Rickettsia, Orientia, Ehrlichia, Coxiella and Bartonella
History of Rickettsial Diseases

- Epidemic typhus - 16th century
- Associated with wars and famine
- WWI and WWII - 100,000 people affected
- Ricketts identifies causative agent of Rocky Mountain spotted fever - 20th century
- Arthropod vectors identified
- Arthropod control measures instituted
Rash of Rocky Mountain Spotted Fever
**Rickettsia, Orientia, Ehrlichia and Coxiella Biology**

- Small obligate intracellular parasites
- Once considered to be viruses
- Separate unrelated genera
- Gram-negative bacteria
  - Stain poorly with Gram stain (Giemsa)
- Reservoirs - animals, insects and humans
- Arthropod vectors (except *Coxiella*)
<table>
<thead>
<tr>
<th>Disease</th>
<th>Organism</th>
<th>Vector</th>
<th>Reservoir</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rocky Mountain spotted fever</td>
<td><em>R. rickettsii</em></td>
<td>TICK</td>
<td>Ticks, rodents</td>
</tr>
<tr>
<td>Ehrlichiosis</td>
<td><em>E. chaffeensis</em></td>
<td>TICK</td>
<td>Ticks</td>
</tr>
<tr>
<td>Rickettsialpox</td>
<td><em>R. akari</em></td>
<td>MITE</td>
<td>Mites, rodents</td>
</tr>
<tr>
<td>Scrub typhus</td>
<td><em>O. tsutsugamushi</em></td>
<td>MITE</td>
<td>Mites, rodents</td>
</tr>
<tr>
<td>Epidemic typhus</td>
<td><em>R. prowazekii</em></td>
<td>Louse</td>
<td>Humans, squirrel fleas, flying squirrels</td>
</tr>
<tr>
<td>Murine typhus</td>
<td><em>R. thypi</em></td>
<td>Flea</td>
<td>Rodents</td>
</tr>
<tr>
<td>Q fever</td>
<td><em>C. burnetii</em></td>
<td>None</td>
<td>Cattle, sheep, goats, cats</td>
</tr>
<tr>
<td>Disease</td>
<td>Organism</td>
<td>Vector</td>
<td>Reservoir</td>
</tr>
<tr>
<td>------------------------------</td>
<td>--------------</td>
<td>----------</td>
<td>-------------------------------</td>
</tr>
<tr>
<td>Rocky Mountain spotted fever</td>
<td><em>R. rickettsii</em></td>
<td>Tick-borne</td>
<td>Ticks, wild rodents</td>
</tr>
<tr>
<td>Rickettsialpox</td>
<td><em>R. akari</em></td>
<td>Mite-borne</td>
<td>Mites, wild rodents</td>
</tr>
<tr>
<td>Scrub typhus</td>
<td><em>O. tsutsugamushi</em></td>
<td></td>
<td>Mites (chiggers), wild rodents</td>
</tr>
<tr>
<td>Epidemic typhus</td>
<td><em>R. prowazekii</em></td>
<td>Louse-borne</td>
<td>Humans, squirrel fleas, flying squirrels</td>
</tr>
<tr>
<td>Murine endemic typhus</td>
<td><em>R. typhi</em></td>
<td>Flea-borne</td>
<td>Wild rodents</td>
</tr>
</tbody>
</table>

**FIGURE 45–1.** Epidemiology of common *Rickettsia* and *Orientia* infections.
Rickettsia and Orientia

Note: *Orientia* was formerly *Rickettsia*
Replication of *Rickettsia* and *Orientia*

- Infect endothelial in small blood vessels - Induced phagocytosis
- Lysis of phagosome and entry into cytoplasm - Phospholipase
- Replication
- Release
Groups of Rickettsia Based on Antigenic Structure

Spotted fever group:
- **R. rickettsii**
  - Rocky Mountain spotted fever
  - Western hemisphere
- **R. akari**
  - Rickettsialpox
  - USA, former Soviet Union
- **R. conorii**
  - Boutonneuse fever
  - Mediterranean countries, Africa, India, Southwest Asia
- **R. sibirica**
  - Siberian tick typhus
  - Siberia, Mongolia, northern China
- **R. australis**
  - Australian tick typhus
  - Australia
- **R. japonica**
  - Oriental spotted fever
  - Japan

