

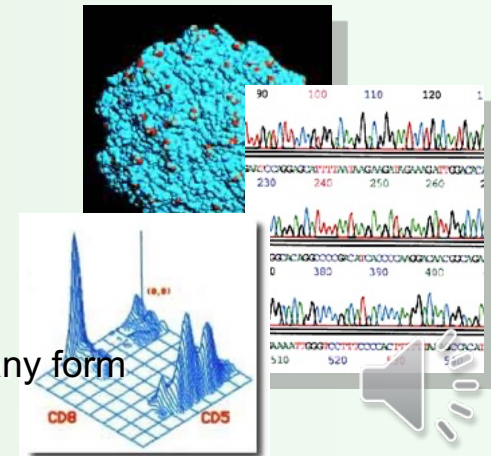
Bugs and Bacteria: Rickettsia

Sheldon Campbell M.D., Ph.D.

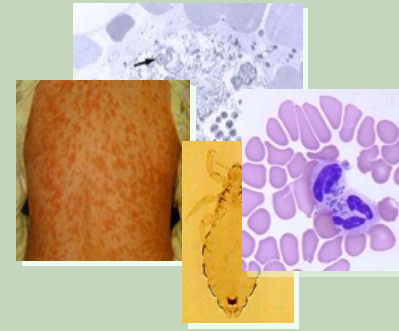
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Pathology and Laboratory Medicine, VA Connecticut

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Practical Bacterial Taxonomy



Medically Important Bacteria

**Normal (pyogenic) Bacteria:
Grow easily in routine
culture**

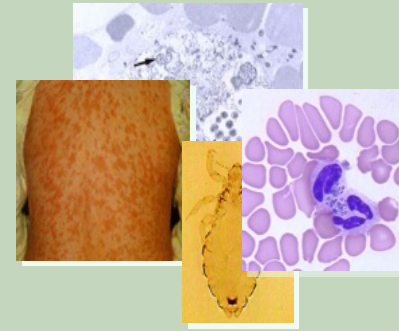
**Weirdo Bacteria:
Often require special procedures**

Aerobic and facultative

**Anaerobes:
Above and below the
diaphragm**



Practical Taxonomy



Weirdo Bacteria

Slow-Growing
Mycobacteria,
Nocardia

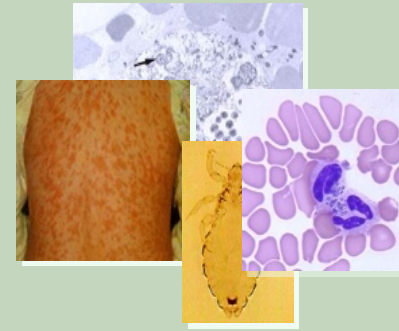
Spirochetes
Treponema
(syphilis), *Borrelia*
(Lyme)

NO Cell Wall / Cell-associated
Mycoplasma,
Chlamydia,
Rickettsia, *Ehrlichia*

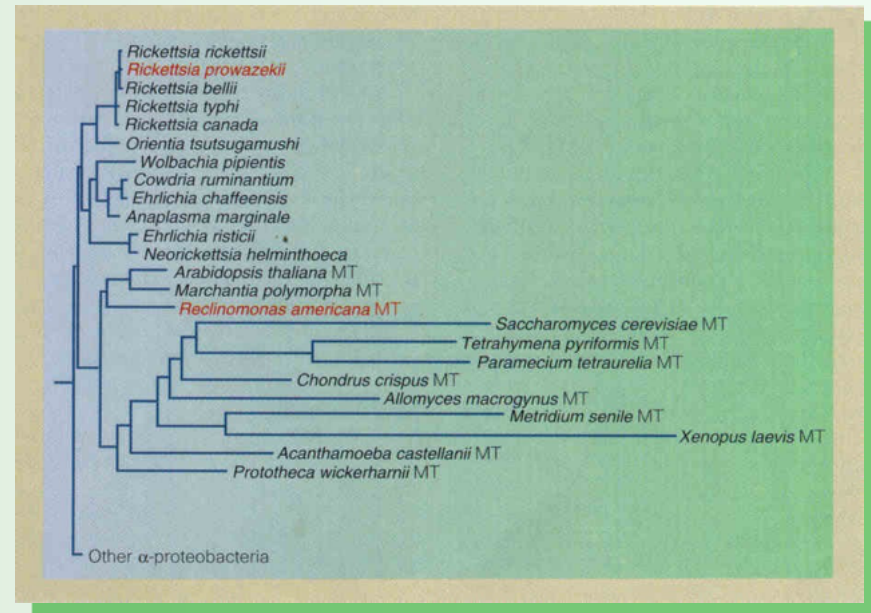
Otherwise Difficult
to Grow
Legionella,
Bartonella



