SCRUB TYPHUS

Chigger mite

Orientia tsutsugamushi under microscope

Characteristic eschar in a patient

Photographs I and II: AFRIMS Bangkok via WHO
Photograph III: WHO

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Review Article

Scrub typhus strikes back: Are we ready?

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Abstract

Scrub typhus has struck back, albeit with renewed vigour, impacting areas with previously known endemicity as also impressing newer expansions. It is not surprising, therefore, that scrub typhus has emerged as a leading cause of public health concern globally as well as in India, but are we ready to take on the challenge?

Over the last decade, there has been a global increase in the number of outbreaks of scrub typhus, be it the military occupied areas or the civil population at large. The incremental outbreaks of scrub typhus, although disconcerting, have nonetheless contributed phenomenally towards better understanding of the dynamics of scrub typhus. There have been significant contributions toward awareness of the disease amongst medical professionals.
Reported outbreaks of scrub typhus in India (till 42nd week of 2018).

Source: Integrated Disease Surveillance Programme (IDSP)
Scheme of Presentation

- Introduction
- Historical Perspective
- Epidemiology & Indian Scenario
- Pathogenesis
- Clinical features & Complications
- Approach to the Disease
- Management
- Prevention & Control
Introduction

- Scrub typhus is a mite borne acute febrile infectious illness that is caused by Orientia tsutsugamushi.
- Gram-negative coccobacillus that is antigenically distinct from the typhus group rickettsiae
- O. tsutsugamushi is maintained by transovarial transmission in trombiculid mites.
- Three strains of O.tsutsugamushi- Karp, Gilliam and Kato
• The mites are both the vector and reservoir of the disease.

• The mite is very small (0.2 – 0.4mm) and can be seen through a microscope or magnifying glass.

• The infected larval mites (chiggers, the only stage that feeds on a host) inoculate organisms into the skin.

• There is no human to human transmission.
Historical perspective

• Historically, in 313 AD, a clinical manual by Hong Ge called “Zhouhofang” had mentioned the clinical description of disease and morphological description of mites.

• 1596 AD, well-known Chinese physician Shizen Li described the characteristics of the disease.

• Japanese researcher started research on this disease in 1879.
The name *Rickettsia tsutsugamushi* was first used in 1930.

The word “tsutsugamushi” is derived from a Japanese word *tsutsuga* meaning something small and dangerous, *mushi*, meaning creature, so it was known as small dangerous creature.
Why is it linked to War?

- Napoleon’s retreat from Moscow was forced by rickettsial disease breaking out among his troops.

- Lenin is said to have remarked, in reference to rickettsial disease during Russian revolution, “either socialism will defeat the louse or the louse will defeat the socialism.”
Major Impact on research during WW2..

- Its impact on immunologically naive Allied troops between 1942 and 1945 resulted in 18,000 cases and 639 deaths (4.0%), as well as an estimated 20,000 cases in Japanese troops.

- First batch of scrub typhus vaccine used to inoculate human subjects was dispatched to India for use by the Allied Land Forces, South-East Asia Command, in June 1945.

- Leading cause of pyrexia of unknown origin (PUOs) in forces of USA during the VietNam conflict.
Scribb typhus is endemic to a part of the world known as the "tsutsugamushi triangle"
Indian Scenario

- In India, the disease had occurred among troops during the Second World War in Assam and West Bengal, and in the 1965 Indo-Pak war.

- There was a resurgence of the disease in 1990 in a unit of an army deployed at the Pakistan border of India.

- Occurrence reported from several states in India including Jammu and Kashmir, Himachal Pradesh, Uttarakhand, Bihar, West Bengal, Meghalaya, Rajasthan, Maharashtra, Karnataka, Tamil Nadu and Kerala.

- Scrub typhus accounts for up to 50% of undifferentiated fever presenting to hospitals.

