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Scrub typhus: A One Health perspective on an emerging vector-borne disease

Gudikandula Krishna and Nallabelly Srinivas

Virus Research and Diagnostic Laboratory, Department of Microbiology, Kakatiya Medical College, Warangal, Telangana, India

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Abstract

Orientia tsutsugamushi is the source of scrub typhus, a new and underappreciated vector-borne zoonotic disease spread by the larval stage of trombiculid mites (chiggers). Despite being historically limited to the "*Tsutsugamushi* Triangle," growing reports from South America, Africa, and the Middle East suggest a wider geographic distribution. This review highlights the interdependent functions of humans, animals, vectors and the environment in the emergence, transmission, prevention, and control of scrub typhus and provides a comprehensive view from a One Health perspective. A comprehensive review of the existing literature was performed, utilizing peer-reviewed publications, systematic reviews, epidemiological reports, and global public health guidelines. Evidence was synthesized across epidemiology, etiology, clinical symptoms, laboratory diagnosis, treatment, environmental variables, and One Health surveillance systems. Scrub typhus is a re-emerging disease driven by climate and environmental changes. Despite advances in diagnostics and predictive tools, disease control remains limited by non-specific symptoms, poor diagnostics, underreporting, and the lack of an effective vaccine. An interdisciplinary One Health approach integrating human, veterinary, and environmental health is essential for efficient surveillance, timely diagnosis, epidemic preparedness, and sustainable disease management. Strengthening integrated surveillance systems, developing rapid point-of-care diagnostics, accelerating vaccine research, and promoting collaborative research and policy efforts will be essential to mitigate the global burden of scrub typhus and improving preparedness for this re-emerging neglected tropical disease.

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Introduction

Scrub typhus is an acute zoonotic disease that can be fatal and is caused by the obligate intracellular bacterium Orientia *tsutsugamushi*, which is transmitted to humans by the bite of infected larval trombiculid mites, commonly called chiggers. The disease, traditionally confined to the "*Tsutsugamushi Triangle*" in the Asia-Pacific region, has recently been reported beyond its traditional boundaries, including in the Middle East, Africa, and South America (Figure 1). The expanding geographic range underscores the increasing global importance of scrub typhus as an emerging vector-borne disease (1, 2).

***Corresponding author:** *krishnagudikandula@gmail.com*
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Fig. 1. Global distribution of the scrub typhus–endemic "*Tsutsugamushi* Triangle," highlighting the regions where the disease is predominantly prevalent.

Scrub typhus is a clinically acute febrile illness characterized by fever, headache, myalgia, rash, and lymphadenopathy. Although the characteristic eschar at the site of the chigger bite is highly suggestive of the condition, it is absent in some cases. Untreated scrub typhus may lead to devastating complications including acute respiratory distress syndrome, myocarditis, meningoencephalitis, acute renal injury, hepatic dysfunction, and multiorgan failure, culminating in significant morbidity and mortality. The disease poses a major public health threat, particularly in endemic areas with limited diagnostic capacity and weak surveillance systems. Environmental changes, climatic fluctuations, urban development, and increased contact between humans and vector habitats favour the reappearance and spread. Improvements in serological and molecular diagnostic techniques, as well as prompt use of doxycycline or azithromycin, have resulted in better clinical outcomes. But the absence of an effective vaccine, and the complicated ecology of mites, rodents, and environmental factors highlight the need for wide-ranging management programmes.

Due to its resurgence and escalating impact, scrub typhus has been recognized as a neglected tropical disease that requires a multidisciplinary strategy. Implementing a One Health framework that encompasses human, animal, and environmental health is crucial for enhancing surveillance, comprehending disease ecology, and formulating efficient prevention and control strategies.

Review scope, search strategy, and objectives

This review highlights the major scientific issues concerning the transmission dynamics of Orientia tsutsugamushi, diagnostic and clinical challenges in resource-limited settings, and the application of One Health approaches to the prevention and control of vector-borne zoonoses. A systematic literature search was performed in major electronic databases including PubMed, Scopus, and Web of Science from inception to May 2026. The search was limited to original peer-reviewed research, systematic reviews, and epidemiological studies on O. tsutsugamushi ecology, human and veterinary epidemiology, diagnostic advances, and integrated One Health control strategies. Studies were eligible if they provided empirical data, methodological insights,

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or clinical evaluations related to the transmission and management of scrub typhus. We excluded non-peer-reviewed editorials, opinion pieces, articles not in English, and research articles that had no apparent methodological connection to scrub typhus ecology or diagnosis.

