Rickettsial Diseases (AFRICOM Focus), Q Fever, and Lyme Disease

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10 February 2012

*Acknowledgement: MAJ Paige Waterman, MD
Objectives

• Familiarization with:
  – Classification
  – Geographic distribution
  – Vector transmission
  – Clinical presentations
  – Disease specific features (risk factors, treatment)

• Clinical case exercises
# Common Rickettsial Infections

<table>
<thead>
<tr>
<th></th>
<th>TICK-BORNE</th>
<th>FLEA-BORNE</th>
<th>LOUSE-BORNE</th>
<th>MITE-BORNE</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Rickettsiae</strong></td>
<td></td>
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</tr>
</tbody>
</table>
| Spotted fever group | R. rickettsii  
R. conorii  
R. Japonica  
R. africae  
R. parkeri | R. felis | R. akari |            |
| Typhus group        |            | R. typhi   | R. prowazekii |            |
| Scrub typhus (Orientia) |            |            |             | O. tsutsugamushi |
| Anaplasma           | A. phagocytophilum |            |             |            |
| Ehrlichia           | E. chafeensis  
E. ewingii  
E. canis |            |             |            |
| Q Fever (Lyme)      | Coxiella burnetii* |            |             |            |
|                     | B. borgdorferi |            |             |            |
## Common things being common

<table>
<thead>
<tr>
<th>Destination</th>
<th>No. travelers</th>
<th>SFG rickettsiosis</th>
<th>TG rickettsiosis</th>
<th>Indeterminate SFG/TG rickettsiosis</th>
<th>Scrub typhus</th>
<th>Anaplasmosis</th>
<th>Acute Q fever</th>
<th>Bartonellosis</th>
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<td>Western Europe</td>
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<td>Eastern Europe</td>
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<td>Sub-Saharan Africa</td>
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<td>South central Asia</td>
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<tr>
<td>Southeast Asia</td>
<td></td>
<td>3</td>
<td>6</td>
<td></td>
<td>5</td>
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<tr>
<td>Australia/New Zealand</td>
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<td>1</td>
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<td></td>
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<td>Oceania</td>
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<td></td>
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<td></td>
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<tr>
<td>North America</td>
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<td>1</td>
<td></td>
<td></td>
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<tr>
<td>Central America</td>
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<td>3</td>
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<td></td>
<td></td>
</tr>
<tr>
<td>Caribbean</td>
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<td>3</td>
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<tr>
<td>South America</td>
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<td>Unknown</td>
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<td></td>
<td></td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td></td>
<td>231</td>
<td>10</td>
<td>4</td>
<td>16</td>
<td>1</td>
<td>11</td>
<td>7</td>
</tr>
</tbody>
</table>

*SFG, spotted fever group; TG, typhus group.*
## Spotted fever group

<table>
<thead>
<tr>
<th>Tick</th>
<th>Flea</th>
<th>Mite</th>
</tr>
</thead>
<tbody>
<tr>
<td><em>R. rickettsii</em></td>
<td></td>
<td></td>
</tr>
<tr>
<td><em>R. conorii</em></td>
<td><em>R. felis</em></td>
<td><em>R. akari</em></td>
</tr>
<tr>
<td><em>R. Japonica</em></td>
<td></td>
<td></td>
</tr>
<tr>
<td><em>R. africae</em></td>
<td></td>
<td></td>
</tr>
<tr>
<td><em>R. parkeri</em></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
R. africae (African tick bite fever)

Distribution map of the principal tick vectors of Rickettsia africae. Dotted line denotes approximate border between A hebraeum (in southern Africa) and A variegatum.

Lancet ID 2003;3:557-564
R. africae (African tick bite fever)

• Incubation 5-7 days
• Acute, febrile, and influenza-like illness
  – severe headache, nausea, fatigue
  – Prominent myalgias (esp. neck)
• Inoculation eschar(s)
  – black crusts surrounded by a red halo
• +/- vesicular rash/aphthous ulcers
• Regional lymphadenitis
• ~50% of patients have multiple eschars
• Rare complications; recovery is the rule

Lancet ID 2003;3:557-564
R. africae (African tick bite fever)
**R. africae** (African tick bite fever)

- Habitat: tall grasses/bush; shade; rainy season
- Typical victims: soldiers, safaris, campers, cattle farmers
  - Aggressive: single host attacked by several ticks, multiple times
- Diagnosis: difficult (clinical)
- Treatment: Doxycycline 100mg BID 7d
  - or until 48hrs post defervescence
- Prevention: PPE; skin exam, careful tick removal
R. conorii (Mediterranean spotted fever AKA Boutonneuse fever)

