



TYPHUS GROUP RICKETTSIOSES: AN UPDATED NARRATIVE REVIEW OF EPIDEMIOLOGY, DISEASE MECHANISMS, CLINICAL SPECTRUM, LABORATORY DIAGNOSIS, MANAGEMENT, AND CONTROL

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DOI: <https://doi.org/10.5281/zenodo.23034025>

How to cite this Article: Dr. Rajeev Kumar Jha*. (2026). Typhus Group Rickettsioses: An Updated Narrative Review of Epidemiology, Disease Mechanisms, Clinical Spectrum, Laboratory Diagnosis, Management, And Control. European Journal of Biomedical and Pharmaceutical Sciences, 13(10), 93–101.

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Article Received on 02/09/2026

Article Revised on 23/09/2026

Article Published on 01/10/2026

ABSTRACT

The typhus illnesses are a set of acute fever-causing infections produced by obligate intracellular bacteria of the genera *Rickettsia* and *Orientia*. Three diseases dominate in humans: epidemic typhus (*Rickettsia prowazekii*), murine or flea-borne typhus (*Rickettsia typhi*), and scrub typhus (chiefly *Orientia tsutsugamushi*). They overlap clinically, sharing fever, headache, muscle pain, rash, and the potential for multisystem involvement, yet they differ markedly in vector, animal reservoir, geographic range, and epidemiological setting. Epidemic typhus follows body-lice infestation in crowded, impoverished, war-affected, or displaced populations. Murine typhus spreads through contamination of skin with infected flea feces and is tied to rodents and other animal hosts. Scrub typhus is passed on by larval trombiculid mites and is a leading cause of acute undifferentiated fever across the Asia-Pacific region, including the Indian subcontinent. Diagnosis is difficult because the early picture resembles malaria, dengue, leptospirosis, enteric fever, common viral infections, and other rickettsioses. Antibody tests may be negative early and may remain positive after past infection, whereas polymerase chain reaction (PCR) can confirm infection sooner when suitable samples are taken. Since late treatment raises the risk of serious complications, therapy is often started empirically when suspicion is high. Doxycycline is the cornerstone drug for all three diseases; azithromycin and a few other agents serve in specific situations. Control rests on vector management, personal protection, sanitation, prompt recognition, effective treatment, and public-health surveillance. Persisting gaps include under-diagnosis, restricted access to molecular testing, the antigenic variability of *Orientia*, sporadic reports of reduced drug responsiveness, and weak surveillance. This review consolidates present knowledge on the principal typhus diseases and outlines priorities for diagnostics, therapy, prevention, and research.

KEYWORDS: Typhus; epidemic typhus; murine typhus; flea-borne typhus; scrub typhus; *Rickettsia prowazekii*; *Rickettsia typhi*; *Orientia tsutsugamushi*; rickettsial disease; doxycycline.

1. INTRODUCTION

“Typhus” has long been used as an umbrella label for several fever syndromes caused by obligate intracellular bacteria. Today the term covers epidemic typhus (*R. prowazekii*), murine typhus (*R. typhi*), and scrub typhus (*O. tsutsugamushi*).^[1-3] Although they are related, these are separate infections with their own vectors, reservoirs, transmission routes, and epidemiology.

Epidemic typhus once ranked among the deadliest infections in human history. Its major outbreaks accompanied wars, famines, mass displacement, and

other conditions of overcrowding and poor sanitation, and it caused enormous losses in armies and refugee populations before antibiotics and modern public-health practice became available.^[1,4] It is now uncommon in many regions, but outbreaks remain possible wherever body-lice infestation and squalid living conditions coincide.

Murine typhus has a wider distribution. Its natural cycle is largely between rodents and fleas, although other mammals and flea species contribute. Because its symptoms (fever, headache, malaise, muscle ache,

digestive complaints, and rash) are nonspecific, it is frequently missed.^[5,6] Recent reports document ongoing transmission in tropical and subtropical regions and renewed activity in some urban and peri-urban areas.

Scrub typhus arises from *O. tsutsugamushi* delivered by larval trombiculid mites (“chiggers”). It is especially significant in South, Southeast, and East Asia, parts of Oceania, and the Indian subcontinent. It is now recognised as a major driver of acute undifferentiated fever in endemic zones and can progress to pneumonia, acute respiratory distress syndrome (ARDS), acute kidney injury, myocarditis, meningoencephalitis, shock, and multiorgan failure.^[7-10]

The burden of typhus stems from both its severity and the difficulty of identifying it early. Presentations mimic many other common febrile illnesses, and dependable laboratory confirmation is often unavailable where resources are limited, which makes early empirical therapy especially valuable. This article reviews the epidemiology, microbiology, pathogenesis, clinical features, diagnosis, treatment, prevention, and future research needs of the main typhus diseases.