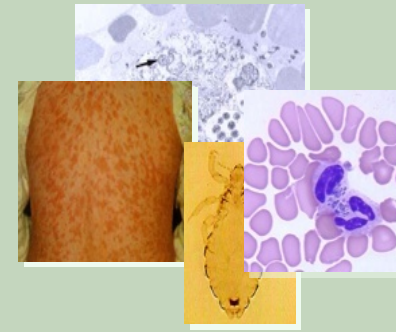
Rickettsiae Basics



- Small, pleiomorphic, **obligate intracellular** bacteria
 - +/- in a vacuole
- **Not visible** on Gram stain
 - **Lack cell wall**
- Stain with acridine orange
- **Do not grow** in typical culture systems
- Ancestral forms became eukaryotic mitochondria



Rickettsia: Spotted Fever Group Diseases

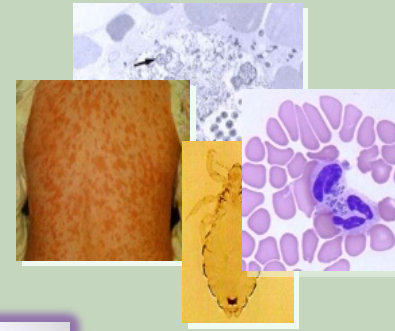


| Disease | Organism | Vector | Geography |
|------------------------------|----------------------|--------|--------------------|
| Rocky Mountain Spotted Fever | <i>R. rickettsii</i> | tick | Western hemisphere |
| Boutonneuse | <i>R. conorii</i> | tick | Africa, India |
| Queensland tick typhus | <i>R. australis</i> | tick | Australia |
| N. Asian tick typhus | <i>R. sibirica</i> | tick | Siberia, Mongolia |
| Rickettsialpox | <i>R. akari</i> | mite | USA, Russia, Korea |

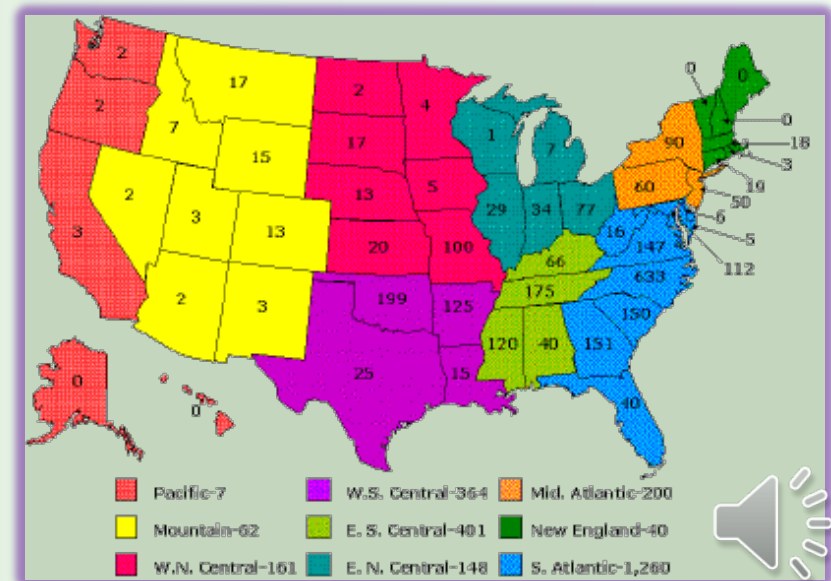


Rickettsia: RMSF

Epidemiology

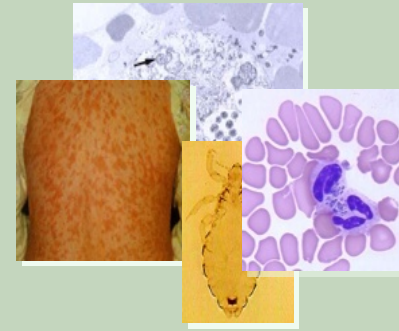


- Spread primarily by *Dermacentor* ticks in the US
- Highest risk in SE, Midwest, northern Rockies
- Tick is vector and main reservoir as well
- Animal reservoirs include dogs and wild animals



