

Podcast (Video Recorded Lecture Series):  
Lyme Disease for the USMLE Step One Exam



No animal was harmed or mistreated in the preparation of the next slides

Howard J. Sachs, MD  
[www.12DaysinMarch.com](http://www.12DaysinMarch.com)  
Email: [Howard@12daysinmarch.com](mailto:Howard@12daysinmarch.com)

# MSK Infections

- Bone and Joint Infections
  - Septic Arthritis
  - Osteomyelitis
  - (Reactive Arthritis)
- Tick Borne (and related) Infections
  - Lyme Disease/Anaplasma (**Ixodes**)
    - Ehrlichiosis (Amblyomma; Lone Star)
  - Babesiosis (**Ixodes**)
  - RMSF (**Dermacentor**)
- Soft Tissue Infections
  - Clostridium perfringens → Myonecrosis
  - Necrotizing fasciitis → GAS
- Viral
  - Parvovirus (RA-like presentation)

# Tick Borne Disease: Lyme Disease

- Background
  - Ixodes tick → Borrelia spirochete
  - Skin infection (1°) disseminates → heart, nervous system, joints

Early Localized → Early Disseminated → Late Disseminated

# Tick Borne Disease: Lyme Disease

- Background
  - Ixodes tick → Borrelia spirochete
  - Skin infection (1°) disseminates → heart, nervous system, joints
- Microbiology: **spirochete**, obligate parasite
  - Genome: comprise **small** linear chromosomes of approximately 1000 kb, and 17 to 21 linear and circular plasmids totaling another 400 to 500 kb
  - **Western blot** correlates with **structural proteins** (flagellin, 41 kDa), **heat shock antigens** (60, 73 kDa), integral membrane protein (39, 66 kDa), **plasma-encoded Ag** (OSP A/31 and B/34 kDa).
    - No need to recall any of these BUT interpretation of diagnostic tests depends on a basic understanding of these.

**IgM Positive: Any two of the following three bands:  
23, 39, 41 kDa**

Structural proteins

Heat shock Ags

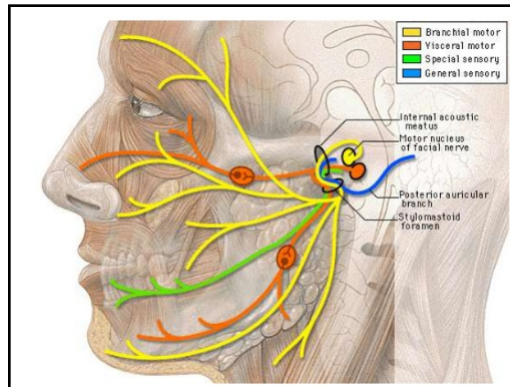
Plasmid encoded Ags

## IgM Panel

23 KD (IgM) Band Blot	<b>REACTIVE</b>
39 KD (IgM) Band Blot	NON-REACTIVE
41 KD (IgM) Band Blot	NON-REACTIVE

## IgG Panel

18 KD (IgG) Band Blot	<b>REACTIVE</b>
23 KD (IgG) Band Blot	<b>REACTIVE</b>
28 KD (IgG) Band Blot	NON-REACTIVE
30 KD (IgG) Band Blot	NON-REACTIVE
39 KD (IgG) Band Blot	<b>REACTIVE</b>
41 KD (IgG) Band Blot	<b>REACTIVE</b>
45 KD (IgG) Band Blot	<b>REACTIVE</b>
58 KD (IgG) Band Blot	<b>REACTIVE</b>
66 KD (IgG) Band Blot	<b>REACTIVE</b>
93 KD (IgG) Band Blot	NON-REACTIVE



