Rickettsia, Ehrlichia, and Borrelia

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EXPOSURE, EXPOSURE, EXPOSURE!!!
&
LOCATION, LOCATION, LOCATION!!!

Differential Diagnosis
- Bacteria
- Viruses
- Fungi
- Parasites
- TB
- Non-TB mycobacteria
- Non-infectious

Rickettsia Microbiology
- Gram negative bacteria
  - fastidious
  - obligate intracellular pathogens

ALWAYS THINK HIV and TBI!!
Rickettsia Pathogenesis

- Vector (tick/louse/flea/mite) bites and feeds (at least 6 hours)
- Regurgitates bacteria into skin bite site
- Bacteria are carried via lymphatics/small blood vessels to general circulation where they invade endothelia cells (primary target)
- Spreads to contiguous endothelial cells, smooth muscle cells, and phagocytes
- Eventually spread via the microcirculation and invade virtually all organ systems
  - Angiitis resulting in local thrombus formation and end organ damage

Rickettsia Rashes

- Rickettsial species cause a petechial rash in early disease that starts on the trunk and spreads outward (centrifugal)
- Two notable exceptions:
  - \( R. \) akari
    - Rash not petechial but papulo-vesicular (looks like chicken pox)
  - \( R. \) rickettsii
    - Centripetal rash (starts on wrists, ankles, soles, and palms and spreads proximally)

Rickettsia Endemic Diseases

- Rocky Mountain Spotted Fever
  - \( R. \) rickettsii
    - Vector: dog tick (Eastern) and wood tick (Western): Dermacentor sp.
  - Endemic regions: Southeastern, Mid-Atlantic, Midwest
  - Peak incidence: May-Sept (when people are outside with potential tick exposure)

- Murine Typhus
  - \( R. \) typhi
    - Vector: flea (cat fleas important: TX and CA)

Rickettsia Epidemic Diseases

- Rickettsialpox
  - \( R. \) akari
    - Vector: mite

- Epidemic Typhus
  - \( R. \) prowazekii
    - Vector: louse

Rocky Mountain Spotted Fever
Rocky Mountain Spotted Fever

- After tick bite, 7-14 day asymptomatic incubation period
- Sudden onset of fever, headache, malaise, myalgia
- Rash, menismus, photophobia, renal failure, diffuse pulmonary infiltrates, encephalopathy
- Gastrointestinal disturbances, hepatomegaly, and jaundice can occur in the later stages
- Thrombocytopenia, anemia, coagulopathy (DIC), hyponatremia

Rocky Mountain Spotted Fever
Rash

- Only small fraction patients have rash first day
- 49% during first three days
- Usually 3-5 days

Three stages:
- Erythematous macule: blanches on pressure
- Macular-papular: results from fluid leakage from infected blood vessels
- Hemorrhage: into center with frank petechiae

Rocky Mountain Spotted Fever
Distribution of Cases

*Note: The map shows the distribution of cases across different regions of the United States, with varying levels of incidence.*
Rocky Mountain Spotted Fever
Late Stage Petechial Rash

- Treatment: Doxycycline and supportive care
- If treated within first 4-6 days of disease, fever subsides 24-72 h
- Outcome: Prognosis largely related to timeliness of initiation of therapy
  Untreated, death occurs 8-15 days

Rocky Mountain Spotted Fever
Diagnosis

- *R. rickettsii*
  - Fastidious organism (difficult to culture)
  - Skin biopsy with immunohistochemical staining of organism (PCR)
  - Serologies (Indirect immunofluorescence, EIA, latex agglutination—not Weil-Felix)
    - Acute and convalescent

Rickettsialpox

- Causative agent: *Rickettsia akari*
- Vector: mouse mite
- Endemic regions: Urban areas (NYC), South Africa, Korea, Russia

Immunohistochemical Stain Endothelial Cells

- Eschar forms at site of mite bite
- Incubation 9 to 14 days
- Papular-vesicular rash (2-3 days after onset) with fever, headache, lymphadenopathy, chills, myalgia
- Diagnosis: Clinical; Serologies (but X-reaction)
- Treatment: self-limited or doxycycline
- Outcome: Excellent, relapse uncommon
**Rickettsialpox**

- Causative agent: *R. prowazekii*
- Vector: Human body louse
- USA reservoir: Southern flying squirrel
- Risk Factors: Crowding and poor sanitation (wartime)

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**Epidemic Typhus**

- Incubation: Approximately one week
- Abrupt onset intense headache, chills, fever and myalgia
- Can have CNS involvement with decreased mental status
- No eschar
- Rash starts fifth day of illness in the axillary folds and upper trunk
  Spreads centrifugally
  Spares face, palms, and soles

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**Epidemic Typhus: Petechial Rash Day 7**
Epidemic Typhus
- Diagnosis: Clinical; Serologies X-react (Weil-Felix)
- Treatment: Doxycycline
- Outcome: under adverse conditions, untreated mortality as high as 40% 

Brill-Zinsser Disease
- Recrudescence of Epidemic Typhus in elderly (waning of immune function)
- Seen most often in immigrants who had the disease during WWII
- Pathogenesis unknown

Ehrlichia
- Small, obligate intracellular gram negative bacteria
- Cause flu-like illness (fever, headache, chills, myalgia, malaise)
- Symptoms of ehrlichiosis are similar to those of rickettsial diseases
  - Dubbed “Spotless” Fever
  - Beware! 20-30% of HME can have rash
- Lab abnormalities: thrombocytopenia, leukopenia, and elevated LFTs