Rationale for a One Health approach

The WHO reports that 60% of recognized infectious diseases and around 75% of emerging infectious diseases (EIDs) are zoonotic (3). The WHO South-East Asian (SEA) region consists of 11 member states and is home to almost a quarter of the world's population. The region is recognized as a hotspot for various emerging and re-emerging zoonotic diseases, including Nipah virus, arboviral infections, Ebola, zoonotic influenza, plague, and the current COVID-19 pandemic (4). The region is particularly vulnerable to new and re-emerging zoonotic diseases owing to factors including population growth, high population density, rapid urbanization, and migration. These elements collectively create settings conducive to the spread of illness (5, 6). The region's dependence on tourism and robust connectivity heightens transmission concerns both within the region and to other areas of Asia and the world. Environmental stress resulting from deforestation, driven by the rapid increase in palm oil production and agricultural development, intensifies human-animal interactions, thereby promoting zoonotic infections. Climate change and altered weather patterns are increasing vector populations and pathogen development, thereby facilitating the transmission of vector-borne diseases. Besides, such variables are influenced by political, cultural and social diversities (7). Also, the increasing consumption and trade in wildlife raise risks and make it harder to control and monitor these diseases, underscoring the urgent need for proactive public health measures. Floods and droughts, driven by climate change and pollution, have played a major role in the proliferation of infectious diseases and pandemics. The risks of zoonotic transmission are increased by pollution-induced desertification, which increases reliance on bushmeat and worsens sanitary conditions in relief camps, underscoring the vital connection between environmental degradation and public health emergencies. Ongoing disease outbreaks and pandemics have exposed deficiencies and highlighted the intricate epidemiological relationships among humans, animals, plants, and the environment, underscoring the necessity for a collaborative global framework that provides integrated solutions through a systemic approach known as “One Health” (OH). This is a cohesive method designed to deliver a thorough evaluation of health concerns, thereby enabling the formulation of suitable preventive and management strategies, as well as inclusive, evidence-based policies to cultivate sustainable health systems and ecosystems (8). To alleviate the constraints posed by the conventional approach to zoonoses, which predominantly treats human and animal health in isolation, the One Health approach underscores the importance of addressing interactions at the human-animal-environment interface.

This review aims to provide a thorough and up-to-date synthesis of existing knowledge on scrub typhus, an emerging neglected vector-borne illness, from a One Health perspective. The review aims to summarize the epidemiology, global burden, and expanding geographic range of scrub typhus and to elucidate the intricate connections among the pathogen, vectors, animal reservoirs, people, and environmental factors that influence disease transmission. The review describes the pathophysiology, clinical features, diagnostic methods, and current treatment strategies for managing the disease. The impacts of climate change, land-use changes and human activities on the resurgence and propagation of scrub typhus are discussed in detail. The review emphasizes the need for integrated surveillance, prevention, and control approaches in a One Health context and for interdisciplinary collaboration among the human, veterinary, and environmental health sectors. It highlights the existing knowledge gaps and sets out future research objectives to aid the development of effective treatments and to enhance readiness for this emerging public health issue.

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Historical perspective

Scrub typhus (ST) is one of the earliest-described vector-borne diseases, with ancient Chinese medical writings describing a scrub typhus-like disease dating back to 313 AD. The Chinese physician Hong Ge described a febrile illness with fever and rash in the medical text Zhouhoufang; subsequent physicians, including Yuan-Fang Chao (610 AD) and Shi-Zhen Li (1596 AD), added further descriptions and recognized the link between the disease and mite bites (9). Initially, it was called "tsutsuga" sickness in Japan, and the first complete description was given by Hakuju Hashimoto in 1810 (Figure 2). Subsequent studies by Japanese investigators in the late nineteenth and early twentieth centuries established the disease as a distinct clinical entity and led to the identification of the causal agent, now called *Orientia tsutsugamushi* (10).