Early Disseminated

# Tick Borne Disease: Lyme Disease

- Background
  - Ixodes tick → Borrelia spirochete
  - Skin infection (1°) disseminates → heart, nervous system, joints
- Microbiology: spirochete, obligate parasite
  - Genome: comprise small linear chromosomes of approximately 1000 kb, and 17 to 21 linear and circular plasmids totaling another 400 to 500 kb
  - Western blot correlates with structural proteins (flagellin, 41 kDa), heat shock antigens (60, 73 kDa), integral membrane protein (39, 66 kDa), plasma-encoded Ag (OSP A/31 and B/34 kDa).
    - No need to recall any of these BUT your diagnostic test depends on these.  
Nice to understand the language of the test.
  - **Survival: expresses different proteins to suit each environment**
  - Organism does not encode for any toxins or lipopolysaccharides, but does encode a large number of **lipoproteins** relative to other bacteria (think **Jarisch-Herxheimer**)
  - **Transmission:** see diagram (interesting but not tested)
  - **Incubation:** 2-3 weeks with infections concentrated in summer months





Lily

← Mouse

No animal was harmed or mistreated in the preparation of the next slides

FYI: Tick



25%



Larva



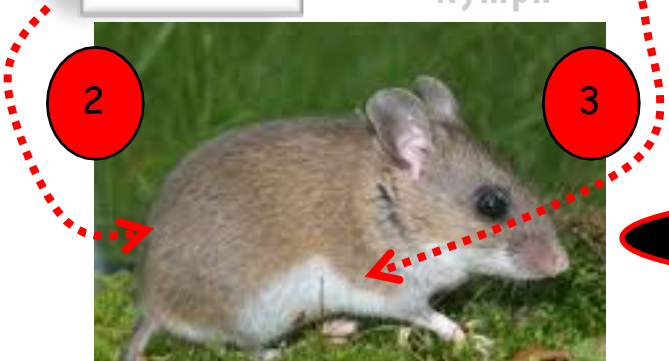
Nymph



50%



Adult Female



2

3



Eggs hatch → larvae

1



Blood meal: acquires infection and/or infects

1° reservoir: spirochete

Blood meal: delicious

Tick Host: not spirochete vector



FYI:  
Human



Nymph



Adult Female



48 h of attachment  
Sense: CO<sub>2</sub> and warmth





Nymph

**Nymph** >> **Adult**  
in transmitting infection.  
Why???



Adult Female

1. **Smaller** and more active in **peak** season.
2. Adults feed more during 'off season' (early and late season)



# Tick Borne Disease: Lyme Disease

- Immunopathogenesis ↔ Clinical Manifestations
  - Acute (Early) Localized (3-30 d post exposure)
    - Tick mouth → human skin (ECM plus flu-like illness)
  - Acute (Early) Disseminated (days to weeks post exposure)
  - Late Disseminated (months to years)

# Tick Borne Disease: Lyme Disease

- Immunopathogenesis ↔ Clinical Manifestations
  - Acute (Early) Localized (3-30 d post exposure)
    - Tick mouth → human skin (ECM plus flu-like illness)
  - Acute (Early) Disseminated (days to weeks post exposure)
    - After inoculation, *Borrelia* begins to multiply rapidly w/ dissemination to distant sites within 2-3 d
    - Skin (disseminated)
    - Cardiac: conduction disease (heart block) and rarely carditis
    - Neuro: (PNS) radiculoneuritis, cranial neuritis; (CNS) lymphocytic meningitis
  - Late Disseminated (months to years)

# Tick Borne Disease: Lyme Disease

- Immunopathogenesis ↔ Clinical Manifestations
  - Acute (Early) Localized (3-30 d post exposure)
    - Tick mouth → human skin (ECM plus flu-like illness)
  - Acute (Early) Disseminated (days to weeks post exposure)
    - After inoculation, *Borrelia* begins to multiply rapidly w/ dissemination to distant sites within 2-3 d
    - Skin (disseminated)
    - Cardiac: conduction disease (heart block) and rarely carditis
    - Neuro: (PNS) radiculoneuritis, cranial neuritis; (CNS) lymphocytic meningitis
  - Late Disseminated (months to years)
    - Has down regulated most target antigens permitting it to hide at low levels in CNS and joints x years.
    - Low bacterial number allow adaptive immune system to react without significant tissue destruction
    - MSK: Intermittent or persistent arthritis of one or a few large joints, esp knee
    - Neuro: encephalopathy, polyneuropathy

Reactive arthritis; rare to find spirochetes in joint

Classic



Common



Early localized (>4 cm)

Requires several days for expansion of the lesion (as opposed to tick bite reaction)