Rickettsia: RMSF

Pathogenesis 1

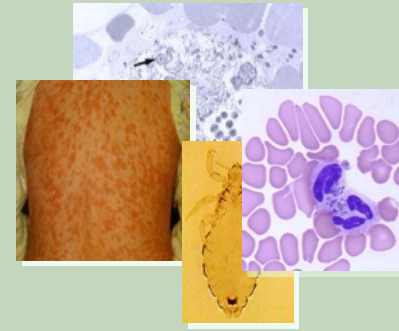


- Organism
 - injected into skin
 - spreads via lymphatics to bloodstream
 - infects **vascular endothelium**
- Spread of organism is directly cell-cell
 - Direct damage by intracellular growth of organisms
 - Rash forms in areas of contiguous vascular damage



Rickettsia: RMSF

Pathogenesis 2

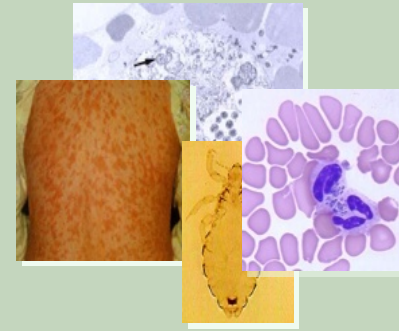


- Loss of vascular integrity
 - Edema; systemic or pulmonary
 - Hypovolemia
 - Hypoalbuminemia
 - Hypotension
- Secondary host inflammatory response
 - Local end-organ injury
 - Thrombocytopenia



Rickettsia: RMSF

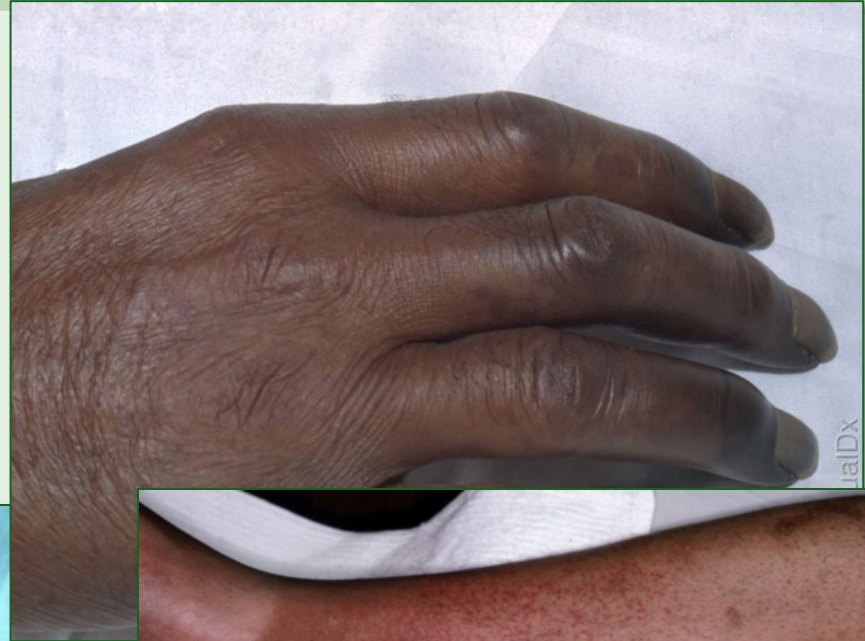
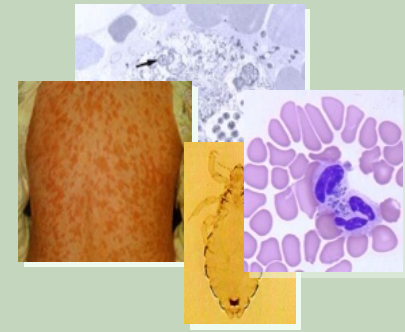
Clinical



