environments, often referred to as "mite zones," during occupational or recreational activities such as farming and forestry (Kelly et al., 2009). Although rare, alternative modes of transmission, including leech-associated infection, have also been documented (Izzard et al., 2010).

Clinically, scrub typhus presents as an acute febrile illness that may progress to pneumonitis, renal impairment, and other systemic complications, with death primarily resulting from multi-organ failure if untreated (Taylor et al., 2015). The disease is generally responsive to antibiotics such as doxycycline, tetracycline, and azithromycin; however, delayed initiation of therapy is associated with severe outcomes and higher mortality, which may reach up to 30% in untreated cases (Watt & Parola, 2003).

Despite ongoing research, no effective vaccine is currently available. Natural infection provides only short-term and strain-specific immunity, and the extensive antigenic diversity among *Orientia* species further complicates vaccine development (Kelly et al., 2009). Given the repeated exposure of rural populations and the expanding geographical range of the disease, the development of effective preventive strategies, including vaccines, remains a critical global health priority. (Fig-1).

Fig. 1 Schematic representation of the key targets for interventions against scrub typhus



The goal of this review is to provide a comprehensive and accurate portrayal of scrub typhus as a newly recognised vector-borne bacterial disease of significant public health importance. It will do this by examining how it spreads, the symptoms it causes, the diagnostic process, available treatments, and methods to prevent its occurrence. It will focus on early diagnosis, effective antibiotic intervention, and tighter surveillance to lower the rising disease burden.

2. Review of Literature

Scrub typhus has been increasingly recognised as an important cause of acute febrile illness and a growing public health concern in many parts of the world, particularly in the Asia–Pacific region. Several studies have reported that scrub typhus contributes significantly to morbidity and mortality due to delayed diagnosis and limited awareness among clinicians (Watt & Parola, 2003). In India, the disease has re-emerged over the past two decades, with reports from multiple states indicating a rising number of cases, especially during monsoon and post-monsoon seasons (Varghese et al., 2015).

The transmission of scrub typhus is closely linked to the ecology of chigger mites, which act as vectors and reservoirs of *Orientia tsutsugamushi*. Research has shown that chiggers thrive in areas with dense vegetation, scrublands, and agricultural fields, increasing infection risk among farmers and outdoor workers (Kelly et al., 2009). Environmental changes such as deforestation, land-use modification, and expansion of agriculture have further intensified human exposure to infected mites (Paris et al., 2013).

Clinically, scrub typhus presents with a wide spectrum of manifestations, ranging from mild febrile illness to severe multi-organ dysfunction. Indian hospital-based studies have documented fever, headache, myalgia, and thrombocytopenia as common features, while severe complications such as acute respiratory distress syndrome, meningoencephalitis, acute kidney injury, and myocarditis have also been frequently reported (Chrispal et al., 2010). International literature similarly highlights the variability of clinical presentation and emphasises that the classical eschar is not universally present, contributing to diagnostic uncertainty (Taylor et al., 2015).

Diagnosis of scrub typhus remains challenging due to its non-specific symptoms and overlap with other endemic febrile illnesses such as dengue, malaria, leptospirosis, and typhoid fever. Studies from India indicate that limited access to reliable laboratory diagnostics, particularly in rural settings, often results in delayed or missed diagnosis (Rapsang & Bhattacharyya, 2013). Globally, although immunofluorescence assay is considered the reference standard, its limited availability has led to reliance on serological tests and clinical judgment (Blacksell et al., 2007).

Early initiation of appropriate antibiotic therapy has been consistently shown to significantly reduce complications and mortality. Both national and international studies confirm doxycycline as the first-line treatment, with azithromycin as an effective alternative, especially in children and pregnant women (Kim et al., 2011). Delayed treatment has been associated with prolonged hospital stay and increased fatal outcomes (Varghese et al., 2015).

Preventive strategies discussed in the literature emphasise vector control, use of personal protective measures, and community awareness. Indian public health studies stress the importance of educating at-risk populations about avoiding mite-infested areas and adopting protective clothing during agricultural activities (Kamarasu et al., 2017). International research further advocates integrated surveillance systems and early warning mechanisms to monitor disease trends and reduce the overall burden of scrub typhus (WHO, 2023).

