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**

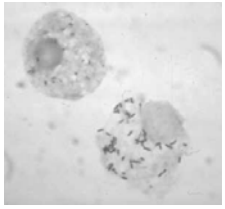
Rickettsia Microbiology

- **Gram negative bacteria**

  - fastidious
  - obligate intracellular pathogens

ALWAYS THINK HIV and TB!!

Rickettsia Microbiology



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
  - *Rickettsia rickettsii*
  - Vector: tick
- Murine Typhus
  - *Rickettsia typhi*
  - Vector: flea (cat fleas important: TX and CA)

Rocky Mountain Spotted Fever

- Causative agent: *Rickettsia 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

Rickettsia Epidemic Diseases

- Rickettsialpox
  - *Rickettsia akari*
  - Vector: mite
- Epidemic Typhus
  - *Rickettsia prowazekii*
  - Vector: louse

Rocky Mountain Spotted Fever

Dog Tick (*Dermacentor variabilis*)

Rocky Mountain Spotted Fever

- **After tick bite, 7-14 day asymptomatic incubation period**
- **Sudden onset of fever, headache, malaise, myalgia**
- **Rash, menigismus, 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 Wood Tick (*Dermacentor andersoni*)

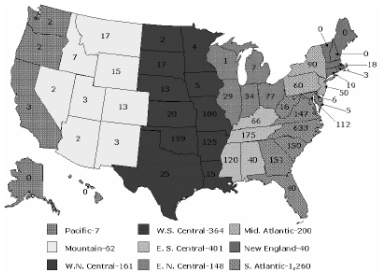
Rocky Mountain Spotted Fever Rash

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

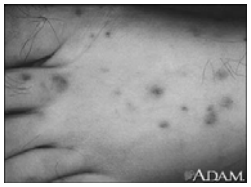
Three stages:

- **<u>Erythematous macule</u>: blanches on pressure**
- **<u>Macular-papular</u>: results from fluid leakage from infected blood vessels**
- **<u>Hemorrhage</u>: into center with frank petechiae**

Distribution of Cases



Rocky Mountain Spotted Fever Early Rash



Rocky Mountain Spotted Fever Late Stage Petechial Rash

Rocky Mountain Spotted Fever

- **Treatment: Doxycycline and supportive care**
- **If treated within first 4-5 days of disease, fever subsides 24-72 h**
- **Outcome:**
  - **Prognosis largely related to timeliness of initiation of therapy**
  - **Untreated, death occurs 8-15 days**

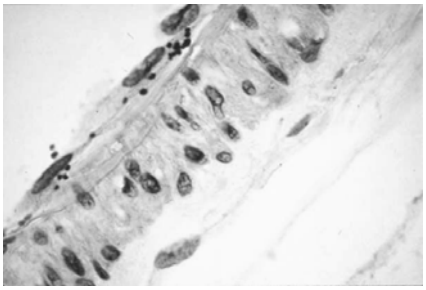
Rocky Mountain Spotted Fever Diagnosis

- ***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**

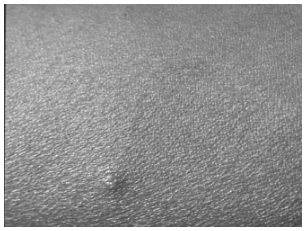
Immunohistochemical Stain Endothelial Cells



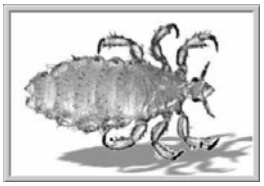
Rickettsialpox

- **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**

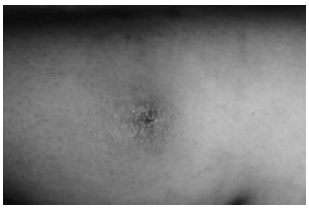
Rickettsialpox



Epidemic Typhus



Rickettsialpox



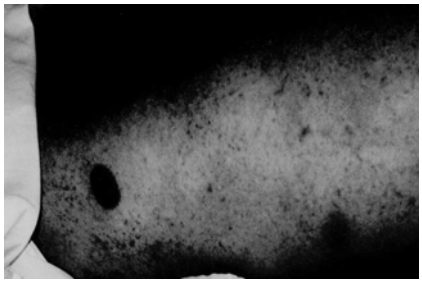
Epidemic Typhus

- 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

Epidemic Typhus

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

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%

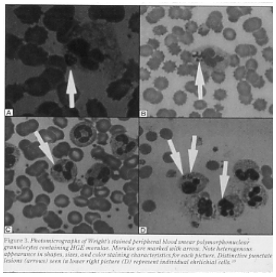
Ehrlichia Pathogenesis

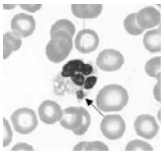
- Bacteria introduced via tick bite
  Except *Ehrlichia sennetsu*: acquired by eating raw fish (Asia)
- Spreads via lymphatics to blood
- Multiple species that infect either granulocytes or monocytes
- Clustered inclusion-like appearance in the host cell vacuoles:
  Morula (Latin for "mulberry")
  Pathognomonic,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

