

An Ongoing Series

Scrub Typhus

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ABSTRACT

Scrub typhus, also known as tsutsugamushi disease, is caused by *Orientia* sp. and approximately 1 million new cases are reported annually. This article discusses the importance of scrub typhus and its clinical presentation, diagnosis, treatment, and prevention.

KEYWORDS: *tsutsugamushi disease; scrub typhus; Orientia sp.; illness, febrile*

Introduction

Background: Scrub typhus, also known as tsutsugamushi disease, is caused by *Orientia* sp., small, coccobacillary gram-negative bacteria that can only survive within cells. Approximately 1 million new cases of scrub typhus are reported annually.¹ Historically, scrub typhus was thought to occur exclusively due to infection with *O. tsutsugamushi* within the “tsutsugamushi triangle,” an area bounded by Korea and Japan to the north, Iran to the west, and Australia to the south. *O. tsutsugamushi* causes the greatest number of identified infections worldwide, the majority within the endemic Asia-Pacific region, but it has also been reported in Africa and South America.² *O. tsutsugamushi* is transmitted to humans via the bite of Trombiculid larval mites, which are often found in areas of dense vegetation. Scrub typhus cases have also been attributed to other recently identified *Orientia* sp. (*O. chuto* in the United Arab Emirates and Africa and “*Candidatus O. chiloensis*” in Chile) without well-established vectors.²

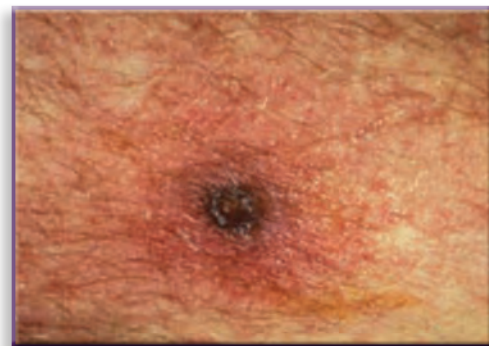
Scrub typhus has been a concern for US military operations in the Indo-Pacific region since World War II with significant associated morbidity and mortality prior to effective antibiotic treatment. The US military was the first to conduct clinical treatment trials of scrub typhus using chloramphenicol in the late 1940s. Although a significant number of cases occurred during the Vietnam conflict, the infections were seldom fatal

due to the availability of effective antibiotic treatment.^{3,4} Even in more recent times, outbreaks have occurred in US military personnel serving in the Asia-Pacific region.⁵ Scrub typhus is considered among the top 20 infectious diseases of significance to the US military.⁶

Clinical Presentation

The first feature of scrub typhus may be development of a black crust or eschar (Figure 1) at the site of the larval mite bite; if present, this should raise concern for infection. Systemic symptoms of scrub typhus usually occur between 5 to 14 days after the mite bite with abrupt onset of high fever, chills, headache, and body aches. The fever usually comes and goes and may be associated with an unexpectedly low heart rate. A widespread, non-itchy rash usually occurs around day 4 or 5 of illness, starting on the trunk as pink lesions then spreading to extremities later in the disease course. Enlarged lymph nodes may develop in the area surrounding the primary lesion. Acute hearing loss can occur, and when combined with a febrile illness should prompt investigation for scrub typhus. Scrub

FIGURE 1 Eschar at the site of a larval mite bite.



Source: Typhus Fevers, CDC.
<https://www.cdc.gov/typhus/scrub/index.html>

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typhus may also occur with a nonspecific febrile presentation, mild systemic symptoms and without an obvious primary lesion. Other infections which may cause similar symptoms including a black crusted lesion, such as rickettsial spotted fevers and cutaneous anthrax, should also be considered.

Scrub typhus is sometimes severe enough to cause organ dysfunction, including acute kidney injury, liver failure, pneumonitis, acute respiratory distress syndrome, cardiac involvement, and bleeding and blood clotting issues.⁷ Patients may experience changes to mental status, meningitis, or meningoencephalitis and may even become comatose. Presence of more severe symptoms is associated with a higher mortality and is more likely to occur in immunocompromised or otherwise weakened patients.

