

FEVER CLINICS

All about acute undifferentiated febrile diseases

Abrupt onset of fever of unknown origin, headache and rashes in an elderly farmer

CASE PROFILE*

Reason for admission

- A 60-year old male farmer presented to the physician with abrupt onset of fever of unknown origin for 5 days, headache and rashes.
- There was no history of travel to another place.
- On physical examination, an eschar was observed in the left upper arm near the axilla.

Laboratory investigations

- Platelet count: 70,000/MI
- Aspartate aminotransferase: 144 U/L
- Alanine aminotransferase: 444 U/L
- Malaria strip test and blood smear for malarial parasite were negative
- Weil Felix reaction and IgM ELISA for scrub typhus (*Orientia tsutsugamushi*) was positive.

Physical examination

An eschar was observed in the left upper arm near the axilla

Travel history

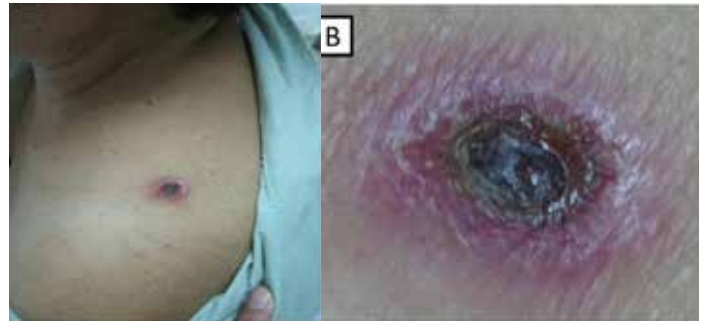
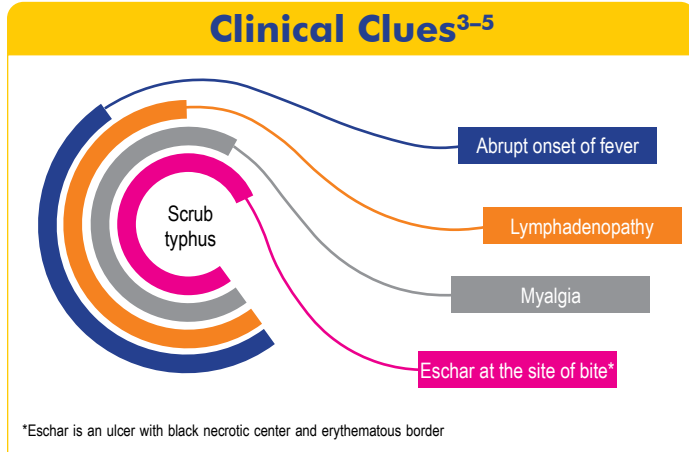
Nil

Diagnosis: Scrub typhus

*Denotes a fictitious case

Scrub typhus: Diagnosis and management

Scrub typhus is a rickettsial infection caused by *Orientia tsutsugamushi* and is transmitted to humans through vector mites^{1,2}



- Lately it is presented as painless ulcers (5–20mm) with black necrotic center surrounded with pink areola (resembling cigarette burn)⁶
- Seen in relatively warm and moist body parts (neck, arm pits, waist, groins, under the breasts)^{1,5,6}