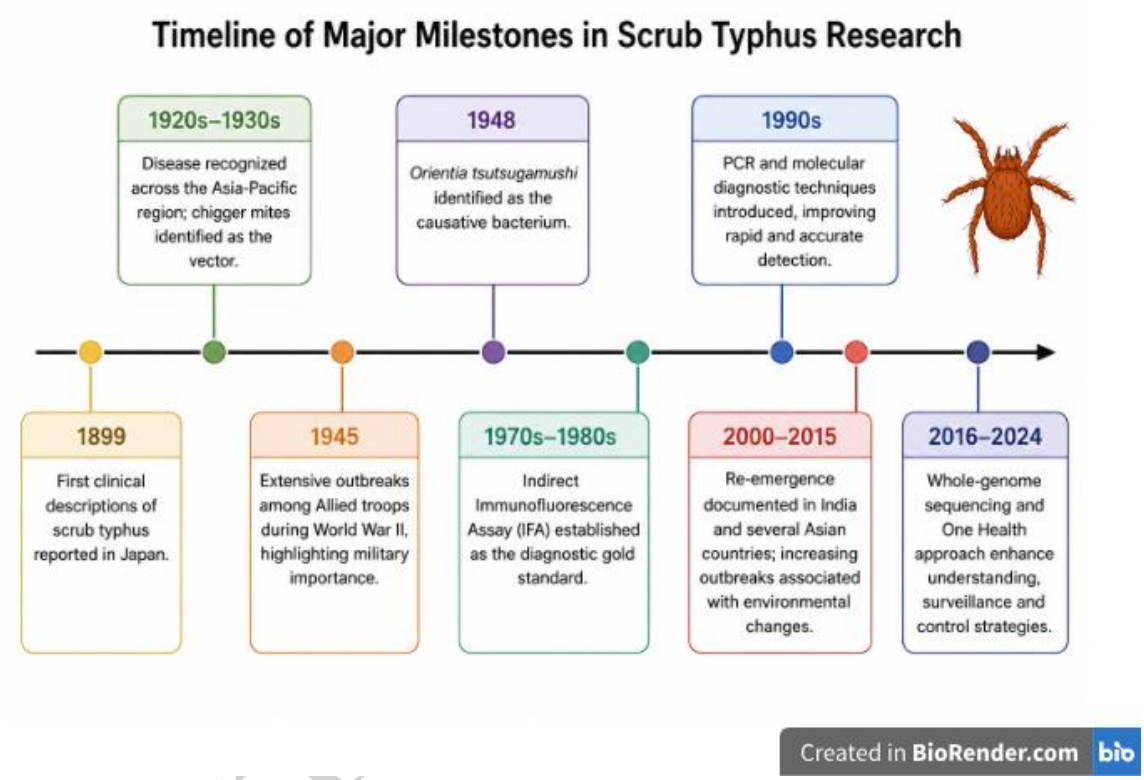


Fig. 2. Timeline highlighting the major milestones in scrub typhus research, including key advances in disease recognition, pathogen identification, diagnostic methods, and genomic surveillance.

In the early twentieth century, infections similar to scrub typhus were increasingly being identified in many countries in the Asia-Pacific region. "Pseudotyphoid fever" was described by Schüffner in 1909 in Sumatra, Indonesia, and subsequent cases have been reported in Taiwan and the Philippines. Other diseases, which were described as "Mossman fever" or "endemic glandular fever" were later identified as manifestations of scrub typhus, and were recorded in North Queensland. In Vietnam, "pseudo-typhus" was described in Saigon in 1915 and in Korea there was a report of an ongoing fever disease during the same period (11). The disease was identified as "tropical typhus" in Malaysia in the 1920s and Fletcher and others undertook research into its origin and epidemiology (12).

Typhus-like infections were reported in the Himalayan regions of India in the 1930s, and endemic transmission was documented in the Simla Hills and the United Provinces (13). Similar observations were made in Burma

and Sri Lanka. Scrub typhus was a major cause of morbidity and mortality among Allied troops in the Asia-Pacific region during World War II, bringing the disease to the forefront. The epidemics stimulated extensive research into the ecology, diagnosis, and prevention of the disease, enabling the early development of vaccines and serological assays.

The "*Tsutsugamushi* Triangle" hypothesis was based on the geographical distribution of recorded cases and extended from northern Japan and eastern Russia to northern Australia, then westward to Pakistan and Afghanistan. For a long time, scrub typhus was believed to be confined to this region. But the evidence gathered in the second half of the twentieth and the early twenty-first centuries put this conception in question. In 1951 Giroud and Jadin reported serological evidence suggestive of scrub typhus in East Africa, but their results were not widely accepted. Additional case reports from the Republic of Congo, Cameroon and Tanzania indicated that the disease occurred beyond its known limits (14).

The global importance of scrub typhus was emphasized by the confirmation of a case in the United Arab Emirates in 2010, which led to the identification of a new species, Candidatus Orientia chuto. Later, indigenous cases were reported in Chile and a new species, Candidatus Orientia chiloensis, was identified by molecular means (15). Further serologic and genetic information from Kenya, Djibouti, Peru, and elsewhere has demonstrated that scrub typhus is present in a significantly larger region than was previously appreciated.