Diagnosis

If the clinical presentation is consistent with scrub typhus, appropriate treatment should be initiated without waiting for confirmation from diagnostic testing.

There are multiple diagnostic testing options and they should be used if available to confirm diagnosis. Serological testing options for scrub typhus include immunofluorescence assay (IFA), rapid diagnostic tests and ELISA. Serology is considered positive with elevated IgM antibodies or a 4-fold increase in IgG antibodies (seroconversion) but may be falsely negative early in the disease process. The gold standard of diagnosis is IFA; however, it is expensive, requires repeat testing, and will not be available in the field. Alternative testing options include polymerase chain reaction (PCR) and the Weil-Felix test. PCR testing on samples from blood or eschar material is as useful as serological testing. Weil-Felix testing has been phased out in resource-rich areas and cannot differentiate *Orientia* sp. from other rickettsial diseases but may be the only option available in resource-poor regions.

Treatment and Prevention

Early treatment of scrub typhus is associated with improved outcomes and decreased mortality. The usual initial treatment for scrub typhus is 100mg of oral doxycycline twice daily for 7 days. If doxycycline is contraindicated, unavailable or if the patient does not improve as expected, alternative antibiotics such as azithromycin and chloramphenicol have been shown to be effective therapy. Rifampin may also be used but only after ruling out tuberculosis. Limited studies have been conducted on the efficacy of the different treatment options with a recent review showing no difference between the different antibiotics on primary outcomes of infection.⁸ Patients are expected to become afebrile within 24 to 48 hours of starting treatment. If a patient is severely ill or worsening despite appropriate oral antibiotics for 48 hours, they should receive IV antibiotic therapy and alternative diagnoses should be seriously considered. Although reported, the significance of antibiotic-resistant scrub typhus is unclear and its clinical significance is unknown.⁹

Prevention of scrub typhus includes avoiding areas with dense vegetation and rodents where the larval mites may be found, using DEET-containing insect repellent, and wearing full-length permethrin-treated gear. No vaccine is currently available to prevent scrub typhus (Figures 2 and 3).

FIGURE 2 Adult and larval mites on the head of a pin.

Source: Typhus Fevers, CDC.
<https://www.cdc.gov/typhus/scrub/index.html>



FIGURE 3 US Armed Forces poster from World War II warning about scrub typhus risk. Wearing permethrin-impregnated clothing is still a mainstay of prevention.

Source: US NLM Digital Collections, NLM, 1945.
<http://resource.nlm.nih.gov/101438591>

Importance in a Deployed Setting

Scrub typhus remains a concern for troops deployed to the Indo Asia-Pacific region, even for brief periods of time and even to urban areas. Scrub typhus is the most common rickettsial disease in South Korea.¹⁰ Rodents captured outside urban foodservice buildings at Yongsan Garrison in Seoul and in areas of tall grass at Dagmar North Training Area were found to carry *O. tsutsugamushi*.^{11,12} In Japan there have been recurrent outbreaks among US Marines at Camp Fuji since the 1930s and rodents trapped in a grassy area near the golf course on Camp Zama were found to harbor mites which carried *O. tsutsugamushi*.^{9,13}

With the recent discovery of scrub typhus cases outside of the Asia-Pacific region it would be prudent to consider scrub typhus from a preventative medicine and differential diagnosis standpoint in other areas of the world as well. If a patient has a clinical presentation concerning for scrub typhus, medical providers should seriously consider it as the cause of illness even outside the “tsutsugamushi triangle,” initiating appropriate antibiotic therapy to prevent severe complications of this potentially fatal infection. Although the US military has made advances in the prevention and treatment of scrub typhus, it is still a factor to consider for military operations in the Asia-Pacific region and beyond.

Disclaimer

The views expressed in this publication are those of the authors and do not reflect the official policy or position of the

Department of the Army, Department of Defense, or the United States Government.

Disclosure

The authors have nothing to disclose.

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