Eschar: A typical scrub typhus marker

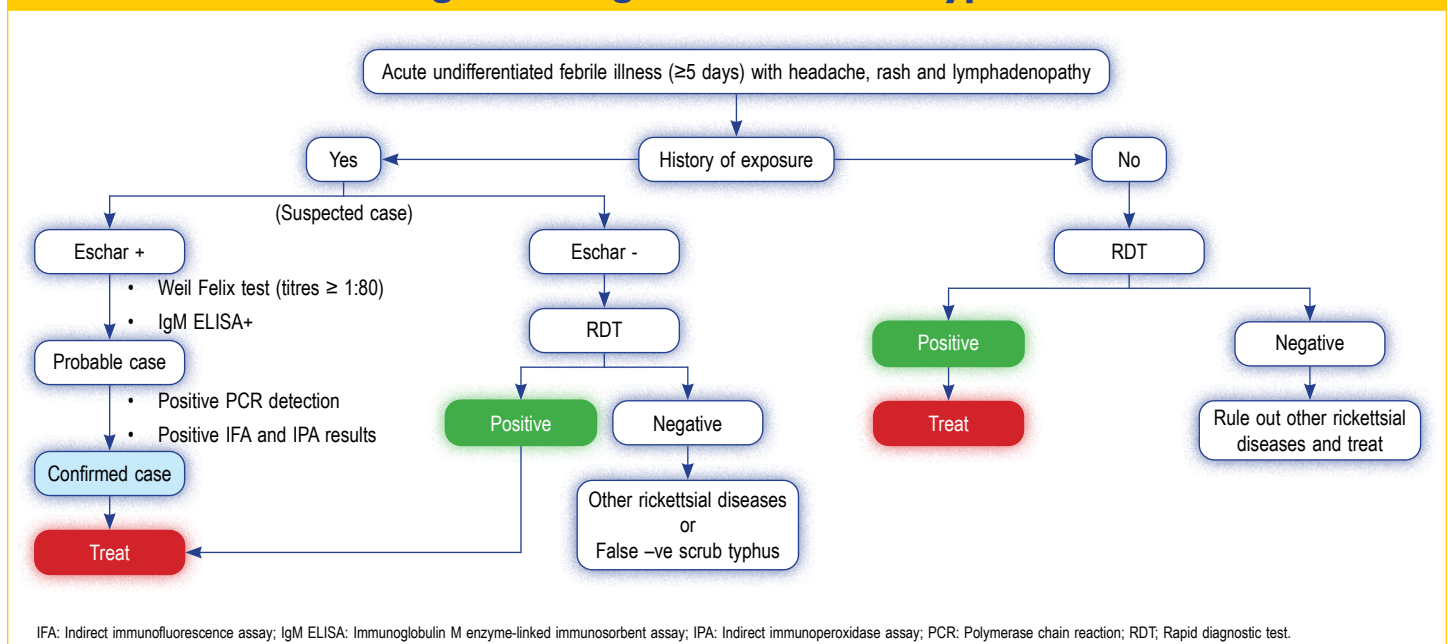
- The incubation period is around 10–12 days. It can also vary from 6 to 21 days³
- Maculopapular rashes develop on the trunk by the end of one week, which may spread to the limbs³
- Eschar at the site of vector bite is a hallmark diagnostic feature for scrub typhus, occurring few days after vector bite¹
- Eschar begins as a papular lesion which further enlarges and undergoes central necrosis

How to predict scrub typhus?⁴

Parameters supporting scrub typhus diagnosis	Parameters against scrub typhus diagnosis
<ul style="list-style-type: none"> • Eschar • Regional lymphadenopathy • Fever ≥ 8 days • CRP > 32 mg/L • ALT/AST > 1 • Defervescence within 48–72 hours of specific therapy 	<ul style="list-style-type: none"> • Bone pain or bleeding manifestations or WBC $< 5,000/\text{mm}^3$ or AST > 500 U/L (Dengue) • Loose stools (Enteric fever) • Bilirubin > 2 mg/dL or ALT < 100 U/L (Malaria) • Bilirubin > 2 mg/dL or ALT > 500 U/L (Hepatitis A)

ALT: Alanine aminotransferase; AST: Aspartate aminotransferase; CRP: C-reactive protein; WBC: White blood cells.

Diagnostic algorithm of scrub typhus^{1,6}



Complications of scrub typhus

The complications associated with scrub typhus are:^{3,5}

- Myocarditis
- Pneumonia
- Meningoencephalitis
- Acute renal failure
- Shock
- Acute respiratory distress syndrome (ARDS)
- Multiorgan dysfunction syndrome (MODS)