- It remains a major underdiagnosed(suspected) cause of undifferentiated fever.
Reservoir of infection at our door

Abundance & distribution of trombiculid mites & Orientia tsutsugamushi, the vectors & pathogen of scrub typhus in rodents & shrews collected from Puducherry & Tamil Nadu, India

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Received September 1, 2015

**Background & objectives:** Human cases of scrub typhus are reported every year from Puducherry and adjoining areas in southern India. However, information on the presence of causative agent, Orientia tsutsugamushi, and its vectors is lacking. Hence, the objective of the study was to find out the vector as well as pathogen distribution in rodents and shrews present in the scrub typhus-reported areas in southern India.

**Methods:** Trombiculid mites were collected by combing rats and shrews collected using Sherman traps and identified to species level following standard taxonomical keys. The serum samples of the animals were used for Well–Felix test and the clots containing blood cells were used for DNA extraction and polymerase chain reaction (PCR).

**Results:** A total of 181 animals comprising four rodent species and one shrew species were collected from 12 villages. High proportion of chiggers was collected from the shrew, Suncus murinus (79.1%) and Rattus rattus (47.6%). A total of 10,491 trombiculid mites belonging to nine species were collected. *Leptotrombidium deliense*, the known vector of scrub typhus pathogen, was the predominant species (35.0%) and the chigger (*L. deliense*) index was 41.1 per animal. Of the 50 animals screened for the pathogen, 28 showed agglutination against OX-K in Well–Felix test indicating the presence of antibodies against *O. tsutsugamushi*, the causative agent of scrub typhus. PCR carried out with the DNA extracted from blood samples of two of the animals were positive for GroEL gene of *O. tsutsugamushi*.

**Interpretation & conclusions:** *L. deliense* index was well above the critical limit of chigger load, indicating that all the villages were receptive for high risk of transmission of scrub typhus to human. Pathogen positivity was higher among animals collected from villages recorded for higher chigger indices due to active transmission between the chigger mites and reservoir host animals. The results are suggestive of routine vector/pathogen surveillance at hot spots to initiate timely preventive measures.

**Key words** Chigger index - *Leptotrombidium deliense* - Orientia tsutsugamushi - Puducherry - scrub typhus - trombiculid mites
Scrub typhus: Clinical spectrum and outcome

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Abstract

Background: Scrub typhus is one of the differential diagnoses for fever with thrombocytopenia. ARDS associated with scrub typhus has high morbidity and mortality. Aim: To evaluate clinical features, lab values, and outcome in patients with scrub typhus and comparison in patients with or without ARDS. Methods: A prospective observational study was conducted on 109 patients with febrile illness and thrombocytopenia during a period of 12 months. All 109 patients were tested with both immune-chromatography test and Weil felix test. Patients having either immune-chromatography test or Weil felix test positive have been included and considered as scrub typhus positive whereas negative for both immune-chromatography and Weil felix test were excluded. Clinical features, lab parameters, and outcome were evaluated in all patients with scrub typhus. Statistical analysis used in this study was T-test. Results: Among 58 patients who were included (After exclusion of 51 patients among total of 109 patients) 34 patients had no ARDS and 24 patients had ARDS. The clinical feature like dyspnoea, cough, low blood pressure (MAP<65 mmHg), IVC collapsibility (by ultrasound) and laboratory parameters like decreased Hemoglobin, Hematocrit, Serum albumin, and increased serum creatinine, serum total bilirubin, SGOT, SGPT, LDH, CPK, and serum lactate were statistically significant (P < 0.001) in scrub typhus patients group with ARDS. The higher titers of Weil-felix can be correlated with more severe form of disease according to our observation. All 34 scrub typhus patients without ARDS recovered completely. Among 24 scrub typhus patients with ARDS, 22 patients recovered, and 2 patients died. Conclusion: Scrub typhus is an important differential diagnosis in a patients having fever with thrombocytopenia. Scrub typhus associated with ARDS has high morbidity and mortality. Early diagnosis and treatment with doxycycline can prevent the occurrence of ARDS.

