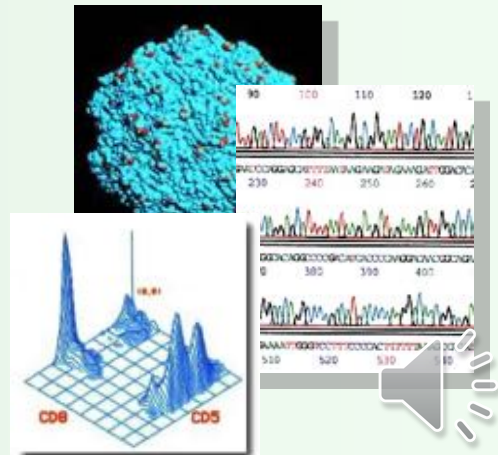


Bugs and Bacteria: Lyme Disease and Other Spirochetes

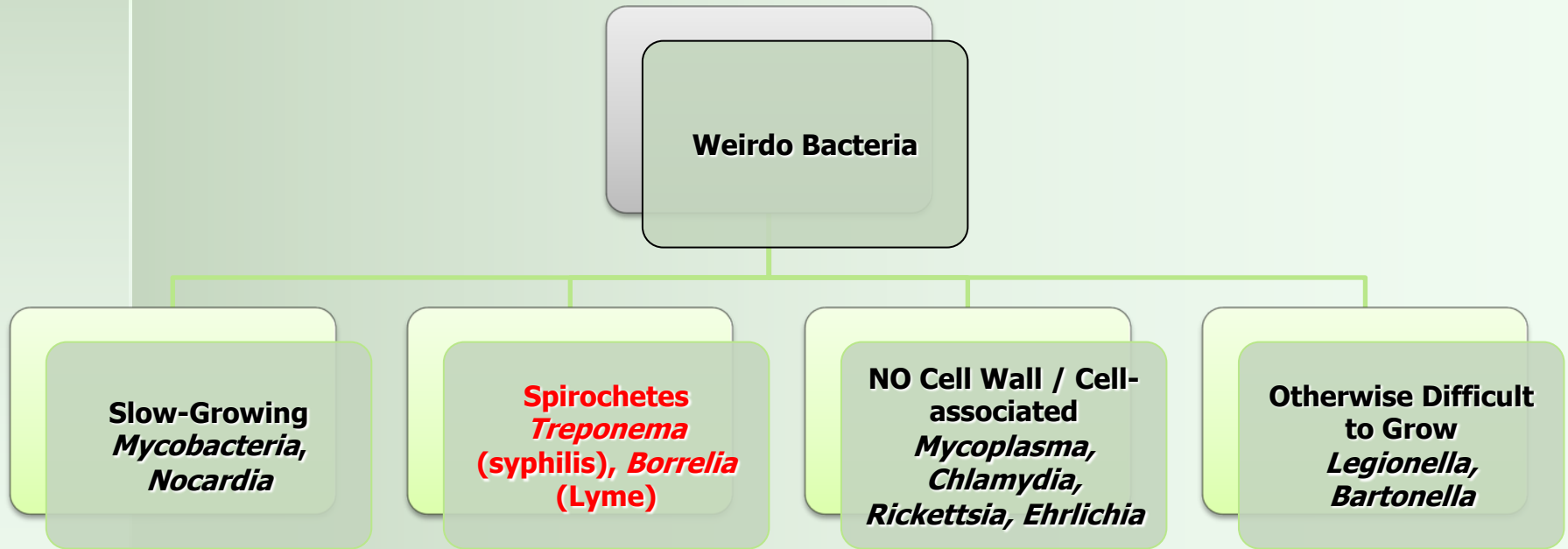
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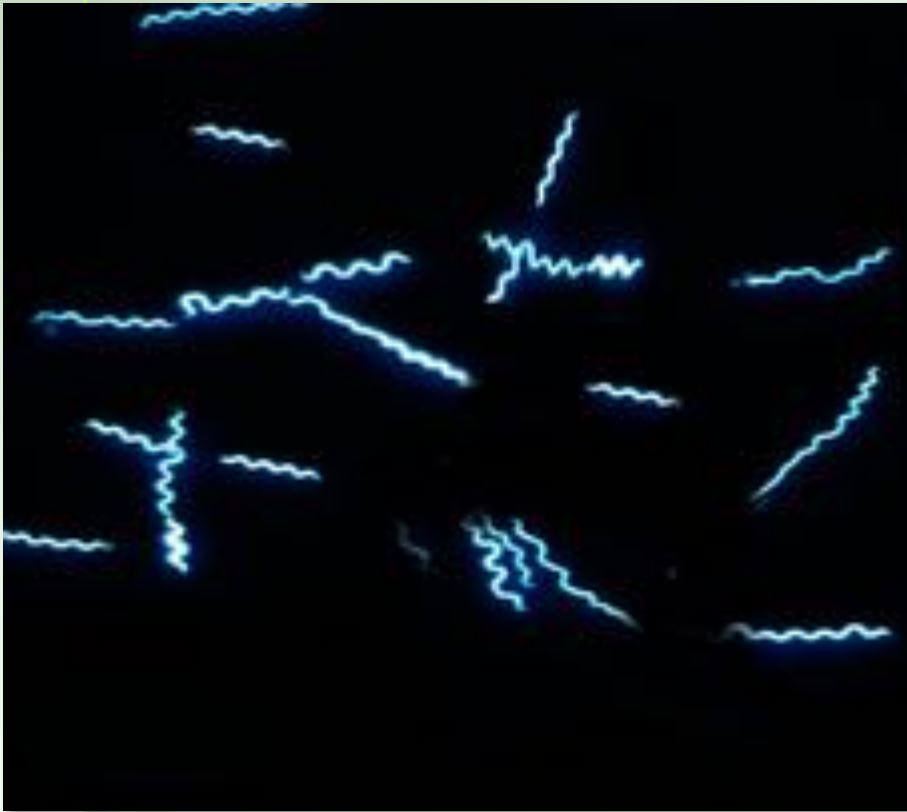