Current global burden of scrub typhus

Scrub typhus is a major but underappreciated cause of acute febrile illness in the tropics and subtropics. Contemporary global estimates suggest that about 3.5 million new infections (95% CI: 2.5–5.1 million) occur annually in 33 countries with established endemic transmission, of which about 1.0 million are symptomatic and almost 0.79 million progress to clinically apparent disease requiring medical attention (16). The disease is associated with significant mortality, with some 44,000 fatalities occurring each year. The burden is heavily concentrated in South and Southeast Asia and the western Pacific region. India accounts for about one-third of global clinical cases and nearly half of projected deaths. Other high-burden countries are South Korea, Pakistan, China, Bangladesh, Indonesia, Malaysia, Japan and Vietnam. Seroprevalence studies show considerable geographical variability, with an estimated overall seroprevalence of 17.6% (95% CI: 10.4–31.3%) in endemic countries (17-19). However, despite these alarming statistics, scrub typhus remains vastly underdiagnosed and underreported due to a lack of surveillance systems, poor diagnostic capacity, and non-specific clinical presentation. Hence, the true burden of the disease is likely to be underestimated, underlining the importance of improved surveillance, better diagnostics and official recognition of scrub typhus as a neglected tropical disease.

Etiology and genetic diversity

Scrub typhus is a substantial contributor to the underdiagnosis of acute febrile illness and is widespread in endemic areas. This condition can affect several organ systems, primarily through vasculitis and perivascular inflammation (20). Mite larvae, or chiggers, which harbor harmful gram-negative bacteria, serve as vectors for humans, transmitting the organisms via their bites. The pathogen persists in nature through transovarial transmission in the vectors and, in some cases, in small mammals that act as reservoirs. Due to numerous intragenomic deletions and duplications, the Orientia genome has an exceptionally high level of repetition. This repetitive character is further shaped by rearrangements involving conjugative and transposable elements within the genome. The 56-kDa type-specific antigen is a distinct outer membrane protein among the structural proteins of *O. tsutsugamushi*. Serological characterization of this outer membrane protein, which exhibits variable regions, has identified several new subtypes across different geographic regions. This demonstrates

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Orientia tsutsugamushi's remarkable genetic flexibility compared with previously recognized prototype strains such as Karp, Kato, and Gilliam.

Neutralizing antibodies can be produced during infection by the 56-kDa type-specific antigen, also referred to as the primary immunogen (21, 22). The development of an effective vaccine has been hampered by the diverse strains of *O. tsutsugamushi* found across endemic regions.

Transmission ecology and reservoir hosts

The larvae (or chiggers) of the trombiculid mites are the main carriers of scrub typhus. They are members of the genus Leptotrombidium spp. In the Asia-Pacific area, *O. tsutsugamushi* is spread by these arthropods (23-27). The lifecycle of a trombiculid mite consists of four major developmental stages: egg, larva, nymph, and adult, with three quiescent stages (Figure 3). The larvae, which range in length from 0.2 to 0.4 mm, are only visible under a microscope or magnifying glass. Additionally, *Apodemus agrarius, Suncus murinus,* and wild rats (R. flavipectus, R. losea, R. confucianus, and R. norvegicus) are the usual food sources for these young mites (28-32). Even though humans are the larvae's accidental hosts, rodent density and climate change may affect the rate of human transmission. The third-stage larvae of O. *tsutsugamushi* infect mammals by feeding on the extracellular fluid of vertebrates (32-34). The main reservoir for *O. tsutsugamushi* is mites. Transovarial transmission is the technique by which later-stage adult mites transfer the ST-causing bacteria to their eggs. *O. tsutsugamushi* is sustained in the vector from one life stage to the next through this method (35). The environment in which host animals reside may significantly affect the occurrence of chigger mites. More specifically, earlier research has shown that temperature has a significant impact on Leptotrombidium mite development and reproduction (especially L. deliense) (36).

The initiation of ST has been associated with environmental factors. Temperature is posited to influence the prevalence of ST. Specifically, elevated temperatures result in heightened outdoor activity levels, which may increase individuals' exposure to chigger bites and the risk of infection. Moreover, invasive plant species such as Leucaena leucocephala, which serve as favored habitats for Leptotrombidium mites, may lead to excessive proliferation of O. *tsutsugamushi*. Finally, socioeconomic transformations that alter land cover, coupled with climate variability, may also lead to the unforeseen emergence of ST in humans.