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 Morula





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

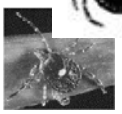
Human Granulocytic Ehrlichiosis (HGE)

- 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

Human Granulocytic Ehrlichiosis (HGE)




Human Monocytic Ehrlichiosis (HME)


Human Granulocytic Ehrlichiosis (HGE)

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

Ehrlichiosis

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

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

RMSF vs. Ehrlichiosis

Rash	RMSF: 90% patients, petechial in 50%
	HME: rash 30% and maculopapular
	HGE: rare
WBC	Leukocytosis rare in either RMSF or Ehrlichiosis
	Leukopenia seen in Ehrlichiosis but rare RMSF
Vasculitis	Hallmark of RMSF; not seen Ehrlichiosis

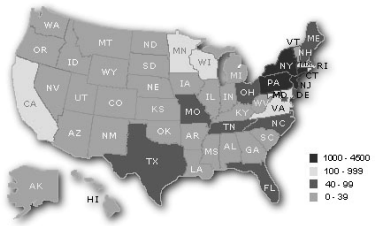
Borrelia

- **Treponemes**
- **Microaerophillic with complex nutritional requirements**

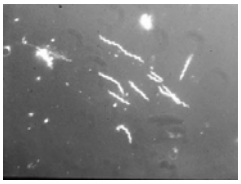
Lyme Disease: *Borrelia burgdorferi*

Relapsing Fevers: *B. recurrentis, B. hermsii*

Lyme Disease



Borrelia



Lyme Disease

Lyme Disease

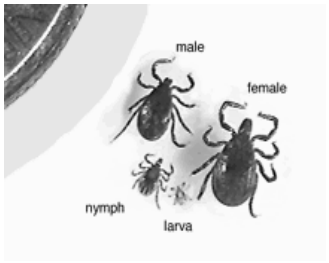
- **Causative Agent: *Borrelia burgdorferi***
- **Accounts for 90% of all vector born illnesses in USA**
- **Vector: Ixodes ticks (deer tick, stage: nymphs)**

Needs at least 24 hours to feed for transmission of treponem

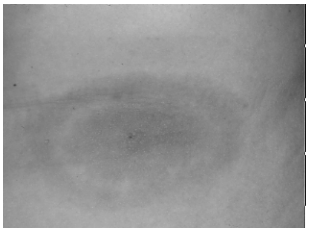
- **Reservoirs: White-footed mouse, white tailed deer, cattle, horses, dogs**
- **Throughout USA, but highest incidence Northeast**

Lyme Disease

Lyme Disease



Erythema Migrans



Lyme Disease

Three stages of infection:

- **Local (acute)**
- **Early Disseminated**
- **Late Disseminated (Persistent)**

Erythema Migrans

Local

- **Rash: Erythema migrans (few days to one month after bite)**

  Migrates outward and exhibits central clearing

  May occur at site of tick bite, but rash does not always correlate (hematogenous spread)

  Treponemes can be isolated from rash

Early Disseminated

- **Few weeks after bite, EM may still be present**
- **Cardiac**
  Heart block, myocarditis, myopericarditis
- **Musculoskeletal**
  Arthralgias and arthritis (knee common, aspirate with *Borrelia*)
- **Neurological**
  Meningitis, Bell's palsy, peripheral neuropathy, encephalitis (rare)

Early Disseminated

Facial Nerve Paralysis - Bell's Palsy

Acrodermatitis chronica atrophicans

Progressive, fibrosing skin process

Extremities: usually extensor surfaces

Starts as a bluish-red discoloration

More common with European *B. afzelii*

Early Disseminated Arthritis

Swollen knee of a youth with Lyme arthritis.

Diagnosis

- **CLINICAL!!!**
- **Demonstration of organism: PCR, staining**
- **Antibody detection (most practical)**

  ELISA followed by Western Blot
  False positives
  False negatives

Late Disseminated (Persistent)

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

Treatment

- **Based on stage of disease**
- **Local (EM), early arthritis, CNS (isolated Bell's Palsy)**

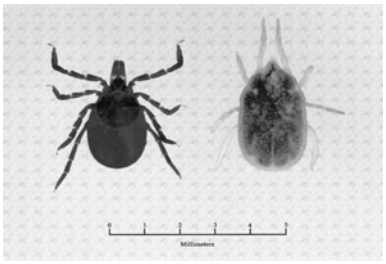
  Oral therapy with doxycycline
- **Disseminated (heart, CNS, chronic arthritis)**

  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%

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



Relapsing Fever

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

Borrelia recurrentis

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

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

Relapsing Fever

- Incubation: One to three weeks
- Onset of high fever with rigors, sever 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

Relapsing Fever

- Diagnosis: Demonstration of spirochete on blood smear (80%)
  - Need special media to culture
- Treatment:
  - Tick-borne: Doxycycline 5 to 10 days
  - Louse-borne: Single dose
  - Monitor for Jarisch-Herxheimer reaction

Take Home Message

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

Relapsing Fever