3. Early Recognition of Clinical Manifestations:

Scrub typhus usually presents as an acute febrile illness with non-specific symptoms, making early clinical recognition challenging. The initial manifestations commonly include sudden onset of high fever, severe headache, myalgia, fatigue, and malaise, which closely resemble other endemic febrile illnesses such as dengue, malaria, and enteric fever (Watt & Parola, 2003; Rapsang & Bhattacharyya, 2013). Due to this clinical overlap, scrub typhus is frequently underdiagnosed, particularly in resource-limited and rural settings.
Careful and thorough physical examination is crucial for early detection. The presence of an eschar—a painless, necrotic, black scab at the site of the chigger bite—is considered a characteristic clinical marker and can strongly support the diagnosis (Kelly et al., 2009). However, the eschar is not universally present and may be absent in a significant proportion of patients or overlooked due to its location in hidden areas such as the groin, axilla, or scalp (Chrispal et al., 2010). Studies have also reported variability in eschar prevalence across different populations and geographic regions, further limiting its reliability as a sole diagnostic indicator (Taylor et al., 2015).
Given these challenges, early recognition of scrub typhus relies on a combination of clinical suspicion, epidemiological history, and careful physical examination rather than a single pathognomonic sign. Prompt identification of early symptoms is essential for timely initiation of antibiotic therapy, which significantly reduces the risk of severe complications and mortality.

4. Timely Clinical Suspicion.

In endemic regions, scrub typhus should be strongly considered in patients presenting with acute febrile illness that fails to respond to routine empirical treatment. Because the early symptoms are non-specific and overlap with other common tropical infections such as dengue, malaria, leptospirosis, and typhoid fever, delayed clinical suspicion is a major contributor to disease progression and increased morbidity (Watt & Parola, 2003; Rapsang & Bhattacharyya, 2013). A high index of suspicion is particularly important during the monsoon and post-monsoon seasons, when vector activity and transmission are heightened.

Several studies from India and other endemic countries emphasize that early clinical suspicion, even in the absence of confirmatory laboratory results, is crucial for initiating timely antibiotic therapy (Varghese et al., 2015). Failure to suspect scrub typhus at an early stage often leads to delays in diagnosis, allowing the infection to progress to severe complications such as acute respiratory distress syndrome, meningoencephalitis, renal failure, and multi-organ dysfunction (Taylor et al., 2015).

Clinical awareness of epidemiological risk factors—such as residence in rural areas, agricultural occupation, and exposure to scrub vegetation—plays a key role in raising suspicion of scrub typhus. Early recognition based on clinical judgment and epidemiological context significantly reduces complications, length of hospital stay, and mortality. Therefore, timely clinical suspicion remains a cornerstone in the effective management and control of scrub typhus in endemic settings.

5. Accurate Diagnosis.

Accurate diagnosis of scrub typhus relies on a combination of clinical assessment and laboratory investigations. In endemic areas, the diagnosis is often initiated based on clinical features such as acute febrile illness, history of environmental exposure, and the presence of an eschar, when identifiable. These clinical indicators are particularly important in the early stages of the disease, as laboratory confirmation may not be immediately available (Watt & Parola, 2003).

Laboratory diagnostic methods include serological tests such as enzyme-linked immunosorbent assay (ELISA) and indirect immunofluorescence assay (IFA), the latter being considered the reference standard. Molecular

techniques like polymerase chain reaction (PCR) offer high specificity in early infection but are often limited to well-equipped laboratories (Blacksell et al., 2007; Kelly et al., 2009). In many rural and resource-limited settings, access to such diagnostic facilities is restricted, leading to underdiagnosis or delayed confirmation.

Given these limitations, symptom-based clinical judgment remains critical, particularly in peripheral healthcare centres. Several studies emphasise that empirical diagnosis based on clinical suspicion and epidemiological context can significantly improve patient outcomes by allowing early initiation of appropriate antibiotic therapy (Varghese et al., 2015). Therefore, strengthening clinical diagnostic capacity alongside expanding laboratory infrastructure is essential for effective management of scrub typhus.