Figure 4. Distribution of the cases of Mediterranean spotted fever (MSF) in the world and incidence of the disease in countries where MSF is endemic.
**R. conorii** (Mediterranean spotted fever AKA Boutonneuse fever)

<table>
<thead>
<tr>
<th>Rickettsia</th>
<th>Vector</th>
<th>Inoculation</th>
</tr>
</thead>
<tbody>
<tr>
<td>R. conorii conorii</td>
<td>Rhipicephalus sanguineus var. sanguineus, Haemaphysalis leporispalustris</td>
<td>100</td>
</tr>
<tr>
<td>R. conorii israelensis</td>
<td>Rhipicephalus sanguineus</td>
<td>100</td>
</tr>
<tr>
<td>R. conorii caspia</td>
<td>Rh. sanguineus var. orbiculatus, Boophilus microplus</td>
<td>100</td>
</tr>
</tbody>
</table>

**Tâche noire**

Unlike African tick bite fever, eschars RARELY multiple in MSF

EID. 2008;14(9):1360-1367
**R. conorii** (Mediterranean spotted fever AKA Boutonneuse fever)

- Incubation 5-7 days
- Fever, HA, maculopapular rash; tache noire
- Ecology of exposure: peridomestic; buildings where dogs kept
- Diagnosis tough (clinical) +/- biopsy (eschar); serology (IFA), PCR, culture
- Treatment: Doxy 100mg BID 5-10 days
- Prevention: PPE
R. akari (Rickettsialpox)

- Morphologically identical to R. rickettsii
- Vector: house mouse mite
  - Liponyssoides sanguineus
- Reservoir: common house mouse
- “urban zoonosis” since 1950s
  - NYC, Boston, West Hartford, Philadelphia, Pittsburgh, Cleveland
- Worldwide: Russia, Korea, South Africa

J Am Acad Dermatol Nov 2004
R. akari (Rickettsialpox)

• Incubation 9-14 days
• Painless bite
• Eschar develops within 1-2 days
• Fever, malaise 1 week later
• Papulovesicular eruption (rash) 2-3 days later
  – Trunk, extremities, oral mucosa
• Generalized lymphadenopathy
• Self-limited (14-21 days)
Rickettsialpox
**R. akari** (Rickettsialpox)

- Labs: mild leukopenia; thrombocytopenia, mild proteinuria
- Definitive Dx: rise in serum *R. akari* Ab during convalescence (CF, IFA)
  - Cross-reactive with RMSF Ab
- Treatment: Doxycycline 100mg BID until clinically improved for 48hrs (~ 5-7 days)
- Prevention: PPE
## "Pox" DDX

<table>
<thead>
<tr>
<th>Feature</th>
<th>Rickettsialpox</th>
<th>Chickenpox&lt;sup&gt;2,3&lt;/sup&gt;</th>
<th>Smallpox (variola major)&lt;sup&gt;2,3&lt;/sup&gt;</th>
</tr>
</thead>
<tbody>
<tr>
<td>Eschar</td>
<td>Yes</td>
<td>No</td>
<td>No</td>
</tr>
<tr>
<td>Incubation period</td>
<td>9-14 days</td>
<td>14 days (range 10-23)</td>
<td>12 days (range 10-14)</td>
</tr>
<tr>
<td>Prodrome</td>
<td>Usually mild, may be severe. Fever, malaise, and headache.</td>
<td>Absent or mild and brief (less than one day)</td>
<td>Usually severe with high fever, headache, backache. Vomiting and severe abdominal pain may be present. Lasts 2 to 4 days.</td>
</tr>
<tr>
<td>Timing and evolution of lesions</td>
<td>Lesion develops at the site of the bite within 24 to 48 hrs and evolves into eschar. Rash begins 2 to 3 days after prodrome. Papules may eventuate in papulovesicles.</td>
<td>Lesions occur in “crops” over 2 to 4 days. Different stages characteristic: macules, papules, vesicles, pustules, crusts</td>
<td>Emerge over 1-2 days and then progress at same rate. The lesions progress over several days from macules (day 1), to papules (day 2), to vesicles (days 3-5), to pustules (days 7-14), to scabs (day 14-20).</td>
</tr>
<tr>
<td>Pruritus/pain</td>
<td>Exanthem usually asymptomatic; occasional pruritus.</td>
<td>Commonly pruritic</td>
<td>Pruritic during healing, otherwise may be painful.</td>
</tr>
<tr>
<td>Distribution</td>
<td>Anywhere. Palms, soles not usually involved.</td>
<td>Starts on trunk and face and spreads centrifugally. Palms, soles may be involved</td>
<td>Begins on the oral mucosa, face, and extremities and spreads centripetally. Palms, soles commonly involved.</td>
</tr>
<tr>
<td>Enanthem Scarring</td>
<td>Minority of cases. Eschar leaves depressed scar, papulovesicles do not.</td>
<td>Common, especially palate. If bacterial superinfection occurs</td>
<td>Starts in mouth</td>
</tr>
</tbody>
</table>