Keywords: Acute respiratory distress syndrome, immunochromatography test, screening criteria, scrub typhus, thrombocytopenia, Weil-Felix test

Introduction

Scrub typhus is a mite borne acute infectious disease caused by Orientia tsutsugamushi. The term scrub means the type of vegetation (Terrain between woods and clearings) that harbors the vector and typhus means “fever with tumor” or empyema. “Tsutsugamushi" insect or mite. Humans are accidental hosts. It affects people of all age. Scrub typhus is endemic in so called “tsutsugamushi triangle” such as Japan, Taiwan, China, and South Korea on the north, India and Nepal on the west, and Australia and Indonesia in the south. with either nonspecific febrile illness or constitutional
The study reveals rickettsial activity amongst rodents at Jammu, Dehradun and Udhampur-Nagrota belt. The results correlate well with the presence of vectors of scrub and tick typhus and corroborate the occurrence of outbreaks of these diseases in the respective areas.
Recent outbreak of scrub typhus in North Western part of India.

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Abstract

BACKGROUND: Scrub typhus usually affects previously healthy active persons and if undiagnosed or diagnosed late, may prove to be life-threatening. Diagnosis of scrub typhus should be largely based on a high index of suspicion and careful clinical, laboratory and epidemiological evaluation.

OBJECTIVE: To describe the diverse clinical and laboratory manifestations of scrub typhus diagnosed in Mahatma Gandhi Medical College and Hospital, Jaipur.

MATERIALS AND METHODS: All cases of febrile illness diagnosed as scrub typhus over a period of 3 months were analysed. Diagnosis was based on ELISA test for antibody detection against 56 kDa antigen.

RESULTS: Forty-two cases of scrub typhus were seen over a period of 3 months (October, 2012-December, 2012). Common symptoms were high grade fever of 4-30 days duration, cough, haemoptysis and breathlessness. Eschar was not seen even in a single patient. Liver enzymes were elevated in nearly all cases (95.9%). Multiple organ dysfunction syndrome (MODS) was present in 16.66% of our patients (7 out of 42). Hypotension (6 patients, 14.2%), renal impairment (9 out of 15 patients, 60%), acute respiratory distress syndrome (4 patients, 9.52%) and meningitis (4 patients, 9.52%) were some of the important complications. There was a dramatic response to doxycycline in nearly all the patients, but initially when the disease was not diagnosed, seven patients had died.

CONCLUSION: Scrub typhus has emerged as an important cause of febrile illness in Jaipur. Empirical treatment with doxycycline is justified in endemic areas.

PMID: 25008815 DOI: 10.4103/0255-0657.136552
Humans are accidental hosts.

Transovarial transmission (from adult to egg) of *O. tsutsugamushi*

Normally the larva (chigger) feeds on small mammals or ground-feeding birds.

Engorged larva

Both the nymph & the adult are free-living in the soil.
• Infections are prevalent in these regions; in some areas, >3% of the population is infected or re-infected each month.

• Immunity wanes over 1–3 years, and the organism exhibits remarkable antigenic diversity.
• Infected chiggers are particularly likely to be found in areas of heavy scrub vegetation during the wet season, when mites lay eggs

• Humans are accidental hosts
Mode of Transmission

- Rats & Mice
- Mites
- Humans (Accidental host)

- No direct person to person transmission
- Mite Islands
An outbreak of scrub typhus in Nepal following the 2015 Gorkha earthquake

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Purpose: To describe the epidemiology and clinical features of 23 cases of scrub typhus seen in a tertiary infectious diseases hospital following the massive April 2015 earthquake in Nepal.

Methods & Materials: In addition to routine clinical examinations and laboratory tests, all patients with undifferentiated fever admitted to the Sukraraj Tropical and Infectious Disease Hospital (STIDH) in Kathmandu, Nepal between August to October 2015 had serum tested by ELISA for IgM antibodies against Orientia tsutsugamushi.