6. Prompt Initiation of Treatment:

Early initiation of appropriate antibiotic therapy is the cornerstone of effective scrub typhus management. Once the disease is clinically suspected, treatment should not be delayed while awaiting laboratory confirmation, as early administration of antibiotics significantly improves patient outcomes (Watt & Parola, 2003). Doxycycline remains the first-line drug of choice for scrub typhus, while azithromycin is widely recommended as an effective alternative, particularly for children, pregnant women, and patients who cannot tolerate doxycycline (Kim et al., 2011).

Several clinical studies have demonstrated that prompt treatment results in rapid defervescence and clinical improvement within 48–72 hours, thereby reducing the duration of illness and hospitalisation (Varghese et al., 2015). In contrast, delayed initiation of antibiotic therapy is strongly associated with disease progression, leading to severe complications such as acute respiratory distress syndrome, meningoencephalitis, renal failure, and multi-organ dysfunction (Taylor et al., 2015).

Empirical antibiotic therapy based on early clinical suspicion has been shown to substantially reduce morbidity and mortality, especially in endemic and resource-limited settings where diagnostic facilities are limited (Rapsang & Bhattacharyya, 2013). Therefore, prompt initiation of appropriate antibiotics is critical for preventing serious organ involvement and reducing fatal outcomes associated with scrub typhus.

7. Prevention and Risk Reduction

Prevention of scrub typhus primarily focuses on reducing human contact with infected chiggers and minimizing exposure to mite-infested environments. Avoidance of dense scrub vegetation, especially during peak transmission seasons, is an effective preventive approach in endemic areas. The use of insect repellents containing approved active ingredients on exposed skin and clothing has been shown to reduce the risk of chigger bites (Kelly et al., 2009). Wearing protective clothing such as long-sleeved shirts, long pants, and closed footwear further limits skin exposure during agricultural and outdoor activities. In addition, maintaining clean surroundings, clearing overgrown vegetation, and controlling rodent populations around human dwellings help reduce vector habitats and lower transmission risk (WHO, 2023). These personal and environmental protective measures are particularly important for rural and occupationally exposed populations.

8. Public Health Awareness and Surveillance

Strengthening public health awareness and surveillance systems is essential for early detection and effective control of scrub typhus. Improved disease surveillance enables timely identification of outbreaks and helps in understanding regional disease patterns (Varghese et al., 2015). Educating healthcare providers to recognize early clinical features and epidemiological risk factors enhances timely diagnosis and treatment, thereby reducing

complications and mortality. Community awareness programs that inform populations about transmission routes, preventive practices, and the importance of early medical consultation have been shown to reduce under diagnosis and disease burden (Watt & Parola, 2003). Integrated surveillance, combined with health education and vector control strategies, plays a critical role in mitigating the rising public health impact of scrub typhus.

Conclusion

Scrub typhus has re-emerged as a significant vector-borne bacterial disease of public health importance, particularly in endemic regions with rural and agricultural populations. The expanding geographical distribution of *Orientia* species, coupled with ecological and environmental changes, has increased human exposure to infected chigger mites, thereby contributing to the rising disease burden. The clinical presentation of scrub typhus is often non-specific, closely resembling other acute febrile illnesses, which frequently leads to delayed diagnosis and inappropriate management.

Early clinical suspicion, careful physical examination for characteristic signs such as eschar, and symptom-based clinical judgment remain crucial, especially in resource-limited settings where advanced diagnostic facilities are not readily available. Although laboratory investigations aid confirmation, prompt initiation of appropriate antibiotic therapy should not be delayed once scrub typhus is suspected. Early treatment with doxycycline or azithromycin has consistently been shown to result in rapid recovery and to prevent progression to severe complications, including multi-organ failure and death.

Preventive measures focusing on reducing exposure to mite-infested environments, adopting personal protective practices, and improving environmental sanitation play an essential role in minimizing transmission risk. Furthermore, strengthening public health awareness and disease surveillance systems is vital for early case detection, outbreak control, and reduction of under diagnosis. Educating healthcare providers and communities enhances timely recognition and appropriate response to the disease.

In the absence of an effective vaccine and given the limited duration of natural immunity, integrated approaches combining early diagnosis, effective treatment, preventive strategies, and robust surveillance are essential. Continued research, improved healthcare infrastructure, and sustained public health efforts are necessary to reduce the morbidity and mortality associated with scrub typhus and to control its growing impact on global health.

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