- Incubation 2-14 days, median 7
 - Fever, myalgia, headache
 - GI symptoms
- Rash
 - 90% of patients have the rash
 - Can occur up to 5d after fever
 - **Extremities first**, then spreads centrally (“centripetal”)
- “Rockies on the wRist”



RMSF on Darker Skin



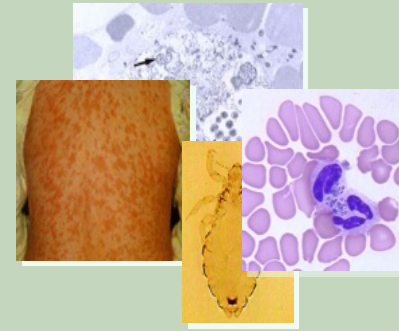
From VisualDx

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Rickettsia: RMSF

Complications

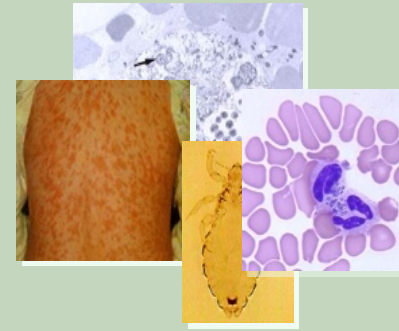


- Neurological:
meningitis/meningoencephalitis
– frequent sequelae
- Renal failure
- Pulmonary edema/interstitial pneumonia
- Skin necrosis/gangrene



Rickettsia: RMSF

Diagnosis

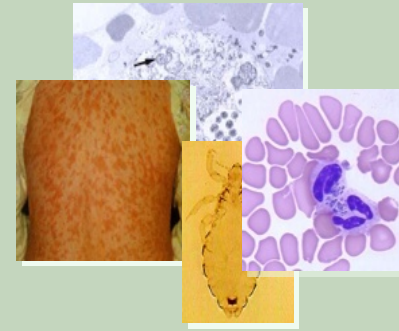


- Characteristic rash (only present in ~90%)
- Clinical presentation and risk factors
- Laboratory
 - Serology only turns positive during recovery
 - **Immunohistology of skin biopsy**
 - PCR on skin biopsies possible



Rickettsia: RMSF

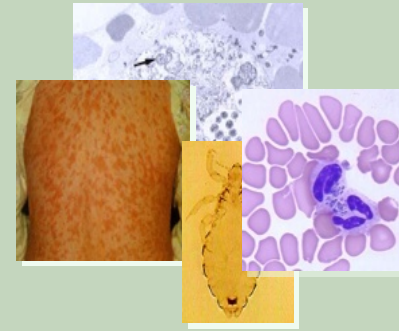
Therapy and Prognosis



- Outcome related to **rapid diagnosis and therapy**; clinical diagnosis is critical
- Treat with a tetracycline or chloramphenicol
- Good prognosis
 - Early treatment
- Bad prognosis
 - Older age
 - Males
 - Dark-skinned persons (rash less apparent)



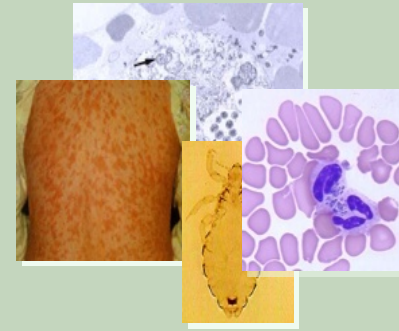
Rickettsia: Other spotted fevers



- Worldwide geographic distribution
- A wide variety of species contribute
- Most cause benign, self-limited illness, but some can be more severe



Rickettsia: Typhus group Diseases



| Disease | Organism | Vector | Eschar |
|-----------------|-------------------------|------------|--------|
| Epidemic typhus | <i>R. prowazekii</i> | body louse | No |
| Brill-Zinsser | <i>R. prowazekii</i> | - | No |
| Murine typhus | <i>R. typhi</i> | rat flea | No |
| Scrub typhus | <i>R. tsutsugamushi</i> | mite | Yes |