2. AIMS OF THE REVIEW

This review aims to

1. Define the principal typhus diseases and their causative organisms.
2. Summarise their epidemiology, vectors, reservoirs, and transmission routes.
3. Examine disease mechanisms and clinical presentations.
4. Appraise available diagnostic tests and their shortcomings.
5. Outline current antimicrobial treatment.
6. Address complications, prognostic considerations, and special situations.
7. Discuss prevention, vector control, surveillance, and priorities for future research.

3. Literature Review Methodology

A narrative approach was adopted. Sources comprised peer-reviewed publications retrieved from PubMed/MEDLINE, public guidance from the Centers for Disease Control and Prevention (CDC), and review articles and systematic reviews on epidemic, murine, and scrub typhus. Search concepts combined terms such as typhus fever, epidemic typhus, *Rickettsia prowazekii*, murine typhus, *Rickettsia typhi*, flea-borne typhus, scrub typhus, *Orientia tsutsugamushi*, diagnosis, serology, PCR, doxycycline, azithromycin, complications, and epidemiology. Systematic reviews, clinical reviews, epidemiological studies, and authoritative clinical guidance were preferred. Recent progress in diagnosis and therapy was emphasised, and older historical works were retained only where they gave essential context.

4. Classification and Causative Agents

4.1 Epidemic typhus

R. prowazekii is a Gram-negative coccobacillus that lives only inside host cells and belongs to the typhus group of *Rickettsia*.^[1,2] Its main vector is the human body louse (*Pediculus humanus corporis*). Infection follows contamination of broken skin or mucous membranes with louse feces, and scratching bite sites helps the bacteria enter.

The organism chiefly targets vascular endothelial cells, and the resulting cell damage and inflammation produce a disseminated vasculitis. Disease can be severe, particularly if treatment is delayed.^[1,2] A zoonotic form linked to flying squirrels has also been described in North America, showing that *R. prowazekii* can persist outside the human-louse cycle.^[11]

4.2 Murine (flea-borne) typhus

Murine typhus, also termed endemic or flea-borne typhus, is caused by *R. typhi*. Rats (*Rattus* spp.) are the classic reservoir and the oriental rat flea (*Xenopsylla cheopis*) a key vector, although other fleas and mammals participate in different ecological settings.^[5,6]

People generally become infected when infected flea feces enter a bite wound or other skin lesion; the flea need not inject the bacteria while feeding. The disease predominates in tropical and subtropical regions but has been recorded in temperate ones. Newer studies describe urban and peri-urban cycles involving domestic and wild animals; in parts of the southern United States, for instance, opossums and cat fleas appear to contribute.^[6]

4.3 Scrub typhus

Scrub typhus is caused by *O. tsutsugamushi*, an obligate intracellular bacterium that is taxonomically distinct from the classical typhus-group rickettsiae and is carried by larval trombiculid mites.^[7,12] *Leptotrombidium* species are important vectors. Mites maintain the bacterium through their life cycle and pass it to humans when the larvae feed; humans are incidental hosts and not part of the essential natural cycle.

The organism shows extensive antigenic and genetic variability. Historically recognised prototype strains include Karp, Kato, and Gilliam, though genomic work reveals far greater diversity.^[8,12] This variability complicates both serological diagnosis and vaccine design.

5. EPIDEMIOLOGY

5.1 Global patterns

Distribution differs by pathogen and vector. Epidemic typhus occurs where crowding, limited bathing and laundering facilities, poverty, conflict, displacement, incarceration, homelessness, and humanitarian crises favour body lice.^[1,2] Improved sanitation has sharply reduced transmission in many countries, yet vulnerable groups still face these conditions.

Murine typhus is found worldwide, mainly in the tropics and subtropics, in settings that sustain rodent and flea populations. Urban growth, inadequate waste management, housing quality, and close animal contact raise risk.^[5,6]

Scrub typhus has long been linked to the Asia-Pacific region, with cases reported from India, Bangladesh, Pakistan, Nepal, Sri Lanka, Thailand, Myanmar, Laos, Vietnam, China, Taiwan, Japan, Korea, Malaysia, Indonesia, and northern Australia.^[7] Detection outside these traditional areas has prompted a reappraisal of its geographic limits. A systematic review concluded that scrub typhus is substantially under-recognised as a cause of fever in Asia^[14], and prospective fever studies frequently find it among the treatable non-malarial causes.