Human Granulocytic Ehrlichiosis (HGE)
- Causative agent: Anaplasma phagocytophilum
- Vectors: Ixodes ticks
- Reservoirs: White-footed mouse, chipmunks, and voles
- Distribution: Northeast
- Incidence: Year round with one peak in July and second in November

Ehrlichia Pathogenesis
- Bacteria introduced via tick bite
  - Except Ehrlichia sennetsu: acquired by eating raw fish (Asia)
- Spreads via lymphatics to blood
- Multiple species that infect either granulocytes or monocytes
- Clustered inclusion-like appearance in the host cell vacuoles:
  - Morula (Latin for “mulberry”)
  - Pathognomonic, but only seen in approximately 20% cases
Human Granulocytic Ehrlichiosis (HGE)

- Can be asymptomatic to fatal
- ARDS with septic shock-like presentation, rhabdomyolysis
- Neurological sequelae include demyelinating polyneuropathy and brachial plexopathy

Human Monocytic Ehrlichiosis (HME)

Causative agent: *Ehrlichia chaffeensis*

- Vectors: Lone star tick (*Amblyomma americanum*)
- Reservoirs: Dog
- Distribution: Southeastern and South Central USA
- Incidence: May-July

Ehrlichiosis

- Diagnosis:
  - Clinical
  - Extremely difficult to culture
  - Light microscopy (limited)
  - PCR
  - Serologies

- Treatment: Doxycycline

RMSF vs. Ehrlichiosis

<table>
<thead>
<tr>
<th>Symptom</th>
<th>RMSF</th>
<th>Ehrlichiosis</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rash</td>
<td>90%</td>
<td>30%</td>
</tr>
<tr>
<td>Leukocytosis</td>
<td>Rare</td>
<td>Rare</td>
</tr>
<tr>
<td>Leukopenia</td>
<td>Seen</td>
<td>Rare</td>
</tr>
<tr>
<td>Vasculitis</td>
<td>Hallmark of RMSF</td>
<td>Not seen Ehrlichiosis</td>
</tr>
</tbody>
</table>
Borrelia

- Treponemes
- Microaerophillic with complex nutritional requirements

Lyme Disease: Borrelia burgdorferi

Relapsing Fevers: B. recurrentis, B. hermsii

Lyme Disease

- Causative Agent: Borrelia burgdorferi
- Accounts for 90% of all vector born illnesses in USA
- Vector: Ixodes ticks (deer tick, stage: nymphs)
- Needs at least 24 hours to feed for transmission of treponem
- Reservoirs: White-footed mouse, white-tailed deer, cattle, horses, dogs
- Throughout USA, but highest incidence Northeast
Title goes here
Early Disseminated Arthritis

Months to years after bite
Chronic destructive arthritis of large joints
End-stage cardiomyopathy
Stroke, meningoencephalitis, dementia, neuropathies
Acrodermatitis chronica atrophicans

Diagnosis

CLINICAL!!!
Demonstration of organism: PCR, staining
Antibody detection (most practical)
ELISA followed by Western Blot
False positives
False negatives

Treatment

Based on stage of disease
Local (EM), early arthritis, CNS (isolated Bell’s Palsy)
Oral therapy with doxycycline
Disseminated (heart, CNS, chronic arthritis)
Intravenous therapy with ceftriaxone
Treatment of seropositive asymptomatic patients is not indicated
**Tick Bite Prophylaxis**

- Based on geographic location and tick characteristics
- Prophylaxis with single dose oral doxycycline indicated if:
  - Deer tick, engorged nymph
  - Endemic area
- Prophylaxis reduces incidence of EM from 3% to 0.4%

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**Ixodes scapularis and Ornithodoros hermsi**  
**Hard vs. Soft ticks**

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**Relapsing Fever**

- Two causative agents:
  - Tick-Borne Relapsing Fever
    - Borrelia hermsii
  - Louse-Borne Relapsing Fever
    - Borrelia recurrentis

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**Borrelia recurrentis**

- Vector: Human louse (*Pediculus humanus*)
  - Epidemic during wars and natural disasters
  - South American Andes and Central and East Africa (not in USA)

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**Borrelia hermsii**

- Vector: Soft ticks (*Ornithodoros*)
  - High altitudes (caves, decaying wood)
  - Night feeder (short feeding time: 5 minutes)
  - World-wide distribution (including Western USA)
- Reservoirs: chipmunk, squirrel, rabbit, rat, rodents

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**Relapsing Fever**

- Incubation: One to three weeks
- Onset of high fever with rigors, severe headache, myalgias, arthralgias, lethargy, and photophobia
- Truncal rash 1-2 duration at the end of first febrile episode (more common in tick-borne disease)
- Multiple relapses with tick-borne disease (louse-borne only one)
Relapsing Fever

- Abrupt termination of primary febrile episode after 3 to 6 days
- Onset of afebrile period associated with hypotension and shock
- Relapse of fever: Tick-borne (7 days); Louse-borne (9 days)
- Relapses last 2-3 days
- Mortality of untreated disease:
  - Tick-borne: 5%
  - Louse-borne: up to 40%

Prevention of Vector Borne Illnesses

- AVOID EXPOSURE!
  - Long sleeved clothing, tuck pant legs into socks
  - DEET reduces risk of tick attachment
  - Examine for ticks and remove
    - Use forceps and grab tick by head and pull straight up

Take Home Message

- Fever, severe headache, and potential exposure
  - Do NOT wait for diagnostic tests!
  - Do NOT wait for rash!
  - TREAT with doxycycline!