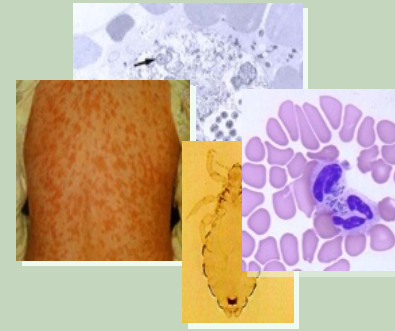
In all forms except scrub typhus, rash progresses from **trunk** to extremities.

The organism infects vascular endothelial cells

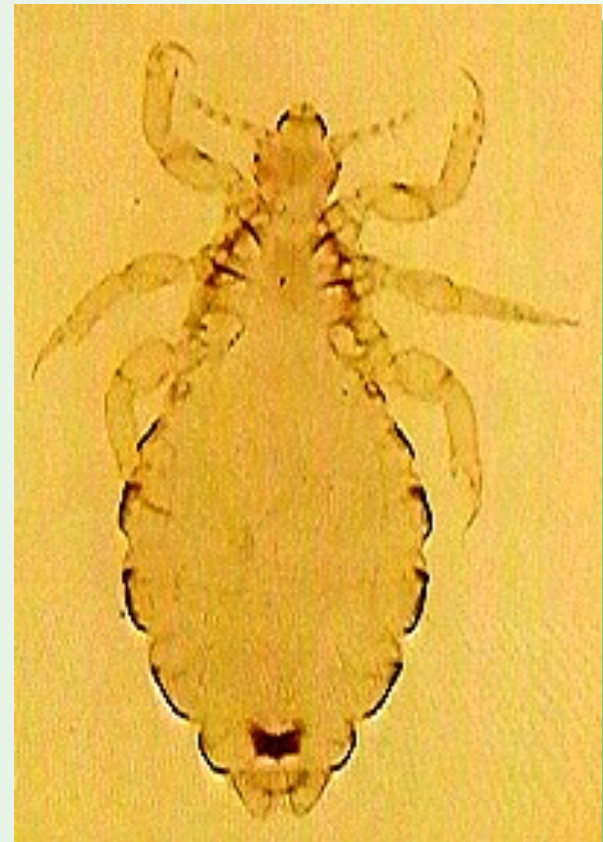


Rickettsia: Typhus group

Epidemic Typhus -- Agent & Vector

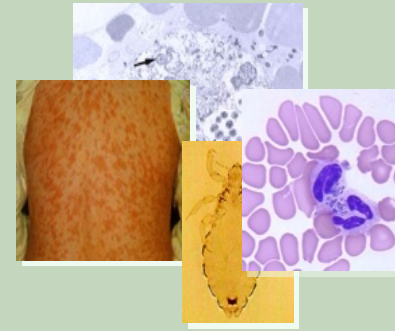


- *R. prowazekii*
- Spread by the **human body louse** (*Pediculus spp.*). Disease is transmitted when louse feces are scratched into a bite



Rickettsia: Typhus group

Epidemic Typhus -- Epidemiology

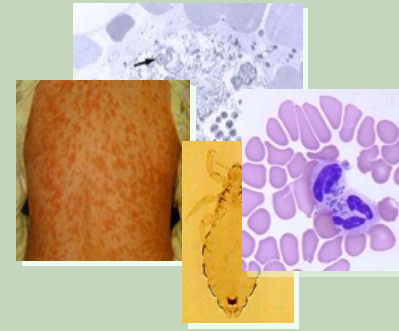


- Incidence parallels **war and famine**; 30 million cases between 1918-22
- Conditions favoring louse infestation -- winter and catastrophe
- Rural highlands of Africa and S. America
- Rare cases acquired in southern US
 - Southern flying squirrel reservoir host