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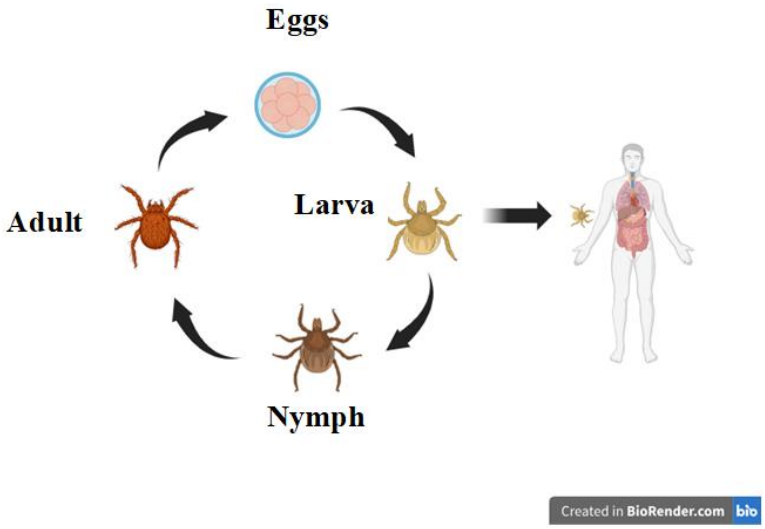


Fig. 3. Life cycle of the mite.

Pathophysiology

The pathogenesis of *O. tsutsugamushi* includes vasculitis resulting from infection of endothelial cells, leading to perivascular infiltration of T cells and monocytes/macrophages. Consequently, a diverse array of inflammatory responses occurs, with both endothelial and non-endothelial cells synthesizing multiple cytokines (37-39). These cytokines can have both advantageous effects, including antibacterial activity, and harmful effects, resulting in tissue damage in the infected host. The dual nature of this immune response can result in serious consequences, including hepatitis, renal failure, meningoencephalitis, and respiratory failure, such as acute respiratory distress syndrome (ARDS) and, on occasion, myocarditis (40-43).

Clinical presentation and management

The incubation period for *Orientia tsutsugamushi* infection is usually 10 to 12 days, with a range of 6 to 21 days. Clinical presentations vary widely, ranging from a mild self-limiting febrile illness to a severe disease with multi-organ dysfunction syndrome (MODS) (44-47). Common symptoms are fever, headache, myalgia, malaise, cough, and gastrointestinal complaints. A maculopapular rash generally appears towards the end of the first week of illness and often starts on the trunk and spreads to the limbs. There is usually regional lymphadenopathy (48, 49).

An eschar at the site of a chigger bite is a characteristic and strong sign of scrub typhus, with an incidence reported to be 7% to 80%. Skin pigmentation, strain-specific changes in eschar development, and lesion location may influence eschar detection (50-52). The eschar is usually a papule that develops into a necrotic black crust and is often found in the groin, axilla, waist and other exposed areas. Differences in the distribution of eschar have been observed between the sexes, probably related to differences in clothing, anatomic folds, and exposure (53, 54).

If left untreated, systemic involvement may occur in the second week of the disease. Complications may involve various organ systems such as the central nervous system (meningitis, encephalopathy, cranial nerve palsies), cardiovascular system (myocarditis, arrhythmias, vasculitis), respiratory system (interstitial

pneumonia, acute respiratory distress syndrome), renal system (acute kidney injury) and gastrointestinal-hepatic system (hepatitis, pancreatitis, diarrhea). Severe cases can progress to Multiple Organ Dysfunction Syndrome (MODS) and have a major impact on morbidity and mortality. The broad spectrum of clinical presentation often causes delay in diagnosis and treatment (55, 56).

Diagnostic modalities

The diagnosis of scrub typhus has evolved from conventional serological methods to the combination of serological and genetic methods. The Weil–Felix O1–K agglutination test, once common, has largely been replaced by the indirect immunofluorescence assay (IFA), which has been the diagnostic gold standard for many decades. A fourfold or greater rise in IgM or IgG antibody titres between acute and convalescent serum samples is confirmatory and increases diagnostic reliability (57-59). Enzyme-linked immunosorbent assays (ELISAs) with whole-cell or recombinant *Orientia tsutsugamushi* antigens have improved diagnostic accuracy and are more amenable to higher throughput than immunofluorescence assays (IFAs). Rapid diagnostic tests (RDTs) that detect anti-Orientia IgM and IgG antibodies are increasingly used, but baseline antibody levels in endemic communities may lead to false-positive results in acute infections (60-63).