Results: Scrub typhus cases surged in Nepal in late 2015 following the Gorkha earthquake. The vast majority of 23 cases diagnosed at STIDH were individuals rendered homeless in the most devastated districts, and living in temporary shelters with a high reported incidence of mouse infestation. Fever and anorexia occurred in 100%, and chills or rigors, myalgia or arthralgia, headache, or nausea occurred in >75%. Physical findings of eschar formation, red eye, or lymphadenopathy were noted in <1/3 of these patients. The majority of patients had significant thrombocytopenia and transaminitis. Although all patients with undifferentiated fever had been empirically started on ceftriaxone, azithromycin and doxycycline were the most effective treatments once the diagnosis of scrub typhus was made. All of the patients treated at STIDH recovered without disease complications or adverse drug effects.

Conclusion: Major causes of undifferentiated fever in Nepal include malaria, dengue, enteric fever, brucellosis, chikungunya, leptospirosis, and scrub typhus. We observed a singular spike in cases of scrub typhus following the 2015 Gorkha earthquake, which we attribute to large-scale human habitat destruction and population dislocation, leading to increased contact with rodents infested with the trombiculid mite vectors of O. tsutsugamushi. Only a minority of patients present with characteristic physical findings, so the diagnosis of scrub typhus can only be established by specific IgM assay. With appropriate diagnosis and treatment, clinical outcomes from scrub typhus can be good, even in resource-limited environments.

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Aftermath Earthquake in Nepal: Burden of Scrub Typhus Cases and Presentations

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Abstract

Background: Scrub typhus, also known as tsutsugamushi disease, is an infectious illness caused by Orientia (Rickettsia) tsutsugamushi. It is widely found in Asian countries and human beings of all ages including children are influenced by it. It can cause death due to late presentation, delayed diagnosis and drug resistance. The clinical features and complications of scrub typhus vary from mild to fatal illness. We describe the epidemiology, clinical features and treatment outcome among scrub typhus cases admitted in Sukraraj Tropical and Infectious Disease Hospital (STIDH), a tertiary center in Kathmandu, Nepal following the massive earthquake of 2015.

Material and methods: Serum samples of twenty-three patients with acute undifferentiated fever admitted to the STIDH were tested positive for orientia tsutsugamushi by IgM ELISA. These patients were admitted between August to October 2015. Detail history taking, clinical evaluation and laboratory parameters of these patients were collected. Most of the patients were from the earthquake affected district and staying in temporary shelter with history of rodent infestation of the environment. Verbal consent was taken from each patient. The data were entered in SPSS version 16 and descriptive statistics was used to analyze the data.

Results: In the study, more than half of the patients (52.2%) were female and the mean (±SD) age of the patients was 37.6 (±13.3) years. Most of the patients (82.7%) were engaged in farm work. About three fifths (60.8%) of the patients were from Dhading district followed by Nuwakot, Sariahi, Kavre and Parsa. Except Sariahi district, all other were affected by earthquake 2015. Majority (87%) of the patients were living in the temporary shelter following devastating earthquake and had history of environmental infestation by rodents. All the patients had fever and anorexia. The mean fever duration before admission was 10.1 (±4.0) days. Clinical features of arthralgia and myalgia (91.3%); nausea, headache and chills or rigor (82.6%) and retroorbital pain (60.9%) among the commonest. Abdominal pain and cough was complained by 47.8% and 43.5% patients respectively. Eschar formation, red eye and lymphadenopathy were the commonest physical finding and noted in 30.4, 30.4% and 26.1% patients respectively. Lymphadenopathy was localized. Most common laboratory parameter was increased in alanine transaminase level and thrombocytopenia and was seen in 73.9% and 60.9% patients respectively. Leukocytosis was seen in 21.7% of patients. Azithromycin or doxycycline was added on ceftriaxone once the diagnosis of scrub typhus was made. The mean fever response time was 1.7 (±1.2) days. All patients were discharged after fever subsides. Clinical recovery and hospital stay was uneventful.