J Am Acad Derm. 2004;51(5)S137-S142
## Typhus group

<table>
<thead>
<tr>
<th>Flea</th>
<th>Louse</th>
<th>Chigger mite</th>
</tr>
</thead>
<tbody>
<tr>
<td><em>R. typhi</em></td>
<td><em>R. prowazekii</em></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td><em>O. tsutsugamushi</em></td>
</tr>
</tbody>
</table>
**R. typhi** (murine/endemic typhus)

- Found sporadically worldwide
  - In US: Hawaii, California, Texas
- Hosts: Rats, cats, mice
  Vector: fleas

WHO, 1998
**R. typhi** (murine/endemic typhus)

- Flea bites (infected feces contaminate skin) or aerosolization
- Incubation 6-14 days
- Fever, headache, rash (triad in 50%)
- Leukocytosis or mild leukopenia
- Anemia (severe with G6PD def)
- +/- hyponatremia, hepatic/renal abnormalities
**R. typhi** (murine/endemic typhus)

- Ecology: Rat fleas; coastal areas
- Diagnosis (clinical): serology (IFA)
  - cross-reactive with *R. prowazekii* and RMSF Ab
- Spontaneous recovery in 2 weeks
- Treatment: Doxycycline 100mg BID for 48-72hrs after fever resolved
- Prevention: PPE
R. prowazekii (louse-borne/epidemic)

WHO, 1998
**R. prowazekii** (louse-borne/epidemic)

- Incubation 6-14 days
- Fever, headache (abrupt), tachypnea, myalgias
- Rash (mac-pap/petechial) on days 4-7
  – spreads peripherally (unlike RMSF)
- CNS disease: confusion, drowsiness, coma
- Shock: multifocal/multi-organ vasculitis
- Recrudescence (Brill-Zinsser disease)
  – Mild illness, elderly, years after initial episode
**R. prowazekii** (louse-borne/epidemic)

- Vector: body louse (*Pediculosis humanus*)
- Reservoir: humans
  - flying squirrels
- Ecology: crowded, war/disasters, famine, poverty
- Diagnosis: serology (IFA), biopsy, PCR
- Treatment: Doxycycline (as endemic)
- Prevention: delousing (permethrin>lindane, malathion)
  - long-acting insecticides
  - prophylaxis (doxycycline)
O. tsutsugamushi (Scrub typhus)

• Chigger-borne zoonosis

• Vector: larval mites
  • “mite islands”

• Tropical Asia, western Pacific islands
O. tsutsugamushi (Scrub typhus)

- Painless bite
- Eschar - painless papule; central necrosis
- Fever, chills, headache, conjunctival suffusion
  - All prior to centrifugal rash
- Cough, tachypnea, pulmonary infiltrates
  - Most common
- Relative bradycardia
- Regional lymphadenopathy
- Acute hearing loss in 1/3 cases
O. tsutsugamushi (Scrub typhus)

- Ecology: active rice fields, agricultural areas, warm humid tropics
- Rats key to population densities
- Diagnosis: clinical; IFA gold standard; PCR, isolation in blood
- Eschar in SE Asia pathognomonic
- Treatment: Doxycycline (resistance possible)
  – Azithromycin, rifampin
- Prevention: topical repellents to clothing, weekly doxycycline
Agents of Ehrlichiosis

• *E. chaffeensis*
  – Infects peripheral monocytes/macrophages
  – Major cause of Ehrlichiosis in USA

• *E. ewingii*
  – Infects neutrophils; immunocompromised

• *E. canis*
  – Asymptomatic
### “Ehrlichiosis”