The advent of molecular diagnostics such as polymerase chain reaction (PCR) has greatly improved the early diagnosis of scrub typhus by detection of bacterial DNA before seroconversion. Typical PCR targets include the 56-kDa, 47-kDa, 16S rRNA and groEL genes. Bacteremia may persist for up to 10 days after the onset of fever, but antibodies usually form after 7–10 days. Therefore, the best diagnostic results are achieved by combining PCR with serological tests (64-66). Eschar swabs and crust specimens are relevant non-invasive samples with high bacterial loads, enabling accurate molecular diagnosis even after treatment initiation (Figure 4).

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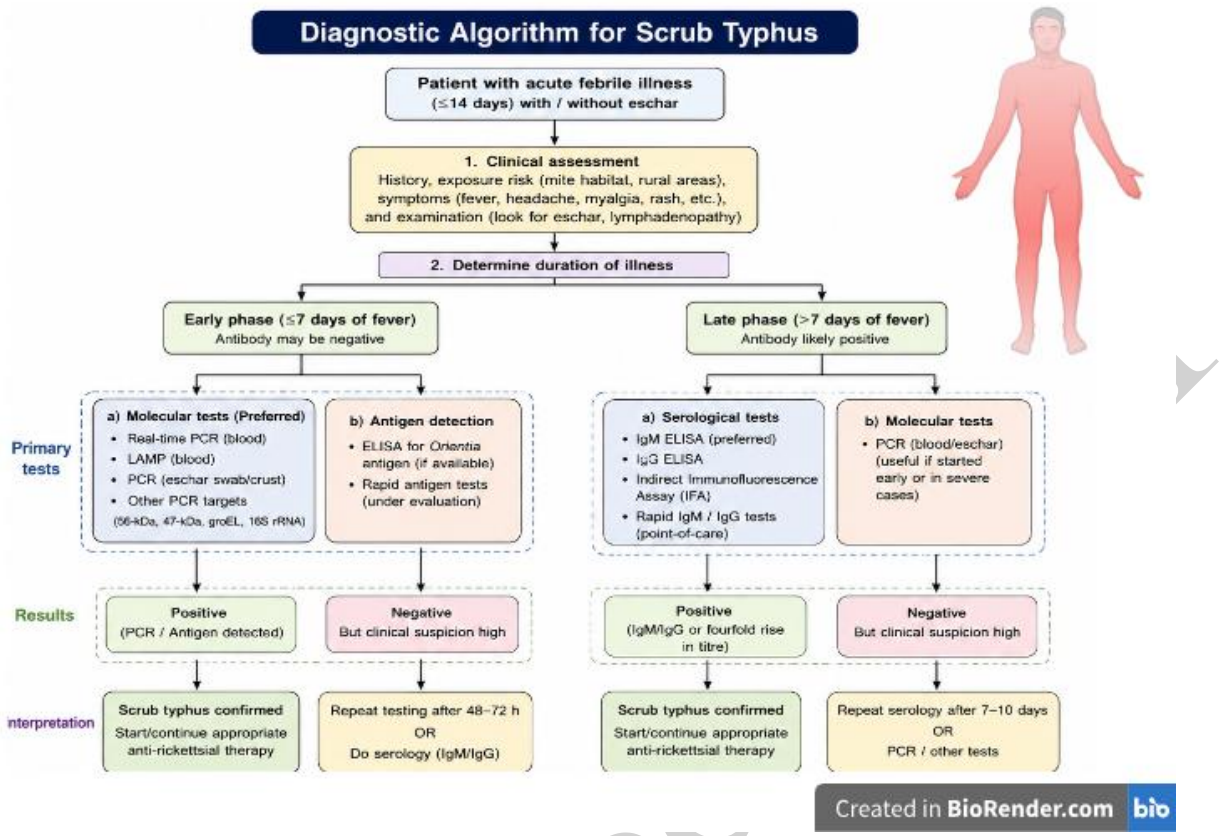


Fig. 4. Diagnostic algorithm of *scrub typhus.*

New molecular techniques such as the loop-mediated isothermal amplification (LAMP) assay enable rapid, sensitive, field-compatible detection without requiring sophisticated laboratory equipment. In addition, multilocus sequence typing (MLST) has been used to study the genetic diversity and evolutionary relationships of *O. tsutsugamushi* strains, but it is still limited. The development of molecular and serological diagnostics has improved early case identification and timely treatment, and reduced morbidity and mortality from scrub typhus (67).