5.2 The situation in India

Scrub typhus is a significant problem in India, having been documented across many states and ecological zones in both rural and peri-urban communities.^[15] Hospital studies report large numbers of confirmed cases, but the real community burden is uncertain because diagnostic practice is inconsistent and surveillance incomplete. A systematic review of Indian data identified thousands of laboratory-confirmed cases with marked regional variation^[15], and further evidence indicates a considerable contribution to acute undifferentiated fever nationally.

Incidence is shaped by season, vegetation, farming activity, occupation, rainfall, temperature, and local mite ecology. Cases may rise during or after the monsoon in some areas, although seasonal patterns vary by region.

6. Transmission and Risk Factors

6.1 Epidemic typhus

The transmission chain is: human → infected body louse → louse feces → human. Lice acquire the bacterium by feeding on infected people; it multiplies in the louse gut and is shed in feces, and scratching then pushes it into small skin abrasions. Risk factors include heavy louse infestation, crowded housing, poor access to washing facilities, inadequate hygiene of clothing and bedding, war and displacement, refugee camps, prisons, homelessness, and disasters.

6.2 Murine typhus

The chain is: animal reservoir → infected flea → flea feces → human. Infection occurs when contaminated feces reach broken skin. Contact with rodents, stray animals, or domestic cats, and living in flea-infested surroundings, increase risk.^[6]

6.3 Scrub typhus

Transmission occurs through bites of infected larval mites. Risk rises with activities that bring people into mite habitat: farming, forestry, grass cutting, outdoor recreation, military exercises, residence near scrub

vegetation, and travel or work in mite-infested areas. Risk depends on local vector distribution and ecology and not on geography alone.

7. Pathogenesis

7.1 Endothelial infection

Invasion of endothelial cells is the central event in typhus-group infections. Bacterial replication within these cells causes injury, inflammatory activation, greater vascular permeability, and microvascular dysfunction.^[1,2] Consequences can include vasodilation, capillary leak, tissue edema, hypotension, ischemia in small vessels, and organ dysfunction. The extent and distribution of this damage shape the clinical picture.

7.2 Host immune response

Control of intracellular rickettsial infection depends on innate and adaptive immunity, including macrophages, natural killer cells, T lymphocytes, and cytokines. Overactivation of inflammation, however, can itself injure tissues. In scrub typhus, endothelial infection combined with immune-mediated inflammation produces systemic vasculitis and capillary leakage, so several organ systems may be affected at once in severe cases.^[7,12]

7.3 Persistence and relapse

A unique feature of *R. prowazekii* is its ability to persist in the body and reactivate years after the original illness, a condition known as Brill-Zinsser disease.^[11,16] It is generally milder than primary epidemic typhus, but is epidemiologically relevant because bacteremia during relapse may restart transmission where body lice are present.

8. Clinical Manifestations

8.1 General features

Typhus typically causes an acute febrile illness with headache, chills, muscle pain, malaise, loss of appetite, nausea, vomiting, rash, and weakness. The textbook picture is not always present, and lack of a rash or eschar does not rule out typhus.

8.2 Epidemic typhus

Incubation is roughly 10 to 14 days.^[1] Onset is usually abrupt, with high fever, severe headache, malaise, and myalgia. A maculopapular rash generally appears several days into the illness, often starting on the trunk before spreading to the limbs. Severe cases may show confusion, delirium, encephalitis, hypotension, renal dysfunction, pneumonia, myocarditis, shock, and multiorgan failure. Without treatment the disease can be fatal, especially in older adults and those with advanced illness.

8.3 Murine typhus

Murine typhus is usually less dramatic. Patients may have fever, headache, chills, malaise, myalgia, nausea, vomiting, abdominal pain, and cough. A systematic review covering more than 2,000 patients found that the

classic triad of fever, headache, and rash was present in only about a third^[5], so the absence of a rash should not be used to exclude the diagnosis. Laboratory changes may include raised transaminases, low albumin, elevated lactate dehydrogenase, and thrombocytopenia.^[5] Neurological involvement is uncommon but can include meningitis, encephalitis, altered consciousness, seizures, and focal deficits.^[6]

8.4 Scrub typhus

Common features are acute fever, headache, myalgia, chills, malaise, lymphadenopathy, rash, cough, and gastrointestinal symptoms. An eschar, a necrotic lesion at the mite bite site, is a valuable diagnostic clue but is not always found, and its reported frequency varies widely between populations.^[7,12] Because eschars often sit in hidden areas such as the armpit, groin, genitals, abdomen, or scalp, thorough skin examination is essential.