<table>
<thead>
<tr>
<th>HME</th>
<th>HGA</th>
<th><em>E. ewingii</em></th>
</tr>
</thead>
<tbody>
<tr>
<td>1987</td>
<td>1994</td>
<td>1999</td>
</tr>
<tr>
<td><em>E. chaffeensis</em></td>
<td><em>A. phagocytophilum</em></td>
<td><em>E. ewingii</em></td>
</tr>
<tr>
<td>Monocyte macrophage</td>
<td>Granulocyte</td>
<td>Granulocyte</td>
</tr>
<tr>
<td>&gt;1600 cases/yr</td>
<td>&gt;2100 cases/yr</td>
<td>~20 (immunocompromised)</td>
</tr>
<tr>
<td>SC, SE, mid-Atl</td>
<td>NE, MW, Pac coast</td>
<td>SC</td>
</tr>
</tbody>
</table>

Dumler JS, Walker DH. *Ehrlichiosis and Anaplasmosis* in Tropical Infectious Diseases 2006.
HME Distribution

- Vector: lone star tick
  - *Amblyomma americanum*
- Reservoir: White-tailed deer
- Only occurs in USA
HGA Distribution

- International distribution
- Vector: *Ixodes* ticks
  - *I. scapularis* (East US)
  - *I. pacificus* (West US)
  - *I. ricinus* (Europe)
  - *I. persulcatus* (Asia)
- Reservoir: white-footed mouse

Clin Lab Med March 2010
Increasing Incidence of *Ehrlichia chaffeensis* and *Anaplasma phagocytophilum* in the United States, 2000–2007

F. Scott Dahlgren, Eric J. Mandel, John W. Krebs, Robert F. Massung, and Jennifer H. McQuiston*

*Division of Vectorborne Infectious Diseases, National Center for Enteric, Zoonotic, and Infectious Disease, Centers for Disease Control and Prevention, Atlanta, Georgia*
## Military importance (Ehrlichiosis)

<table>
<thead>
<tr>
<th>Group, disease</th>
<th>Causative agent</th>
<th>Mode</th>
<th>Geographic</th>
</tr>
</thead>
<tbody>
<tr>
<td>Canine</td>
<td><em>E. canis</em></td>
<td>Tick bite</td>
<td>SE Asia, SW US, Venezuela</td>
</tr>
<tr>
<td>HME</td>
<td><em>E. chaffeensis</em></td>
<td>Tick bite</td>
<td>Americas, Europe, Thailand</td>
</tr>
<tr>
<td>HGA</td>
<td><em>A. phagocytophilum</em></td>
<td>Tick bite</td>
<td>USA, Europe, Asia</td>
</tr>
<tr>
<td>Sennetsu fever</td>
<td><em>Neorickettsia sennetsu</em></td>
<td>unknown</td>
<td>Japan, Malaysia</td>
</tr>
</tbody>
</table>

CID, 2002
Ehrlichiosis

- Incubation 5-14 days
- Rash rare; NO vasculitis
- Ecology:
  - grassy areas, forest edge, un-mowed areas
  - May-Sept in USA
- Diagnosis: paired serology; peripheral blood smears (morulae=cytoplasmic inclusions); PCR
- Treatment: Doxycycline 100mg BID ~ 3d after afebrile (~5-7 days)
- Prevention: PPE
# Ehrlichiosis and Anaplasmosis

<table>
<thead>
<tr>
<th>Symptom or sign</th>
<th>Patients, % (no. evaluated)</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>HME</td>
<td>HGA</td>
</tr>
<tr>
<td>Fever</td>
<td>97 (633)</td>
<td>93 (521)</td>
</tr>
<tr>
<td>Myalgia</td>
<td>57 (250)</td>
<td>77 (516)</td>
</tr>
<tr>
<td>Headache</td>
<td>80 (240)</td>
<td>76 (385)</td>
</tr>
<tr>
<td>Malaise</td>
<td>82 (234)</td>
<td>94 (288)</td>
</tr>
<tr>
<td>Nausea</td>
<td>64 (143)</td>
<td>38 (258)</td>
</tr>
<tr>
<td>Vomiting</td>
<td>33 (192)</td>
<td>26 (90)</td>
</tr>
<tr>
<td>Diarrhea</td>
<td>23 (197)</td>
<td>16 (95)</td>
</tr>
<tr>
<td>Cough</td>
<td>26 (155)</td>
<td>19 (260)</td>
</tr>
<tr>
<td>Arthralgias</td>
<td>41 (211)</td>
<td>46 (504)</td>
</tr>
<tr>
<td><strong>Rash</strong></td>
<td><strong>31 (286)</strong></td>
<td><strong>6 (357)</strong></td>
</tr>
<tr>
<td>Stiff neck</td>
<td>3 (240)</td>
<td>21 (24)</td>
</tr>
<tr>
<td>Confusion</td>
<td>19 (279)</td>
<td>17 (211)</td>
</tr>
<tr>
<td>Laboratory finding</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Leukopenia</td>
<td>62 (276)</td>
<td>49 (336)</td>
</tr>
<tr>
<td>Thrombocytopenia</td>
<td>71 (247)</td>
<td>71 (336)</td>
</tr>
<tr>
<td>Elevated serum AST or ALT level</td>
<td>83 (276)</td>
<td>71 (177)</td>
</tr>
</tbody>
</table>