A novel field-applicable rapid molecular technique for identifying pathogenic infections has been developed, utilizing the clustered regularly interspaced short palindromic repeats (CRISPR) and CRISPR-associated (Cas) proteins of the bacterial immune system (68). The CRISPR-Cas system employs an RNA-guided endonuclease to confer sequence-specific protection against an invading nucleic acid sequence, such as that from a plasmid or virus. The RNA used by the RNA-guided endonuclease is referred to as guide RNA (gRNA) or CRISPR RNA (crRNA) and is derived from the invading nucleic acid sequence. The previously published diagnostic approach included a Cas12a protein with a gRNA complementary to the target DNA sequence, together with a T-nucleotide-rich protospacer-adjacent motif (PAM). The binding of Cas12a to target DNA activates its trans-cleavage activity, enabling it to cleave adjacent single-stranded DNA. Jennifer Doudna and her team developed a molecular diagnostic method known as DNA Endonuclease-Targeted CRISPR Trans Reporter (DETECTR), using Cas12a and isothermal amplification. Multiple pathogens, such as human papillomavirus (HPV), severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), severe fever with thrombocytopenia syndrome virus (SFTSV), and human immunodeficiency virus (HIV), were identified using the DETECTR platform, and Cas12a-based pathogen diagnostics are presently employed in clinical settings (17, 69).

However, applying CRISPR-Cas12a platforms for *Orientia tsutsugamushi* diagnosis in low-resource settings faces challenges. High sequence diversity in target genes (such as 56-kDa) can impair guide RNA binding. Furthermore, cold-chain reliance for reagents and high costs present key operational barriers for routine field implementation in endemic regions.

Treatment/management

Tetracycline, azithromycin, doxycycline, and rifampicin are all efficacious antimicrobials for the treatment of scrub typhus. Research has investigated multiple dosing protocols for doxycycline and azithromycin, encompassing an initial loading dose followed by maintenance doses. The typical treatment duration for doxycycline is 7 days, while for azithromycin it is 3 days. Tetracycline and rifampicin are recognized as effective therapies for scrub typhus (70, 71).

The administration of prophylactic medication at a weekly dosage of 200 mg of doxycycline is contentious, predominantly advised for those with significant occupational hazards, such as agricultural workers (72). However, despite the interventions, some patients may develop life-threatening complications such as MODS that require a multidisciplinary management strategy involving ICU care. A new multicentric randomized controlled trial has demonstrated the efficacy of a 7-day intravenous combination therapy with doxycycline and azithromycin in severe scrub typhus. Patients in the intensive care unit (ICU) often require intensive supportive interventions such as IV fluids, but patients with ARDS may require mechanical ventilation. Prompt symptomatic therapy and appropriate antibiotic therapy can significantly improve the patient's recovery without permanent end-organ damage (18).

One Health perspective of scrub typhus

Human health component

Scrub typhus is an important cause of acute febrile illness in endemic areas and contributes significantly to morbidity and mortality. Diagnosis is difficult due to non-specific clinical manifestations and limited access to reliable diagnostic facilities in resource-limited settings. Improvement of surveillance systems is a must for early detection, outbreak surveillance and disease control (60).

Animal health component

The principal reservoir hosts of *Orientia tsutsugamushi* are rodents that maintain the bacteria in the environment. Other small mammals and domestic animals may act as facilitators of pathogen circulation and markers of disease activity in endemic areas (64).

Environmental Health Component

Temperature changes, land-use changes, urbanization, and ecological disturbances are among the environmental factors that influence the dispersal of chigger mites and their reservoir hosts. These changes could impact transmission and the likelihood of human infection (73).

Human–animal–environment interface

Scrub typhus is an example of the interconnection of human, animal and environmental health. Human activities, such as agriculture, forestry, and outdoor occupations, increase exposure to infected vectors and reservoir hosts. Optimal surveillance, prevention, and control of the disease will require a One Health approach that integrates the medical, veterinary, and environmental sectors (74, 75; Figure 5).

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Fig. 5. One Health framework illustrating the interconnections among human, animal, and environmental health and the key factors influencing disease emergence and public health.

Impact of climate change on scrub typhus emergence

Climate and other environmental changes may lead to unexpected events and rising incidence trends, as they affect the survival, development, reproduction, behaviour, and population dynamics of vectors and hosts. Changes in climate and environment can assist the spread and growth of both, therefore increasing the global threat of vector-borne diseases (76). The scale of human activities is changing due to rapid urbanization and deforestation, which alter the balance between natural and social environments and influence the distribution of chiggers and the probability of human contact with infected chiggers. Chiggers serve as reservoirs and important vectors of scrub typhus. They are resilient and have a wide range of habitats. This suggests that the bacterium's natural cycles have been effectively preserved over millennia and across a wide geographic range. However, little is known about which environmental factors are important in this process and how they influence the occurrence of human cases (77).