Rickettsia: Typhus group

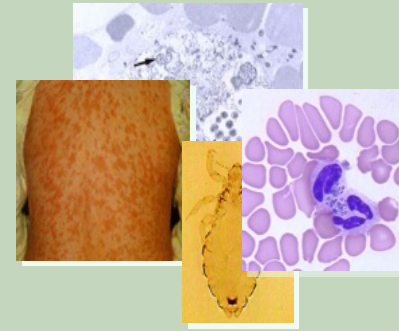
Epidemic Typhus -- Clinical



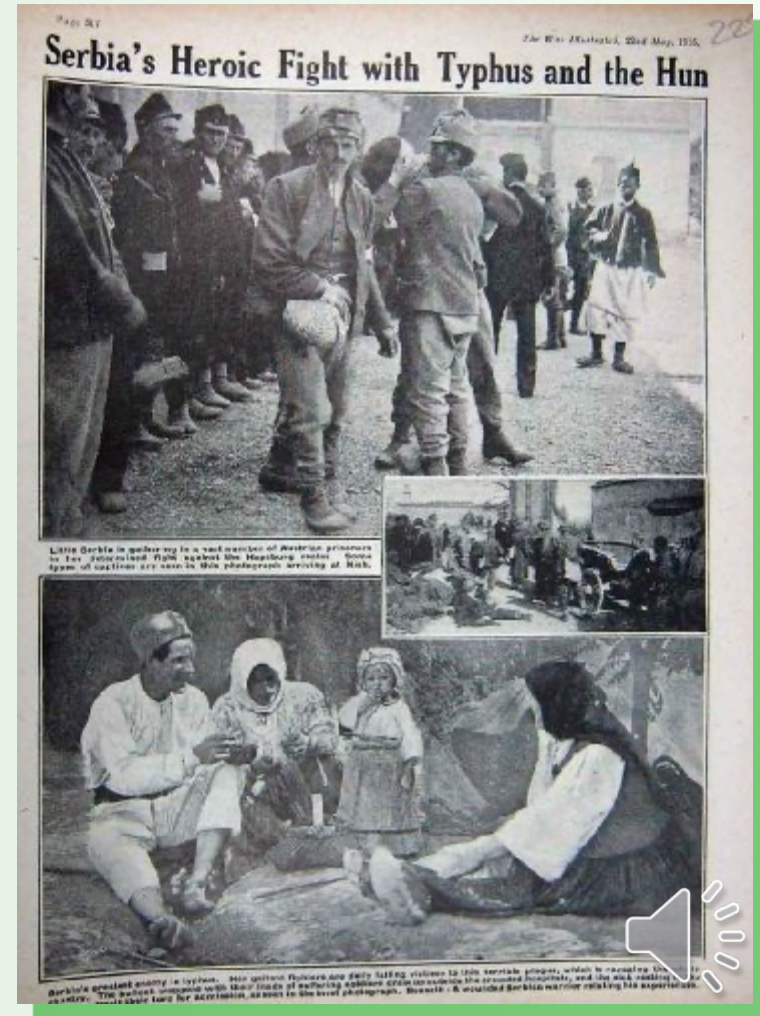
- Abrupt and severe onset
- Headache, fever, myalgia, rash
- Rash
 - begins on **trunk and axilla** and spreads peripherally (“centrifugal”)
 - begins as pink, blanching macules, darkens, sparing palms and soles
- Mortality up to 40% in vulnerable populations
 - Less with available therapy
- “Typhus on the Trunk”



Epidemic Typhus in History

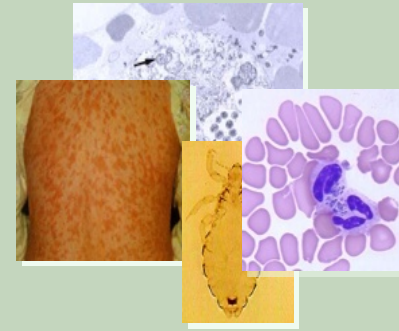


- Enormous impact on history
 - Probably one of the Plagues of Athens
 - During Napoleon's retreat from Moscow in 1812, more French soldiers died of typhus than were killed by the Russians.
 - During World War I typhus caused three million deaths in Russia and more in Poland and Romania.
 - Major contributor to concentration-camp deaths during WWII; Anne Frank apparently died of typhus.