CID, 2007; 45 (Suppl 1)
**Q fever (Coxiella burnetii)**

- Worldwide distribution
  - USA, no cases in New Zealand
- Zoonosis: wildlife and arthropod (tick) reservoir
- Transmission via cattle, sheep, goats
- Localizes to uterus/mammary glands
- Infectious particles inhaled or ingested
- 1 organism can cause clinical infection
From Lancet 1984: 12 people were playing poker in the same room as a parturient cat. All 12 handled either the cat or litter and all 12 were diagnosed with acute Q fever (placentas carry $10^9$ organisms).
Q fever (*Coxiella burnetii*)

- **3 clinical presentations (major)**
  - Febrile illness: self-limited; most common
  - Pneumonia (with fever): severe HA, retro-orbital pain
  - Hepatitis (with fever): “doughnut” granulomas”
  - * 60% asymptomatic

Complications:
- Endocarditis (culture negative; chronic)
- Optic neuritis
- Encephalitis
Q Fever (*Coxiella burnetii*)

- Ecology: farmers, vets, abattoir/lab workers
- Diagnosis: paired serology (Ph II, Ph I)
  - Culture (USAMRIID, CDC)
- Treatment:
  - Acute: fluoroquinolone or Doxy x 21 days
  - Chronic/endocarditis: FQ + rifampin or doxy + hydroxychloroquine x 18 mo.
- Prevention: educate (livestock, dairy)
  - disposal of birth products (animals)
  - quarantine/restriction of infected animals
  - caution high risk patients (valve disease)
Lyme disease (Borrelia sp.)

Agent: B. afzelii, B. garinii
Vectors: I. ricinus – Europe
I. persulcatus – E. Europe, Russia

Agent: B. burgdorferi
Vectors: I. scapularis – East
I. pacificus - West

Lancet 2003; CDC.gov
Common presenting symptoms

Early Infection
• Rash (erythema migrans) in ~ 70-80%
  – at site of tick bite after 3-30 days
  – Gradually expands over several days
  – Central clearing (Bull's-eye); warm but not painful
  – occasional additional EM lesions days later
• +/- fatigue, chills, fever, headache, swollen lymph nodes

Late Infection
• Encephalomyelitis
• Arthritis in 60% untreated
  – Intermittent attacks of joint swelling, pain
  – Large and small joints
  – Can develop chronic arthritis

Steere AC. Borrelia burgdorferi (Lyme Disease, Lyme Borreliosis) in PPID.2005.
Lyme disease (*B. borgdorferi*)
Lyme Disease Manifestations

• Neuroborreliosis (5%)
  – Can occur at any time
  – Early: aseptic meningitis; cranial nerve palsies; peripheral neuritis/paresis
  – *Borrelia* DNA (PCR) in CSF

• Carditis
  – Conduction disturbances (AV block – complete block)

• Arthritis
  – Intermittent attacks of inflammation
  – Synovial fluid positive for *Borrelia* DNA (PCR)
  – US>Europe