Prevention and control strategies

Minimizing exposure to infected chigger mites, early diagnosis, and treatment are the main strategies for the prevention and control of scrub typhus. Personal preventive measures include wearing long-sleeved clothing, using insect repellents, avoiding sitting or reclining on unprotected ground, and limiting exposure to vegetation infested with mites (78-80). Control of vectors and reservoirs through vegetation removal, improved sanitation, and rodent control can contribute to environmental management. Promoting preventive measures in endemic areas requires community awareness and health education. Without a vaccine that works for most people,

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surveillance, rapid case identification, and rapid antibiotic treatment are key to controlling the disease. Chemoprophylaxis with doxycycline has been effective in high-risk patients but is not generally recommended (81, 82).

Advanced technologies and future directions

Genomics and Proteomics

Whole-genome sequencing and proteomic analysis have contributed to advances in our understanding of the genetic diversity, antigenic variation, virulence mechanisms, and host-pathogen interactions of *Orientia tsutsugamushi*. These technologies allow the identification of new diagnostic biomarkers and vaccination targets (83).

Artificial intelligence in diagnosis

Scrub typhus diagnosis is being explored using artificial intelligence (AI) and machine learning algorithms to analyze clinical, laboratory, and epidemiological data. AI-assisted diagnostic methods can improve early detection, especially in resource-limited settings with restricted access to advanced laboratory testing (84).

Predictive modelling

Geospatial mapping, climate-based forecasting and predictive modelling are now essential tools for locating disease hotspots and predicting outbreaks. The combination of environmental, meteorological and epidemiological data can aid targeted monitoring and timely public health actions (18).

One Health surveillance frameworks

One Health surveillance systems integrating human, animal, vector and environmental data have improved understanding of scrub typhus transmission dynamics. These multidisciplinary frameworks enhance epidemic preparedness, risk assessment and disease management techniques (85).

Vaccine candidates

For several decades, *O. tsutsugamushi* has been studied, but the major antigenic variability among the strains has prevented the development of a licensed vaccine. Recent progress in recombinant protein, DNA, subunit, and multi-epitope vaccine approaches has shown promising preclinical results, offering hope for the development of broadly protective vaccines (86).

Challenges and research gaps

Scrub typhus is emerging as a major public health problem, but several hurdles remain. Diagnosis is difficult due to non-specific clinical features, variable prevalence of eschar, and limited availability of reliable diagnostic facilities in endemic areas. The antigenic diversity of *Orientia tsutsugamushi* is broad, and there is no cut-off value for diagnostic purposes, further reducing diagnostic accuracy (87). Underreporting, inadequate surveillance systems and insufficient knowledge of medical professionals also cause delays in diagnosis and treatment. Environmental changes, such as climate fluctuations, deforestation, and land-use changes, still affect disease transmission patterns and make control efforts more difficult (88, 89). Questions on pathogen diversity, vector ecology, host-pathogen interactions, and the role of environmental factors in disease emergence still need to be answered. The absence of a safe and broadly protective vaccine underscores the importance of continued research on vaccine development, improved point-of-care diagnostics, predictive modeling and integrated One Health surveillance frameworks.

Conclusion

Scrub typhus is a major but little-known zoonotic disease that is becoming more common in both endemic and previously non-endemic areas. Recent advances in molecular diagnostics, genomic surveillance, and understanding of host–vector–pathogen interactions have improved our knowledge of its epidemiology and pathogenesis. Effective disease control continues to be hampered by the lack of a licensed vaccine, late

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diagnosis, nonspecific clinical signs, poor surveillance, and concerns about antibiotic resistance. A One Health approach integrating the environmental, animal and human health sectors is required for sustainable prevention and control of scrub typhus. Enhanced interdisciplinary surveillance, vector and reservoir monitoring, environmental risk assessment and data exchange can facilitate early epidemic detection and targeted interventions.

Future efforts should focus on investment in coherent surveillance systems, rapid, affordable point-of-care diagnostics, vaccine research, monitoring of antimicrobial resistance and predictive models that encompass climate and ecological data. Policymakers should promote intersectoral collaboration, improvements in healthcare infrastructure in endemic areas, and the development of public awareness and capacity. Multidisciplinary research will be key to reducing the global impact of scrub typhus and improving preparedness for this re-emerging neglected tropical disease.

Ethical approval

This article is a review based exclusively on previously published studies and publicly available data. No human participants or animals were involved in this research. Therefore, ethical approval was not required.

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Conflict of interest statement

The authors declare no financial or personal conflicts of interest that could have influenced the work reported in this paper.

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