Rickettsia: Murine Typhus



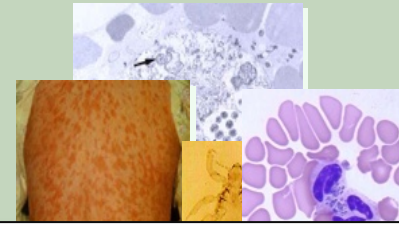
- *R. typhi*
- Worldwide; temperate and subtropical near oceans
- Reservoir is usually a rat; vector is fleas
- Abrupt onset, usually milder than epidemic typhus
- 50% develop a rash
 - Petechial in <10%
 - no particular pattern of development
- Fever, headache, chills, myalgia, N&V
- Rare neurological or organ dysfunction



Rickettsia: Typhus group

Scrub typhus:

Epidemiology



- *Orienta tsutsugamushi*
- Endemic to Far East
 - Reported recently in the Middle East, southern Chile, and Africa
- Mice are reservoir
- Spread by chiggers (larval mites)

IMAGES IN CLINICAL MEDICINE

Scrub Typhus

Chang-Seop Lee, M.D., Ph.D., and Jeong-Hwan Hwang, M.D.
N Engl J Med 2015; 373:2455 | December 17, 2015 | DOI: 10.1056/NEJMicm1503639

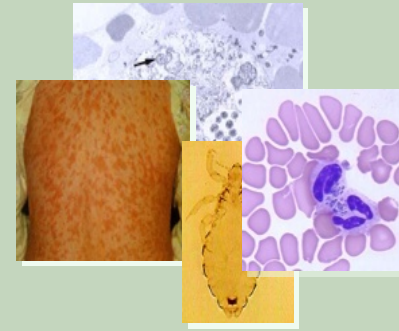
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Article [Slide](#)

A 65-year-old woman was admitted with fever and rash that had developed 3 days and 1 day before admission, respectively. On physical examination, an erosion 1.5 cm by 1.5 cm with a torn bulla was observed in the right axilla, and a generalized, nonpruritic, maculopapular rash was found over the whole body (Panels A and B). The daily appearance of eschar was evaluated by dermoscopy, and routine photography was performed from the first through the fourth hospital day (Panels C

Rickettsia: Typhus group

Scrub Typhus: Clinical



- Organism proliferates locally at bite site
 - Papule → Ulcer → **Eschar**
- Tender lymphadenopathy, regional → systemic
- Sudden onset of fever (up to 104°-105°F), chills, headache, myalgia
- Rash in <50%, trunk to extremities
- Some patients have neurological complications
- Mortality 0-30%, tending to zero with effective therapy.

Detection of *Orientia* spp. Bacteria in Field-Collected Free-Living *Eutrombicula* Chigger Mites, United States

Kaiying Chen, Nicholas V. Travanty, Reuben Garshong, Dac Crossley,
Gideon Wasserberg, Charles S. Apperson, R. Michael Roe, Loganathan Ponnusamy