Conclusion: From the study, it can be concluded that scrub typhus has emerged as an important cause of febrile illness in Nepal after massive earthquake of 2015 so; it demands the continuous surveillance in the health care setting. Scrub typhus should be considered in the patient presenting with acute undifferentiated fever and can be confirmed by sensitive test as characteristic clinical findings seen only in small number of cases. Rodent infestation of the environment around temporary shelter increases the risk of acquiring scrub typhus and such history increases clinical suspicion in the diagnosis. Azithromycin and doxycycline are the effective antibiotics. Appropriate diagnosis and treatment can reduce the complication of scrub typhus even in resource-limited environment.
Pathogenesis

- Chigger inoculates *O tsutsugamushi* pathogens
- Bacteria multiply at the inoculation site, and a papule forms that ulcerates and becomes necrotic, evolving into an eschar, with regional lymphadenopathy that may progress to generalized lymphadenopathy within a few days
- Perivasculitis of the small blood vessels occurs. The endothelium is involved;
- *O Tsutsugamushi* stimulates phagocytosis by the immune cells, and then escapes the phagosome. It replicates in the cytoplasm and then buds from the cell
Clinical Manifestations

COURSE OF ILLNESS

- Mild and self-limiting to fatal.
- Incubation period of 6–21 days
- Scrub typhus lasts for 14 to 21 days without treatment.
- Death may occur end of 2\textsuperscript{nd} week due to complications.
Clinical Manifestations

- Fever is high grade (>104 °F)
- Severe headache, Profuse sweating, Conjunctival injection
- Myalgia, cough, and gastrointestinal symptoms (Nausea, vomiting, and/or diarrhea are prominent)
- Fever Lasts for long periods in untreated patients .
  Median 14.4 days, range 9 to 19 days
Seasonal deviation and habitat diversity

• Scrub typhus was historically known to occur in post monsoon season, however reports of occurrence of outbreaks in cooler months has widened the seasonal window of scrub.

Outbreak of scrub typhus in southern India during the cooler months.

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Abstract

Orientia tsutsugamushi, the agent of scrub typhus, is a strict intracellular bacterium which is found in many parts of Asia including India. During the past few years, the number of patients with rickettsial infection and scrub typhus has increased, especially during the cooler months. We report in this study a recent outbreak of scrub typhus recorded during the cooler months (October 2001 to February 2002) in patients admitted to our hospital with acute febrile illness associated with diverse signs and symptoms. Overall, 28 patients were clinically and serologically confirmed to have scrub typhus. Fever for more than one week was the only common manifestation. Myalgias was the next most common feature (52%), and rash was observed in only 22% of the cases. Seventeen patients treated with doxycycline recovered in 1 to 3 days, as well as two patients who received chloramphenicol. In five patients who received ciprofloxacin, fever subsided only after five days. Finally three patients (10.7%) died, including one patient treated with doxycycline. These data indicate that scrub typhus is a reemerging infectious disease in India with a possibility of drug resistance. This reemergence emphasizes the need for further prospective studies to design effective control measures.


[Indexe for MEDLINE]
Symptoms and Signs

• The classic case description includes an eschar (fewer than 50%) where the chigger has fed, regional lymphadenopathy, and a transient maculopapular rash.
  – fewer than 40% develop a rash (on day 4–6 of illness).
  – comprises 5 to 40 macular, then papular and vesicular spots.
  – Non-pruritic
  – The rash typically begins on the abdomen and spreads to the extremities. The face is also often involved.
  – Rarely, petechiae may develop.
• Eschar
  – Painless papule often at the site of the infecting chigger bite
  – Subsequent central necrosis then occurs forming eschar with black crust
Eschar—Characteristics

- Single
- Black necrosis ... hallmark
- 66-97% cases
- Missing should not exclude diagnosis
Eschar....Missed when

- Scalp
- Groin
- Inguinal
- Axillary area
Eschar distribution

MALES

- Arms [5.6]
- Head [0.5]
- Neck [1.0]
- Axilla [16.7]
- Back [4.5]
- Abdomen [11.1]
- Buttocks [2.5]
- Groin [21.3]
- Thighs [8.6]
- Legs [0.5]

FEMALES

- Arms [3.0]
- Head [2.6]
- Neck [2.5]
- Axilla [10.9]
- Back [6.6]
- Abdomen [21.4]
- Buttocks [2.1]
- Groin [14.4]
- Thighs [7.4]
- Legs [0.4]
Signs

• Relative bradycardia

• Lymphadenopathy - Tender lymph node, usually proximal to site of mite bite

• Hepatomegaly and splenomegaly can be observed.
• **Respiratory-**
  – Cough
  – Acute Respiratory Distress Syndrome
  – Pathogenesis of ARDS in scrub typhus not known, thought to be immunological response of the lung to the infection without direct invasion of the organism and diffuse alveolar damage without evidence of vasculitis.