Typhus group:
- **R. prowazekii**
  - Epidemic typhus
  - South America and Africa
  - Recrudescent typhus
  - Worldwide
  - Sporadic typhus
  - United States
  - Murine typhus
  - Worldwide

Scrub typhus group:
- **O. tsutsugamushi**
  - Scrub typhus
  - Asia, northern Australia, Pacific Islands
Pathogenesis and Immunity

- No known toxins or immunopathology
- Destruction of cells
  - Leakage of blood into tissues (rash)
  - Organ and tissue damage
- Humoral and cell mediated immunity important for recovery
  - Antibody-opsonized bacteria are killed
  - CMI develops
Spotted Fever Group
Rickettsia rickettsii

- Rocky Mountain spotted fever

Fluorescent Ab staining  Vector - Tick

From: G. Wistreich, Microbiology Perspectives, Prentice Hall
Epidemiology - *R. rickettsii*
Rocky Mountain Spotted Fever

- Most common rickettsial infection in USA
  - 400 - 700 cases annually
  - South Central USA
- Most common from April - September
- Vector - Ixodid (hard) tick via saliva
  - Prolonged exposure to tick is necessary
- Reservoirs - ticks (transovarian passage) and rodents
  - Humans are accidentally infected
Rash of Rocky Mountain Spotted Fever
Clinical Syndrome - Rocky Mountain Spotted Fever

- Incubation period - 2 to 12 days
- Abrupt onset fever, chills headache and myalgia
- Rash appears 2-3 days later in most (90%) patients
  - Begins on hands and feet and spreads to trunk (centripetal spread)
  - Palms and soles common
  - Maculopapular but can become petechial or hemorrhagic
- Complications from widespread vasculitis
  - Gastrointestinal, respiratory, seizures, coma, renal failure
  - Most common when rash does not appear
- Mortality in untreated cases - 20%
Laboratory Diagnosis - \textit{R. rickettsii}

- Initial diagnosis - clinical grounds
- Fluorescent Ab test for Ag in punch biopsy - reference labs
- PCR based tests - reference labs
- Weil-Felix test - no longer recommended
- Serology
  - Indirect fluorescent Ab test for Ab
  - Latex agglutination test for Ab
Treatment, Prevention and Control

*R. rickettsii*

- Tetracycline and chloramphenicol
  - Prompt treatment reduces morbidity and mortality
- No vaccine
- Prevention of tick bites (protective clothing, insect repellents)
- Prompt removal of ticks
- Can’t control the reservoir
Rickettsia akari

• Rickettsialpox
Typhus Group
Rickettsia prowazekii

- Epidemic typhus
- Brill-Zinssser disease

Fluorescent-Ab staining  Vector - Louse

From: G. Wistreich, Microbiology Perspectives, Prentice Hall
Epidemiology - *R. prowazekii*
Epidemic typhus

- Associated with unsanitary conditions
  - War, famine, etc.
- Vector - human body louse
  - Bacteria found in feces
- Reservoir
  - Primarily humans (epidemic form)
  - No transovarian transmission in the louse
- Sporadic disease in Southeastern USA
  - Reservoir - flying squirrels
  - Vector - squirrel fleas
Clinical Syndrome - Epidemic typhus

• Incubation period approximately 1 week
• Sudden onset of fever, chills, headache and myalgia
• After 1 week rash
  – Maculopapular progressing to petechial or hemorrhagic
  – First on trunk and spreads to extremities (centrifugal spread)
• Complications
  – Myocarditis, stupor, delirium (Greek “typhos” = smoke)
• Recovery may take months
• Mortality rate can be high (60-70%)
Clinical Syndrome - Brill-Zinssser Disease

- Recrudescent epidemic typhus
  - Commonly seen in those exposed during WWII
- Disease is similar to epidemic typhus but milder
- Rash is rare
- High index of suspicion need for diagnosis
Laboratory Diagnosis - *R. prowazekii*

- Weil-Felix antibodies - not recommended
- Isolation possible but dangerous
- Serology
  - Indirect fluorescent Ab and latex agglutination tests
  - Epidemic typhus - IgM followed by IgG Abs
  - Brill-Zinsser - IgG anamnestic response
Treatment, prevention and Control