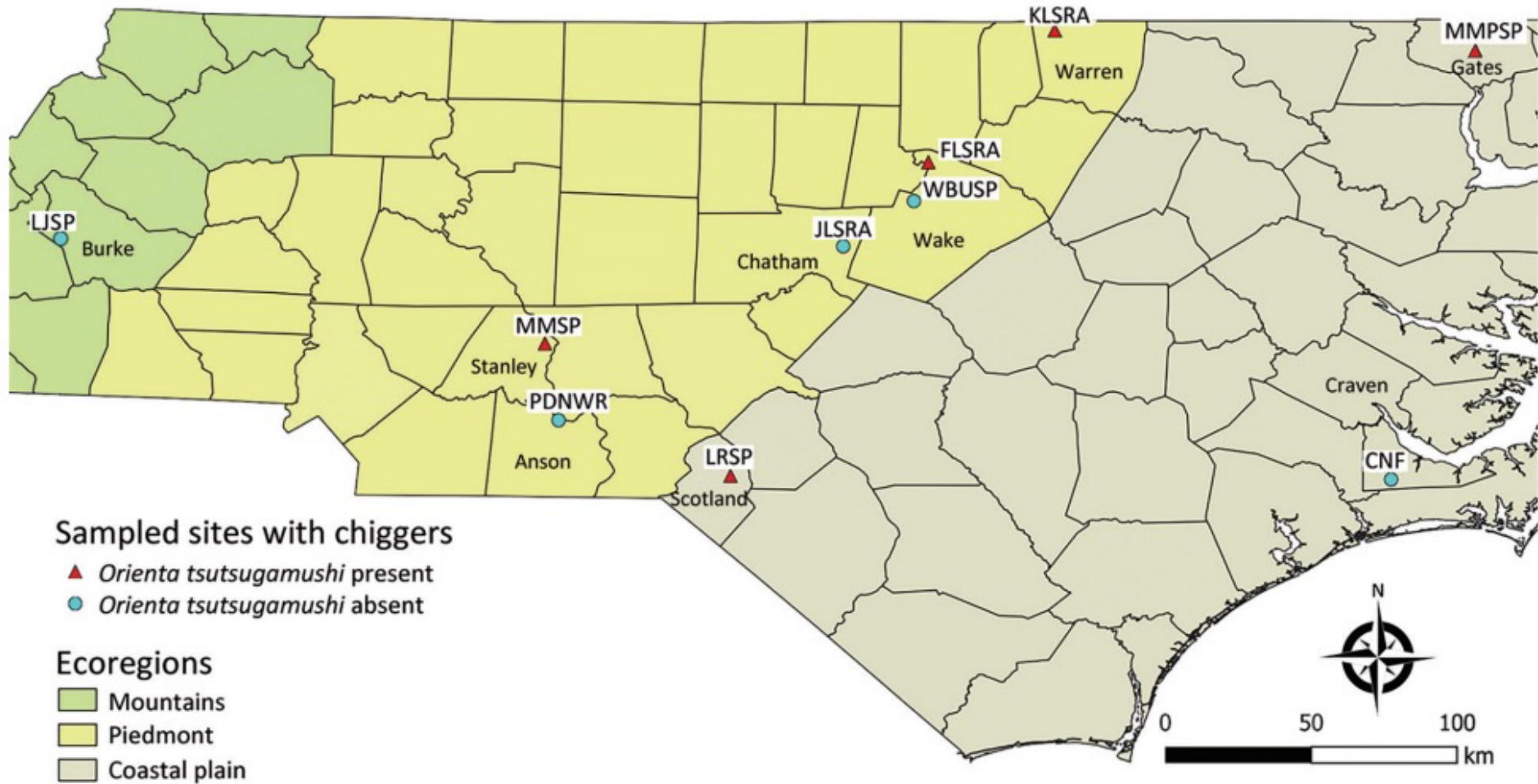
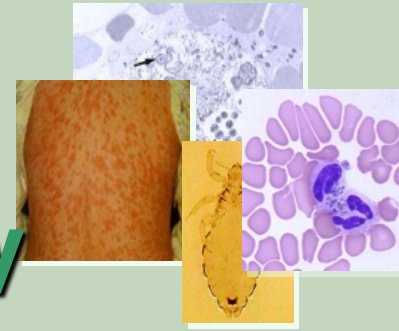


Figure 1. Study area for investigation of *Orientia* spp. bacteria in field-collected free-living *Eutrombicula* chigger mites, North Carolina, USA. Free-living chiggers were collected from 10 sites in 8 counties. CNF, Croatan National Forest; FLSRA, Falls Lake State Recreation Area; JLSRA, Jordan Lake State Recreation Area; KLSRA, Kerr Lake State Recreation Area; LJSP, Lake James State Park; LRSP, Lumber River State Park; MMPSP, Merchant Millpond State Park; MMSP, Morrow Mountain State Park; PDNWR, Pee Dee National Wildlife Refuge; WBUSP, William B. Umstead State Park.

Rickettsia: Typhus group

All Types: Diagnosis/Therapy



- Diagnosis is usually clinical, with serologic confirmation
 - PCR or antigen tests investigational
- All respond to **tetracyclines** or **chloramphenicol**
 - Quinolones and macrolides are promising as well
 - Defervescence and reduction of symptoms usually rapid after appropriate treatment – if not, suspect another illness