• **Neurological**
  – Involvement of blood vessels in the central nervous system may produce meningitis
  – Mental changes are usual and range from slight intellectual blunting to coma or delirium

• In severe cases, evolution to a multiple-organ dysfunction syndrome with hemorrhage can be observed

• Relapse is usually less severe than the first attack
Complications

Neurological findings may suggest meningoencephalitis.
Delirium, confusion, seizures

Multi-organ failure

Death may occur as a result of these complications

Spontaneous abortion may occur during pregnancy if infected

Acute hearing loss or tinnitus
Spike in scrub typhus

Majority of Acute Encephalitis Syndrome (AES) patients hospitalised between August and October in the last three years had scrub typhus.

- Scrub typhus is an acute illness caused by a bacterium Orientia Tsutsugamushi, which is transmitted by the bite of an infected mite larva present in the soil.

% of patients tested positive for scrub typhus in 2017
EDITORIAL

Acute encephalitis in India: An unfolding tragedy

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Complications

Overwhelming pneumonia with ARDS–like presentation
Acute Kidney Injury
Atypical pneumonia,
Myocarditis, Congestive heart failure
Pulmonary edema
Circulatory collapse
Disseminated intravascular coagulation (DIC).
Complications

• Some patient recover spontaneously.

• Case-fatality rate for untreated classic cases is 70% (the fatality rate ranges from 0 to 30%).

• Scrub typhus is not more severe in HIV-infected patients, and surprisingly, HIV suppressive factors appear to be produced during infection.
Renal Manifestation in Scrub Typhus during a Major Outbreak in Central Nepal

Abstract
Renal involvement and acute kidney injury (AKI) are common clinical manifestations seen in scrub typhus, a vector-borne tropical disease. There are no data on renal manifestation in scrub typhus in Nepal. We conducted a prospective study to analyze the incidence, urinary abnormalities, course, severity, outcome, and the predictors of AKI in patients with scrub typhus during a major outbreak in Central Nepal. Total 1398 patients admitted with acute febrile illness were subjected for Scrub Typhus Detect™ Immunoglobulin M (IgM) enzyme-linked immunosorbent assay (ELISA) test, of which 502 (35.90%) patients tested positive and were included in the study. Mean age of the patients

Multivariate analysis of Scrub typhus revealed that the presence of pneumonia, shock and ARDS predicted the development of AKI.

AKI occurred in fifth and sixth day of fever. ICU admission was required for 18.73% of patients and 8.57% required ventilator support. Mortality rate was 1.79%, which was higher among patients with AKI (2.96% vs. 1.0%; \( P = 0.106 \)). Multivariate analysis revealed that the presence of pneumonia, shock, and acute respiratory distress syndrome predicted the development of AKI.

Keywords: Acute febrile illness, acute kidney injury, albuminuria, hematuria, scrub typhus.
Older age and high Serum Creatinine independent predictor of poor outcome in patients with Scrum typhus admitted in ICUs.
Study design influences the reported eschar rates in ST and MSF significantly. NERD is likely to be a vastly underdiagnosed entity, and clinicians should consider and test for the disease more often.
Differential Diagnosis

- The most common signs are similar to a variety of other infectious diseases
- typhoid fever
- Malaria
- leptospirosis
- dengue fever
- Brucelosis
- Chickenguenia etc.
Lab Parameters

• Leucocytosis or leucopenia may be present, but mostly normal WBC count.

• Lymphocyte count is decreased

• Liver enzyme levels are increased in 60% of cases.

• Thrombocytopenia may be sufficient to cause bleeding.