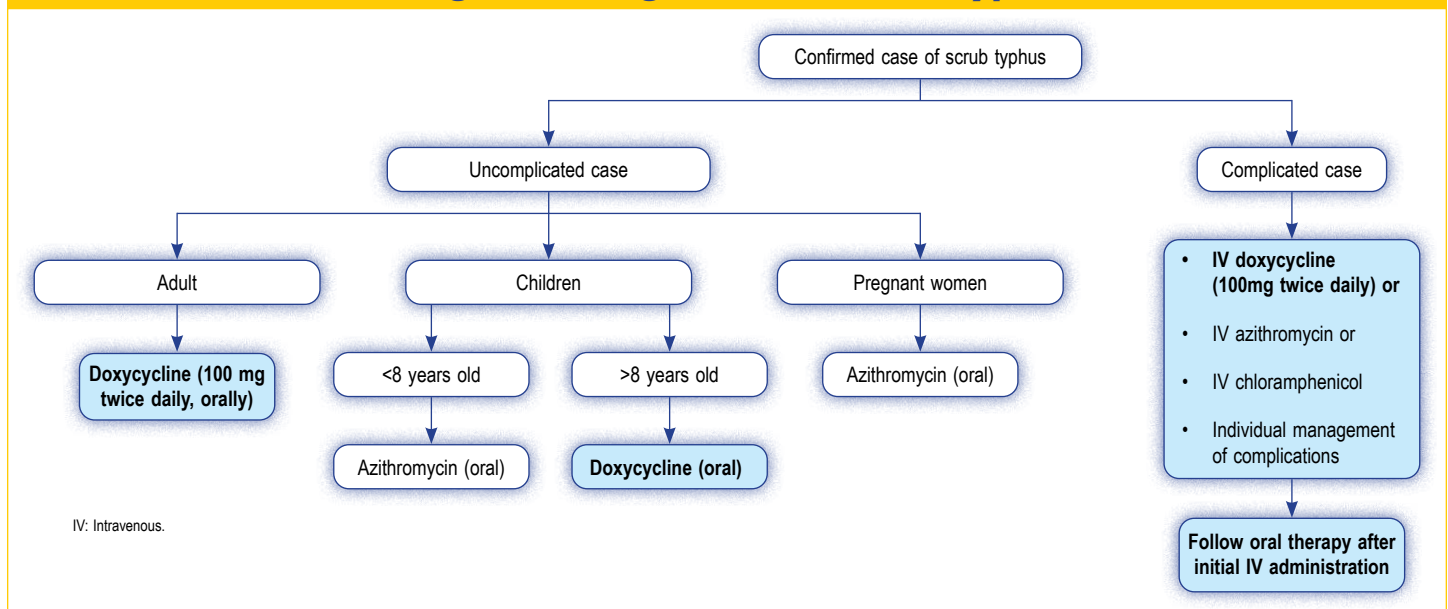
- Gastro-intestinal bleeding
- Sepsis

All cases of scrub typhus should be treated with antibiotics

Recommended antibiotics are:^{1,6}

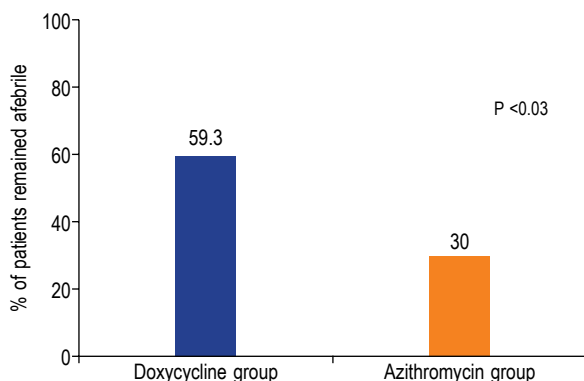
- **Doxycycline**
- Azithromycin
- Chloramphenicol

Management algorithm of scrub typhus^{1,6}



Doxycycline is better than azithromycin in scrub typhus

Doxycycline therapy showed higher fever resolution rate compared to azithromycin⁷



Clinical pearls

- Doxycycline is recommended as the drug of choice for scrub typhus
- Doxycycline therapy should be initiated in all categories of complicated scrub typhus
- Doxycycline therapy is better than azithromycin for scrub typhus