9. Complications

Serious complications are particularly associated with scrub typhus but can occur in any typhus.

- **Respiratory:** Involvement ranges from mild pneumonitis to severe pneumonia and ARDS. Recent systematic evidence identifies ARDS as an important and often fatal complication in hospitalised scrub typhus.^[17]
- **Renal:** Acute kidney injury may result from systemic inflammation, endothelial dysfunction, hypotension, and multiorgan involvement, often with electrolyte disturbance and metabolic acidosis.^[18]
- **Neurological:** Encephalopathy, meningitis, meningoencephalitis, seizures, delirium, and altered consciousness have been described, notably in severe scrub and murine typhus.^[6,18]
- **Cardiovascular:** Myocarditis, arrhythmia, hypotension, and circulatory shock may occur.
- **Hematological and hepatic:** Thrombocytopenia, abnormal white cell counts, anemia, raised liver enzymes, low albumin, and coagulation disturbances are seen; severe disease can lead to disseminated intravascular coagulation and multiorgan failure.

10. Laboratory Diagnosis

10.1 Diagnostic difficulty

Typhus usually presents as undifferentiated fever. In endemic areas the differential includes malaria, dengue, enteric fever, leptospirosis, influenza and other viral infections (including COVID-19), acute bacterial infections, other rickettsioses, viral hepatitis, and meningitis or encephalitis. Clinical and epidemiological information must therefore be weighed together with laboratory findings.

10.2 Serology

Indirect immunofluorescence assay (IFA), ELISA, immunoperoxidase assays, and rapid

immunochromatographic tests are available for scrub typhus.^[19,20] The main limitation is that antibodies may not yet be detectable early in illness. A four-fold rise in titre between acute and convalescent samples is stronger evidence of recent infection than a single result.^[19] In endemic settings, interpreting IgM is especially tricky because it can persist and false positives occur; a recent study underlined the risks of relying on one IgM result.^[21]

10.3 Weil-Felix test

This older agglutination test exploits cross-reactivity between rickettsial antibodies and certain *Proteus* antigens. Its sensitivity and specificity are poor, and current CDC guidance advises against routine use for scrub typhus.^[19] Its persistence in low-resource settings reflects a lack of better options and not good performance.

10.4 PCR

PCR detects rickettsial or *Orientia* DNA in blood or tissue during acute illness and is therefore useful before antibodies appear. For scrub typhus, targets include genes for the 56-kDa and 47-kDa antigens and other conserved or species-specific regions.^[13,20,22] Performance depends on bacterial load, sampling time, specimen type, assay design, and strain variation.

10.5 Culture and immunohistochemistry

Isolating rickettsiae needs specialised facilities and is impractical for routine work. Immunohistochemistry may help with selected tissue samples in reference laboratories.

11. Differential Diagnosis

Because typhus commonly presents as acute undifferentiated fever, the differential is wide (Table 1).

Table 1: Key differential diagnoses of typhus fever.

Disease	Overlapping features	Helpful distinguishing points
Malaria	Fever, chills, headache, thrombocytopenia	Exposure or travel history; blood smear or rapid antigen test
Dengue	Fever, headache, myalgia, thrombocytopenia, rash	Leukopenia, local epidemiology, NS1 antigen or serology
Leptospirosis	Fever, headache, myalgia, renal and hepatic involvement	Contact with contaminated water or animals; conjunctival suffusion
Enteric fever	Prolonged fever, headache, abdominal symptoms	Gastrointestinal features; microbiological culture
Scrub typhus	Fever, headache, rash	Eschar, mite exposure, positive serology or PCR
Murine typhus	Fever, headache, rash	Flea or rodent exposure; serological or molecular confirmation
Epidemic typhus	Fever, headache, rash, confusion	Body-louse exposure; epidemiological setting
Viral infections	Fever, rash, malaise	Specific viral tests; epidemiological clues

A careful exposure history is vital, covering recent travel, rural or agricultural exposure, vegetation contact, insect or mite bites, body lice, fleas, rodents, domestic animals, homelessness, overcrowding, and contact with affected people.