• Hyperbilirubinemia and increased Creatinine
Lab Parameters

• The most common radiologic abnormalities includes
  – Bilateral reticular opacities (49%)
  – Cardiomegaly (29%)
  – Congestive heart failure (19%)
<table>
<thead>
<tr>
<th>Test</th>
<th>Principle</th>
<th>Time taken</th>
<th>Time of Positivity</th>
<th>Sensitivity &amp; specificity</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Serologicala</td>
<td>Based on antigenic similarity with OX-K strain of <em>Proteus mirabilis</em></td>
<td>6(\pm)18 h</td>
<td>5(\pm)10 days (usually second week)</td>
<td>Poor sensitivity Good Specificity</td>
</tr>
<tr>
<td>b Immunofluorescent assay (IFA)</td>
<td>Detects IgM fluorescent anti-human antibody to detect antibody in patient serum Tests IgM &amp; IgG similar to IFA</td>
<td>2 h</td>
<td>3(\pm)4 days</td>
<td>Highly sensitive and specific GOLD STANDARD</td>
</tr>
<tr>
<td>Indirect immuno-peroxidase Assay (IIP) Enzyme linked immunosorbent assay (ELISA)</td>
<td>Uses Light Microscope Uses outer membrane proteins as Antigen Detects both IgM &amp; IgG Based on chromatography Detects both IgM &amp; IgG</td>
<td>2 h 30 min</td>
<td>3(\pm)4 days (7 days for IgM, end of second week for IgG)</td>
<td>Highly sensitive and specific IgM capture assays most sensitive</td>
</tr>
<tr>
<td>C. Immunochromatographic Test (ICT)</td>
<td>Detects rickettsial DNA before antibody response Eschar/Lymph node biopsy/ Skin Biopsy as sample Recombinant 56 kDa protein used as antigen Uses amplification and detection of DNA Cell culture of organisms in monolayer cells Can use ELISA or Immunochromatography to detect antibodies LAMP detects antigen</td>
<td>30 min</td>
<td>More than 5 days after onset</td>
<td>Good sensitivity and specificity</td>
</tr>
<tr>
<td>2. Moleculara</td>
<td>Polymerase chain reaction (PCR)</td>
<td>Few hours</td>
<td>Positive on Day 1</td>
<td>Highly sensitive and specific</td>
</tr>
<tr>
<td>b Rapid flow assay</td>
<td></td>
<td>15 min</td>
<td>Positive after day 2 of fever up to 10 days</td>
<td>Sensitive and specific</td>
</tr>
<tr>
<td>c Loop-mediated isothermal amplification assays (LAMP)</td>
<td></td>
<td>2(\pm)3 h</td>
<td>Day 1 (for sample)</td>
<td>Most sensitive and specific</td>
</tr>
<tr>
<td>3. CultureIn vitro</td>
<td></td>
<td>27 days</td>
<td>Day 2 of onset</td>
<td></td>
</tr>
<tr>
<td>4. Rapid tests</td>
<td></td>
<td>Few min. 2(\pm)3 h</td>
<td>After 7 days Day 2 of onset</td>
<td>Sensitive and specific(???)</td>
</tr>
</tbody>
</table>
Diagnosis

• Serologic assays
  – indirect fluorescent antibody (gold standard)
  – indirect immunoperoxidase
  – enzyme immunoassays
  
  – Serological methods are most reliable when a four-fold rise in antibody titre is looked for.
  – When a single measurement is performed, the most common cut off titre is 1:50

• PCR amplification of Orientia genes from eschars, lymphnodes and blood
  
• O.tsutsugamushi specific gene (56-kDa protein-encoding gene)
WEIL FELIX TEST

- The Weil-Felix test detects cross-reacting antibodies to *Proteus mirabilis* OX-K. The Weil- Felix test is still used because of its low cost.
  - notoriously unreliable and no longer advised.
  - Fifty per cent of patients have a positive test result during the second week