*R. prowazekii*

- Tetracycline and chloramphenicol
- Louse control measures
- Vaccine available for high risk populations
Rickettsia typhi

- Murine or endemic typhus
Epidemiology - *R. typhi* 
Murine or endemic typhus

- Occurs worldwide
- Vector - rat flea
  - Bacteria in feces
- Reservoir - rats
  - No transovarian transmission
  - Normal cycle - rat to flea to rat
- Humans accidentally infected
Clinical Syndrome- Murine Typhus

• Incubation period 1 - 2 weeks
• Sudden onset of fever, chills, headache and myalgia
• Rash in most cases
  – Begins on trunk and spreads to extremities (centrifugal spread)
• Mild disease - resolves even if untreated
Laboratory Diagnosis - *R. typhi*

- Serology
  - Indirect fluorescent antibody test
Treatment, Prevention and Control

*R. typhi*

- Tetracycline and chloramphenicol
- Control rodent reservoir
Scrub Typhus Group
Orientzia (Rickettsia) tsutsugamushi

- Scrub typhus
- Japanese “tsutsuga” = small and dangerous and “mushi” = creature
- “Scrub” - associated with terrain with scrub vegetation
Epidemiology - *O. tsutsugamushi*

Scrub Typhus

- **Vector** - chiggers (mite larva)
- **Reservoir** - chiggers and rats
  - Transovarian transmission
  - Normal cycle - rat to mite to rat
- **Humans are accidentally infected**
Clinical Syndrome - Scrub Typhus

• Incubation period - 1 to 3 weeks
• Sudden onset of fever, chills, headache and myalgia
• Maculopapular rash
  – Begins on trunk and spreads to extremities (centrifugal spread)
• Mortality rates variable
Laboratory Diagnosis - *O. tsutsugamushi*

- Serology
Treatment, Prevention and Control

*O. tsutsugamushi*

- Tetracycline and chloramphenicol
- Measures to avoid exposure to chiggers
Coxiella
Coxiella burnetii

- Q fever (Q for query)

Fluorescent-Ab Stain

From: G. Wistreich, Microbiology Perspectives, Prentice Hall
Replication of *Coxiella burnetii*

- Infection of macrophages
- Survival in phagolysosome
- Replication
- Lysis of cell
Pathogenesis and Immunity - *C. burnetii*

- Inhalation of airborne particles
- Multiplication in lungs and dissemination to other organs
- Pneumonia and granulomatous hepatitis in severe cases
- In chronic disease immune complexes may play a role in pathogenesis
- Cellular immunity is important in recovery
Pathogenesis and Immunity - *C. burnetii*

- Phase variation in LPS
  - Acute disease - Antibodies to phase II antigen
  - Chronic disease - Antibodies to both phase I and phase II antigens
Epidemiology - C. burnetii

Q fever

- Stable “spore like”
- Infects many animals including sheep, goats, cattle, and cats
- High titers in placentas of infected animals
- Persists in soil
- Found in milk of infected animals
- No arthropod vector
- Disease of ranchers, veterinarians, and abattoir workers
Clinical Syndrome - Q Fever

- **Acute Q fever**
  - Can be mild or asymptomatic
  - fever, chills, headache and myalgia
  - Respiratory symptoms usually mild (atypical pneumonia)
  - Hepatomegaly and splenomegaly can be observed
  - Granulomas in the liver are observed histologically

- **Chronic Q fever**
  - Typically presents as endocarditis on a damaged heart valve
  - Prognosis is poor
Treatment, Prevention and Control

*C. burnetii*

- Acute Q fever - tetracycline
- Chronic Q fever - combination of antibiotics
- Vaccine is available but it is not used in the USA
Bartonella
Epidemiology - *B. henselae*
Cat-scratch Disease

• Acquired from cat bite or scratch and possibly from cat fleas
Clinical Syndrome
Cat-scratch Disease

- Benign disease
- Chronic regional lymphadenopathy
Laboratory Diagnosis - *B. henselae*

- Serology
Treatment - *B. henselae*

- Does not respond to antimicrobial therapy