Early disseminated

Classic



Common



Early localized

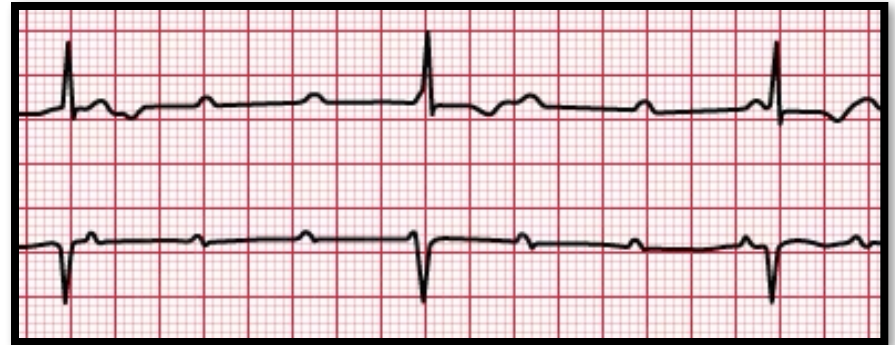
Febrile illness (esp in summer)  $\Rightarrow$  Undress

(Don't ask if they have a rash...  
you have to seek the rash!)

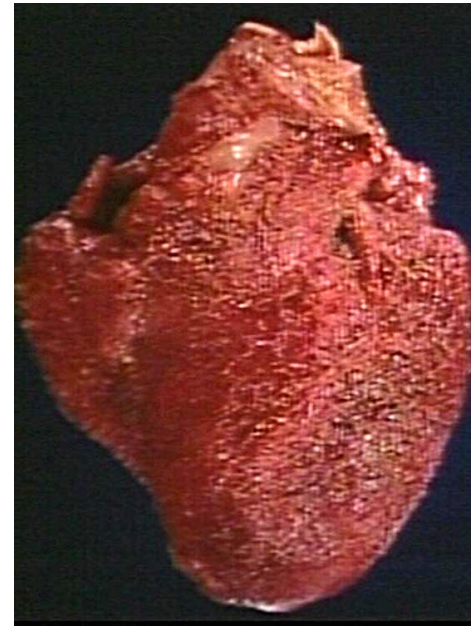


## Early disseminated disease

Dysrhythmia  
1° → 3° Heart Block



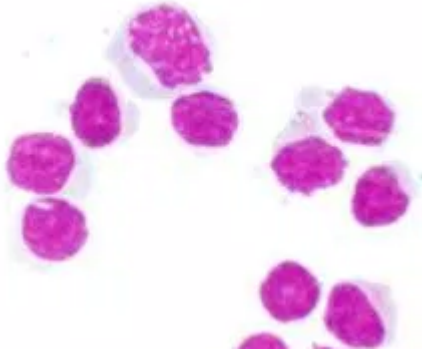
Cardiomyopathy (rare):  
S3, rales, MR  
JVD, elevated PCWP



Myopericarditis:  
Positional pain  
Friction rub



## Early Disseminated



Lymphocytic Meningitis



Cranial Neuropathy



Radiculoneuritis  
(most commonly missed)

## Late Disseminated Disease



Oligoarticular (few joints)  
Knee joint is most characteristic with large effusion

Synovial Fluid Analysis:  
Septic or Inflammatory?

# Tick Borne Disease: Lyme Disease

- Diagnostics
  - Not visible on light microscopy; difficult to culture
  - Visualize: silver stains or immunofluorescence (skin).
  - Serologic Testing:
    - **ELISA** (whole cell-based): false (+) seen due to X-reactivity.
    - **Western (immuno-) blot**: antibodies to specific antigens
      - Early: IgM plus two bands (Osp C, 39, 41 kDa) of three tested
      - Late (>3 wks): IgG plus five bands (ten bands tested)
- Treatment
  - Doxycycline (**rx of coinfection w/ Anaplasma**; doesn't cover Babesia) OR Cephalosporin
- Special Notes
  - Antibodies persist x years so all tests interpreted in view of symptoms.
  - Be familiar with coinfection (Anaplasma, Babesia)

Coinfection...