- Weil felix test is based on cross reactions which occur between antibodies produced in acute rickettsial infections with antigens of OX (OX19, OX 2 and OX K ) strains of proteus.
  - Typhus group (R.prowazekii, R typhi) react with P.vulgaris OX 19
  - Scrub typhus reacts with P.mirabilis OX K
  - Spotted fever group react with OX2 and OX19.
Diagnosis

- Biopsy of an eschar or generalised rash
  - Pathological hallmark: lymphohistiocytic vasculitis
  - Endothelial injury causes loss of vascular integrity. Egress of plasma and plasma proteins and microscopic and macroscopic hemorrhages.
  - Histologic change in biopsies of eschars shows focal areas of cutaneous necrosis surrounded by a zone of intense vasculitis with perivascular collection of lymphocytes and macrophages
Case Definition

• **Suspected/clinical case:** Acute undifferentiated febrile illness (UFI) of 5 days or more with or without eschar should be suspected as a case of Rickettsial infection. (If eschar is present, fever of less than 5 days duration should be considered as scrub typhus.)

• **Probable case:** A suspected clinical case with an IgM titer > 1:32 and/or a four-fold increase of titers between two sera confirm a recent infection.
• **Confirmed case:**
  • The one in which:
  • Rickettsial DNA is detected in eschar samples or whole blood by PCR OR,
  • Rising antibody titers on acute and convalescent sera detected by Indirect ImmuneFluorescence Assay (IFA) or Indirect Immunoperoxidase Assay (IPA)

**Supportive laboratory investigations:**
• Total Leucocytes Count during early stages may be normal but may be elevated to more than 10,000/cu mm later in the course of disease.
• Thrombocytopenia (low platelet count), usually <1,50,000/cu mm is seen in majority of patients.
• Elevated liver transaminases (AST, ALT) is also seen in many patients.
Diagnosis...Bedside

• Isolation of *O. tsutsugamushi* can be done in cell culture or in inoculated mice.

• Chest radiography may reveal pneumonitis especially in the lower lung fields.

• In meningitis, there is a predominant mononuclear response
Treatment

• **Pediatric treatment**: Azithromycin for less than 8 years: 10mg/kg orally single dose

• For more than 8 years: Doxycycline 2.2mg/kg orally twice daily for 3 days after resolution of fever (usually 5-10 day course)
Adult treatment:

- Doxycycline (100 mg bid orally for 7–15 days),
  - but can also be given in a single dose or for short periods (3 to 7 days), although relapse can occur.

- Azithromycin (500 mg orally for 3 days) especially for the pregnant patients.

- Alternatives:
  - Ciprofloxacin 10 mg/kg twice daily for 5-10 days
  - Chloramphenicol 25 mg/kg/dose 6 hourly for 5-10 days
  - Rifampicin
Treatment

• Rifampin (600 to 900 mg/day) may be used especially in doxycycline resistant areas and a combination therapy is recommended.
  – Known to have a good CNS penetration, hence valuable in Scrub Meningitis.
Treatment

- Rapid defervescence after antibiotic treatment is so characteristic that it is used as a diagnostic test for O. tsutsugamushi infection (resolution of fever expected within 24-36 hours.)

- Failure of defervescence should lead to suspicion of other diseases like Malaria.
• **Prophylaxis:**

  • Single oral dose of chloramphenicol or tetracycline given every five days for a total of 35 days, with 5-day non-treatment intervals (for endemic regions).

  • No vaccine is available for scrub typhus.
Prevention/Control/Precautions:
- Early case detection by healthcare workers is needed.
- Other strategies are to make public aware and give preventive information like:
  - Wear protective clothing including boots
  - Insect repellents containing benzyl benzoate, DEET, permethrin, diethyl toluamide, during travel in rural areas of endemic countries.
  - Do not sit or lie on bare ground or grass; use a suitable ground sheet or other ground cover
  - Clear vegetation spray insecticides on the soil to break up the cycle of transmission
Conclusion

• Common disease
• Changes in presentation, disease distribution
• Acute Encephalitis syndrome
• Complications
• Poor prognostic markers
• Good index of suspicion can save life
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Thank You