Steere AC. *Borrelia burgdorferi* (Lyme Disease, Lyme Borreliosis) in PPID.2005.
<table>
<thead>
<tr>
<th>Indication</th>
<th>Treatment</th>
<th>Duration, days (range)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tick bite in the United States</td>
<td>Doxycycline, 200 mg in a single dose³,⁴; (4 mg/kg in children ≥8 years of age) and/or observation</td>
<td>...</td>
</tr>
<tr>
<td>Erythema migrans</td>
<td>Oral regimen⁵,⁶</td>
<td>14 (14–21)⁹</td>
</tr>
<tr>
<td>Early neurologic disease</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Meningitis or radiculopathy</td>
<td>Parenteral regimen⁶,⁷</td>
<td>14 (10–28)</td>
</tr>
<tr>
<td>Cranial nerve palsy</td>
<td>Oral regimen⁶</td>
<td>14 (14–21)</td>
</tr>
<tr>
<td>Cardiac disease</td>
<td>Oral regimen⁶ or parenteral regimen⁶,⁷</td>
<td>14 (14–21)</td>
</tr>
<tr>
<td>Borreliotic lymphocytoma</td>
<td>Oral regimen⁵</td>
<td>14 (14–21)</td>
</tr>
<tr>
<td>Late disease</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Arthritis without neurologic disease</td>
<td>Oral regimen⁶</td>
<td>28</td>
</tr>
<tr>
<td>Recurrent arthritis after oral regimen</td>
<td>Oral regimen⁶ or parenteral regimen⁶,⁷</td>
<td>28 (14–28)</td>
</tr>
<tr>
<td>Antibiotic-refractory arthritis</td>
<td>Symptomatic therapy⁸</td>
<td>...</td>
</tr>
<tr>
<td>Central or peripheral nervous system</td>
<td>Parenteral regimen⁶</td>
<td>14 (14–28)</td>
</tr>
<tr>
<td>Acrodermatitis chronica atrophicans</td>
<td>Oral regimen⁶</td>
<td>21 (14–28)</td>
</tr>
<tr>
<td>Post–Lyme disease syndrome</td>
<td>Consider and evaluate other potential causes of symptoms; if none is found, then administer symptomatic therapy⁸</td>
<td>...</td>
</tr>
</tbody>
</table>

1. Rat-infested grain stores
2. Close living quarters, poverty
3. Sheep or cattle exposure
4. Transitional vegetation
5. Land navigation exercises

A. Spotted fever (*R. rickettsii*)
B. Q fever (*C. burnetii*)
C. Scrub typhus (*O. tsutsugamushi*)
D. Murine typhus (*R. typhi*)
E. Louse-borne Typhus (*R. prowazekii*)
RMSF

- *R. rickettsii*
- Vector: *Dermacentor variabilis, D. andersoni*
- Fever, rash (90%), HA,
- abdominal pain, conjunctival injection
- Can be fatal early if untreated

[cdf.gov/rmsf/symptoms](http://cdc.gov/rmsf/symptoms)  [cdf.gov/rmsf/stats](http://cdc.gov/rmsf/stats)
Case #1

• 35yo USMC medic in Iraq x 7 months
• En route CONUS – fever 104°F
• Now daily fever/chills + retro-orbital HA, lower back and bilateral calf pain
• ROS: sore throat, watery diarrhea x 6 days
• Exposures: insect bites, slept in revamped Iraqi chicken factory, goats roaming, walked in brackish water, ate local Iraqi-prepared food
Case #1

- **PE:**
  - T-103°F, HR-90, BP-110/60, O$_2$ Sat-99% (RA)
  - Unremarkable

- **CXR, abdominal CT both normal**
Case #1 part B

- 23yo USMC – becomes ill 3 days after #1
- Similar fever, chills, sore throat, diarrhea
- ROS: blisters on feet (waded through sewage); only ate MREs, did not sleep in chicken factory (500yds away)
- PE: T-106°F, HR-104, BP-120/70, O₂ Sat - 98%
  - Mild jaundice o/w normal
Lab data

Patient 1
- **Na-130** (137-145)
- **K-3.0** (3.6-5.0)
- **Alkphos-310** (36-126)
- **AST-125** (17-49)
- **ALT-130** (7-56)
- **Tbili 1.8** (0.2-1.3)
- **WBC 4.5** (4.0-11.0) 74N/E2
- **Plt-120** (150-450)

Patient 2
- **Na-130**
- **K-2.9**
- **Alkphos-137**
- **AST-173**
- **ALT-131**
- **Tbili-2.8**
- **WBC-4.8**
- **Plt-45**
Case #1

- Differential?