References: 1. Rahi M, et al. In: Thomas S. (eds) Rickettsiales. Springer, Cham. 2016. 2. Chaudhry R, et al. Indian J Med Res. 2019;149(6):790–4. 3. Chakraborty S, et al. Indian J Dermatol. 2017;62(5):478–85. 4. John Antony Jude Prakash. Res Rep Trop Med. 2017;8:73–83. 5. Jain D et al. Med Pharm Rep. 2019;92(1):36–42. 6. National guideline for prevention, treatment and control of scrub typhus in Bhutan, 2016. Available from http://www.health.gov.bt/wp-content/uploads/afd-files/2014/11/STyphus_Guideline.pdf. Last accessed on 19 Feb, 2020. 7. K. Phimda, et al. Antimicrobial Agents and Chemotherapy. 2007;51(9): 3259–63.

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DOXT Injection

Doxycycline hydrochloride 100 mg



Dr. Reddy's Laboratories Ltd., Global Generics India, 7-1-27, Ameerpet, Hyderabad - 500 016, India. www.drreddys.com

Composition: Each capsule contains Doxycycline 100mg + Lactic acid bacillus spores-5 billion. **Therapeutic Indications:** For adult patients prone to intra-abdominal bacterial infection & antibiotic associated diarrhoea. **Dosage and Administration:** In Adults for the treatment of acute infections is two capsules per day (as a single dose or in divided doses) followed by a maintenance dose of one capsule/day. In the management of more severe infections, two capsules daily should be given throughout treatment. **Contraindications:** Doxycycline is contraindicated when hypersensitivity to any of the Tetracycline's. **Drug interactions:** Anticoagulant, co-administration of Tetracyclines with penicillin, Antacid, OC pills, Antiepileptic's etc. **Warnings & Precautions:** During tooth development (last half of pregnancy, infancy and childhood to the age of 8 years) may cause permanent discoloration of the teeth (yellow-gray-brown). Evaluate for Clostridium difficile-associated diarrhoea. Limit sun exposure. Overgrowth of non-susceptible organisms, including fungi & superinfection. Dosage adjustment required in patients with hepatic impairment. **Adverse reactions:** In patients receiving tetracyclines include anorexia, nausea, vomiting, diarrhoea, rash, photosensitivity, urticaria, and hemolytic anemia. **Special population:** Can be prescribed in the elderly in the usual dosages. Not recommended for use in paediatric population due to complexity of dose calculations with a combined dosage form. Pregnancy Category D. Tetracyclines are excreted in human milk; Doxycycline use during nursing should be avoided if possible.

Further information available upon request.

Date: March 20, 2020

Composition: Combi-pack contains (A) Vial of Doxycycline for injection USP 100mg (B) Ampoule of Sterile water for Injection IP 10ml. **Therapeutic Indications:** Broad spectrum antibiotic for infection by Rickettsia, sexually transmitted disease, Respiratory tract infection, specific bacterial infections etc. **Dosage and Administration:** In Adults usual dosage is 200 mg on first day in one or two infusions, subsequently as per disease severity 100/200 mg daily. In Syphilis dosage can be 300 mg daily for 10 days. Infusion should be for 1-4 hours. In Paediatric patients weighing >45kg adult dose can be used. In paediatric patients weighing <45kg and greater than 8 years of age dose of 2.2mg/kg of body weight can be administered every 12 hours. **Contraindications:** Doxycycline is contraindicated when hypersensitivity to any of the Tetracycline's. **Drug interactions:** Anticoagulant, co-administration of Tetracyclines with penicillin, Antacid, OC pills, Antiepileptic's etc. **Warnings & Precautions:** during tooth development (last half of pregnancy, infancy and childhood to the age of 8 years) may cause permanent discoloration of the teeth (yellow-gray-brown). Evaluate for Clostridium difficile-associated diarrhoea. Limit sun exposure. Overgrowth of non-susceptible organisms, including fungi & superinfection. **Adverse reactions:** In patients receiving tetracyclines include anorexia, nausea, vomiting, diarrhoea, rash, photosensitivity, urticaria, and hemolytic anemia. **Special population:** Pregnancy Category D. Tetracyclines are excreted in human milk. Doxycycline use during nursing should be avoided if possible.

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