12. Treatment

12.1 Guiding principles

Early antimicrobial therapy is the mainstay. When clinical and epidemiological suspicion is considerable, treatment should not wait for laboratory confirmation. CDC guidance explicitly stresses early treatment for epidemic, murine, and scrub typhus.^[19,23,24] Untreated scrub typhus carries a substantial mortality that varies widely between studies.^[26]

12.2 Doxycycline

Doxycycline is the first-line drug for the major typhus infections. The usual adult dose is 100 mg twice daily, and paediatric doses are weight-based.^[19,23,24] In epidemic and flea-borne typhus, therapy continues for at least three days after fever settles and until clinical improvement, which generally means 7 to 10 days.^[23,24] For scrub typhus the same rule applies: at least three days after fever resolves and until the patient improves.^[19] Benefit is greatest with early initiation, and delay increases complication risk.

12.3 Azithromycin

Azithromycin is an important alternative for selected scrub typhus patients, especially when doxycycline is unsuitable. Systematic reviews report broadly similar outcomes to doxycycline in many studies, though the evidence is limited by study heterogeneity.^[10,25] In pregnancy and some paediatric situations, the choice should be individualised using current guidance and specialist input.

12.4 Other agents

Chloramphenicol and rifampicin have been studied in scrub typhus. Their use depends on clinical circumstances, local susceptibility, contraindications, drug interactions, and guidelines. Evidence for them is less consistent than for doxycycline, and severe cases

should be managed with infectious-disease expertise and local protocols.

12.5 Supportive care

Severe typhus may require intravenous fluids, oxygen, respiratory support, electrolyte correction, renal replacement therapy, haemodynamic support, control of seizures or encephalopathy, and treatment of secondary complications. Patients with ARDS or multiorgan failure may need intensive care.

13. Antimicrobial Resistance and Therapeutic Challenges

Reduced drug susceptibility in scrub typhus is a growing concern. Doxycycline remains standard, yet treatment failures and slow responses have been reported in some endemic areas. Interpretation is complicated because poor response can reflect late treatment, severe disease, reinfection, pharmacological variation, host factors, or true reduced susceptibility. Systematic reviews of controlled trials generally find doxycycline, azithromycin, and some other agents effective, though evidence quality varies.^[10,25] A recent meta-analysis comparing doxycycline and azithromycin found no statistically significant difference in several key outcomes, although heterogeneity and study quality limit certainty.^[25] Continued surveillance and well-designed trials are needed.

14. Prevention and Control

14.1 Epidemic typhus

Prevention centres on louse control and better hygiene: regular bathing, laundering of clothing and bedding, reducing overcrowding, prompt detection of infestation, delousing of affected groups, appropriate treatment of garments and bedding, and rapid identification and treatment of cases. Permethrin-treated clothing and suitable pediculicides may be used in relevant settings following public-health guidance.^[23]

14.2 Murine typhus

Prevention means reducing flea and rodent exposure through rodent control, proper waste disposal, removing rodent food sources, flea control on domestic animals,

avoiding flea-infested animals, repellents, and environmental sanitation. As transmission cycles differ between places, programmes should be tailored to local ecology.

14.3 Scrub typhus

Prevention is harder because mites are widespread in natural habitats and no licensed human vaccine is widely available. Recommended measures include avoiding prolonged contact with mite-infested vegetation where possible, wearing long sleeves and trousers, using repellents, treating clothing and gear with approved permethrin products where indicated, promptly removing and washing outdoor clothing, and raising awareness among farm and outdoor workers. CDC notes that permethrin-treated clothing protects against chiggers, but clothing-grade permethrin products must not be applied to skin.^[27]

15. Vaccines and Future Preventive Approaches

No broadly available vaccine gives durable protection against scrub typhus. Development is hampered by the antigenic diversity of *O. tsutsugamushi* and incomplete understanding of protective immunity.^[8,12] An effective vaccine would be of great value in endemic regions. Approaches under investigation include recombinant antigens, conserved outer-membrane proteins, subunit vaccines, vector-based vaccines, DNA and RNA platforms, and multivalent formulations designed to overcome strain variation. Progress will depend on a better grasp of antigenic variation, cellular immunity, and what separates protective from non-protective responses.

16. Public-Health Significance

Typhus matters because it combines high illness burden, potential mortality, and diagnostic difficulty. Epidemic typhus shows how disease follows social conditions and can re-emerge quickly when populations face displacement, crowding, poverty, and poor sanitation. Murine typhus highlights the role of zoonotic and urban ecological cycles, which can be altered by changes in wildlife, pet ownership, housing, and the environment. Scrub typhus illustrates the challenge of controlling vector-borne disease in rural and peri-urban settings, where the mite habitat is extensive and conventional vector control is hard to apply at scale. Clinician awareness is therefore critical: in endemic regions, typhus should be considered in any patient with acute unexplained fever, especially when clinical or epidemiological clues exist.