- Malaria smears (-)

- Blood, stool, urine cultures (and CSF #1) (-)

- Acute HIV, RPR (-)

- Viral, Dengue, Hepatitis A/B/C (-)

- Leptospirosis Ab (-)

- Q fever
Current Recommendations of the Tri-Service Infectious Diseases Q Fever Working Group

- Clinical syndrome potentially consistent with acute Q fever → Include doxycycline 100 mg po BID for 21 days in therapeutic regimen
  - Send acute (now) and convalescent (in 2 weeks) serum to USAFSAM for Q fever IFA testing
  - If negative testing no further action required
  - Confirmed Q fever
    - Obtain Infectious Diseases consult and transthoracic echo (TTE) upon redeployment to CONUS
    - Repeat serologies at USAFSAM every 3 months for 1 year then every 6 months for 1 year
    - Anti-phase IgG ≥ four-fold higher than previous test and anti-phase II IgG the same or decreasing?
      - Other clinical evidence of inflammatory disease?
        - Yes → TEE + Coxiella PCR on whole blood (CDC)
        - No → Repeat serology in 3 months
      - If either abnormal then treat with minimum of 18 months doxycycline + hydroxychloroquine

Fever, sweats, weight loss, chest pain, elevated erythrocyte sedimentation rate, C reactive protein, liver-associated enzymes, white blood cell count, rheumatoid factor
**Chronic Q fever: Review of the literature and a proposal of new diagnostic criteria**

<table>
<thead>
<tr>
<th>Table 5 Dutch consensus guideline on chronic Q fever diagnostics.</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Proven chronic Q fever</strong></td>
</tr>
<tr>
<td>1. Positive <em>C. burnetii</em> PCR in blood or tissue$^a$</td>
</tr>
<tr>
<td>2. IFA $\geq$ 1:800 or 1:1024 for <em>C. burnetii</em> phase I IgG$^b$</td>
</tr>
<tr>
<td><strong>Probable chronic Q fever</strong></td>
</tr>
<tr>
<td>IFA $\geq$ 1:800 or 1:1024 for <em>C. burnetii</em> phase I IgG$^b$</td>
</tr>
<tr>
<td><strong>Possible chronic Q fever</strong></td>
</tr>
<tr>
<td>IFA $\geq$ 1:800 or 1:1024 for <em>C. burnetii</em> phase I IgG$^b$ without manifestations meeting the criteria for proven or probable chronic Q fever</td>
</tr>
</tbody>
</table>

**OR**

- Valvulopathy not meeting the major criteria of the modified Duke criteria$^{29}$

**AND**

- definite endocarditis according to the modified Duke criteria$^{29}$
  - Known aneurysm and/or vascular or cardiac valve prosthesis without signs of infection by means of TEE/TTE, $^{18}$FDG-PET, CT, MRI or abdominal doppler ultrasound

**OR**

- proven large vessel or prosthetic infection by imaging studies ($^{18}$FDG-PET, CT, MRI or AUS)
  - Suspected osteomyelitis or hepatitis as manifestation of chronic Q fever
  - Pregnancy
  - Symptoms and signs of chronic infection, such as fever, weight loss and night sweats, hepatosplenomegaly, persistent raised ESR and CRP
  - Granulomatous tissue inflammation, proven by histological examination
  - Immunocompromised state
Case #2

- 44yo Indian subsistence farmer with fever x 7 days
- Fever unremitting, initially abrupt onset
- Previously well
- One day severe frontal HA, N/V, photophobia, DOE and now tender swelling in left groin
- No travel
- Chickens on farm
- Married, 2 children – all healthy
- Vegetarian; makes yogurt
- Water – well or river (wife gathers)
- No TOB, ETOH, drugs, meds, allergies
- Childhood vaccines (WHO) completed
More clinical information

- Following incubation (6-21 d), sx appear
- After initial sx (F, HA, chills, fever, ↓ hearing, conjunctivitis/suffusion, LAD), ulcer seen then centrifugal rash within 1 wk
- 2nd wk (if untreated):
  - Splenomegaly
  - Pneumonia
  - Myocarditis
  - Delirium
  - Death

- Diagnosis?

**Scrub Typhus**
African tick bite fever

- *R. africæ*
- *Amblyomma* tick
- ↑ tourists (~5%)
- HA, myalgias, eschar/s
- Vesicular rash, mouth blisters 30%
- Reactive arthritis (5%)
- Self-limited

Scrub typhus

- *Orientia tsutsugamushi*
- Mites
- Loggers, rice farmers, military
- F, LAD (70%), eschar (50%)
- PNA, CNS, DIC, renal failure
- Indep. predictor mort: met. acidosis (↑ ast, wbc, ↓ plt)
Case #3

40yo male Thai subsistence farmer is brought to clinic with report of headache, chills, hearing loss, and cough. You note an eschar on his leg and elicit confusing responses to simple questions. What would be your drug of choice for treatment?

A. Doxycycline
B. Atovaquone
C. Azithromycin
D. Gentamicin
40yo male Thai subsistence farmer is brought to clinic with report of headache, chills, hearing loss, and cough. You note an eschar on his leg and elicit confusing responses to simple questions. What would be your drug of choice for treatment?

A. Doxycycline
B. Atovaquone
C. **Azithromycin**
D. Gentamicin
Case #4
A 44-year-old male traveler returning from Tanzania presents 7 days after return with fever and respiratory symptoms. Among rickettsial diseases to be considered, which of the following is most likely to be the cause of his illness?

A. Ehrlichiosis
B. Spotted fever group rickettsiosis
C. Bartonellosis
D. Typhus group rickettsiosis
A 44-year-old male traveler returning from Tanzania presents 7 days after return with fever and respiratory symptoms. Among rickettsial diseases to be considered, which of the following is most likely to be the cause of his illness?

A. Ehrlichiosis

B. **Spotted fever group rickettsiosis**

C. Bartonellosis

D. Typhus group rickettsiosis
#5
Which of the following is the most commonly used treatment for rickettsial disease among returning international travelers?

A. Tetracycline  
B. Minocycline  
C. Septra  
D. Doxycycline
Which of the following is the most commonly used treatment for rickettsial disease among returning international travelers?

A. Tetracycline
B. Minocycline
C. Septra
D. Doxycycline
During war with many displaced people, which organism would you be most concerned about because of its high mortality rates, complications, and epidemic potential?

A. *Orientia tsutsugamushi*
B. *Rickettsia rickettsii*
C. *Rickettsia prowazekii*
D. *Rickettsia typhi*
#6

During war with many displaced people, which organism would you be most concerned about because of its high mortality rates, complications, and epidemic potential?

A. *Orientia tsutsugamushi*

B. *Rickettsia rickettsia*

C. *Rickettsia prowakezii*

D. *Rickettsia typhi*
QUESTIONS?
Ehrlichia disease

<table>
<thead>
<tr>
<th>HME</th>
<th>HGA</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Fever (&gt;95%), HA (60-75%), myalgias (60%), nausea (40-50%), arthralgias (30-35%), malaise (30-80%)</td>
<td>• Similar symptoms</td>
</tr>
</tbody>
</table>
| • **Rash** 30-40% (↑ HIV, peds)  
  – After 5d onset | • Less rash (10%) |
| • Cytopenias, ↑ transaminases, ↓ sodium | • CNS – lower rates |
| • **CNS** disease 20% (cognitive impairment predictor) | • **Morulae** 8-20% |
| • Pulmonary 20-25%, bldg | • 1 % case fatality |
| • 3% case fatality | |
## Ehrlichia vs. Lyme

<table>
<thead>
<tr>
<th>HGA (HGE)</th>
<th>Lyme</th>
</tr>
</thead>
<tbody>
<tr>
<td>• <em>I. scapularis/pacificus</em></td>
<td>• <em>I. scapularis/pacificus</em></td>
</tr>
<tr>
<td>• Small mammal reservoir</td>
<td>• Small mammal reservoir</td>
</tr>
<tr>
<td>• May-Jul</td>
<td>• May-Jul</td>
</tr>
<tr>
<td>• 5-11d incubation</td>
<td>• 7-10d incubation</td>
</tr>
<tr>
<td>• M:F – 2:1</td>
<td>• 1:1</td>
</tr>
<tr>
<td>• Age 43-60</td>
<td>• 1.7x more freq &lt; age 15</td>
</tr>
<tr>
<td>• Leukopenia – 50%</td>
<td>• Leukopenia – rare</td>
</tr>
<tr>
<td>• ↓Plt – 92%</td>
<td>• ↓Plt – rare</td>
</tr>
<tr>
<td>• Anemia – 50%</td>
<td>• Anemia – 12%</td>
</tr>
<tr>
<td>• ↑LFT – 91%</td>
<td>• ↑LFT – 19%</td>
</tr>
</tbody>
</table>

- M:F: Male to Female ratio
- ↓: Decrease
- ↑: Increase
Questions

• Which rickettsial disease has an animal reservoir? Q fever (*Coxiella burnetii*)
• Which antibiotic is the best empiric choice if concerned re: a rickettsial disease? Doxy
• What type of bacteria causes both Spotted fever group and Typhus group of disease? Gram-negative obligate intracellular
• More likely to have multiple eschars? *R. africae* (African tick bite fever)