17. Emerging Diagnostic Technologies

Fast, affordable point-of-care tests are a leading research priority. An ideal test would

- Be highly sensitive in the first days of illness;
- BE highly specific in endemic areas;
- Be inexpensive and need minimal laboratory infrastructure;
- Give results quickly;

- Distinguish active infection from past exposure;
- Perform reliably across diverse strains.

PCR and other nucleic-acid amplification methods offer clear advantages for early diagnosis, but infrastructure, reagent cost, technical expertise, and pathogen diversity limit their routine use in many endemic settings. Antigen-detection and new molecular platforms may add options, and future tests may combine molecular and serological markers to improve accuracy across illness stages.

18. Research Priorities

1. **Surveillance.** Typhus is probably under-diagnosed and under-reported; standardised systems are needed to measure incidence, distribution, seasonality, and burden.
2. **Point-of-care diagnostics.** Tests that reliably detect infection in the first week would greatly improve management.
3. **Resistance monitoring.** Standardised susceptibility testing and molecular surveillance are needed to detect emerging resistance and guide recommendations.
4. **Vaccines.** Broadly protective scrub typhus vaccines are especially needed given strain diversity and the large population at risk.
5. **Vector ecology.** More work is required on mite, flea, and louse ecology, including effects of climate, land use, urbanisation, agriculture, and environmental change.
6. **Host-pathogen interaction.** Better understanding of endothelial infection, immunity, persistence, and severe-disease mechanisms may reveal new therapeutic targets.

19. DISCUSSION

Typhus fever comprises clinically related but epidemiologically distinct infections, united by their capacity to cause acute systemic illness through intracellular bacterial infection and vascular and inflammatory injury. Epidemic, murine, and scrub typhus should be separated at the bedside: the first is tied to body lice and social conditions, the second to fleas and animal reservoirs, and the third to infected mites and environmental exposure.

Clinical overlap is considerable. Fever and headache are common to all, and rash is frequently absent. The eschar of scrub typhus is useful when found, but its absence does not exclude the disease, and the classic triad of fever, headache, and rash is too insensitive to identify murine typhus reliably.^[5]

Laboratory confirmation is complicated by the timing of the immune response: serology may be negative early yet positive long after past infection, and PCR sensitivity varies with specimen type and timing. The practical lesson is that diagnosis should integrate epidemiology, clinical findings, and laboratory evidence and not rest on

one test. When typhus is plausible and a patient has unexplained acute fever, treatment should not be needlessly postponed pending confirmation.^[19,23,24]

Doxycycline remains highly effective when given promptly, yet serious complications follow late therapy, and the continued burden of scrub typhus in South Asia and elsewhere underscores the need for vigilance. Control strategies also differ: louse control for epidemic typhus, flea and rodent control for murine typhus, and personal protection and environmental awareness for scrub typhus.

Growing recognition of scrub typhus beyond its historic “tsutsugamushi triangle” has implications for surveillance. Molecular and epidemiological studies show broader diversity and distribution of *Orientia*^[8,12], so geographic assumptions should never replace exposure-based clinical assessment.

20. CONCLUSION

Despite advances in antimicrobial therapy and public health, typhus remains an important group of vector-borne bacterial diseases. Epidemic, murine, and scrub typhus differ in agent, vector, reservoir, and epidemiology, but all can present as acute fevers that are hard to tell apart from other common infections. Early recognition is essential because delayed treatment can cause serious complications, especially in scrub and epidemic typhus. Doxycycline remains the principal treatment, with azithromycin appropriate in selected cases, particularly scrub typhus.

Laboratory diagnosis remains a challenge: serology is widely available but limited by antibody timing and persistence, while PCR enables early confirmation but is not universally accessible. Affordable, sensitive, specific, rapid point-of-care tests should be a major research goal. Prevention needs an integrated approach combining vector control, sanitation, personal protection, early case detection, effective treatment, and surveillance. Future work should target improved diagnostics, resistance monitoring, understanding of pathogen diversity and host immunity, vector ecology, and vaccine development.

Maintaining clinical awareness is especially important in endemic areas and in people with relevant environmental or vector exposure. Strengthening diagnostic and surveillance capacity will be key to reducing illness and death from these preventable and treatable infections.

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