Practical Taxonomy



Spirochete Basics

Morphology



- .1-.5 μm x 5-20 μm
- Gram-negative type cell wall with outer membrane
- Axial filaments; possibly precursors of eukaryotic flagella



Spirochete Basics

General characteristics

- Three pathogenic genera: *Treponema*, *Borrelia*, *Leptospira*
- Many non-pathogenic species are commensals or free-living
- **Don't Gram stain well**, if at all
- **Difficult to culture**



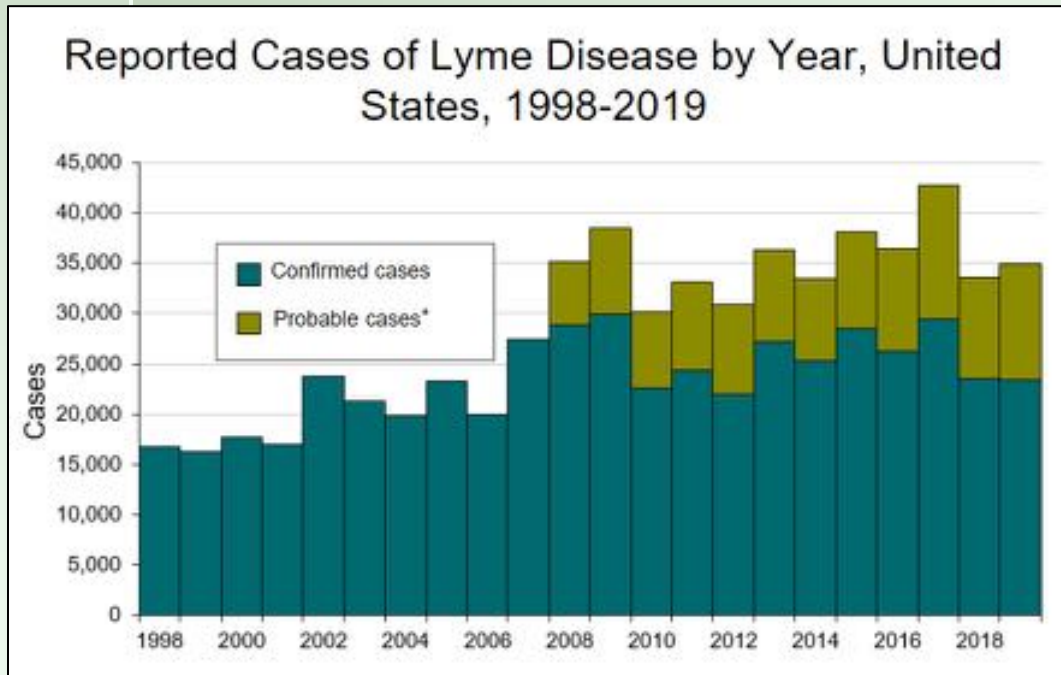
Lyme Disease History

- Disease named in 1975
 - A cluster of children in Lyme, CT with 'Lyme Arthritis'
 - Parts of the syndrome described elsewhere earlier
- A **tick-transmitted disease** caused by *B. burgdorferi*



Lyme Disease

An emerging infection

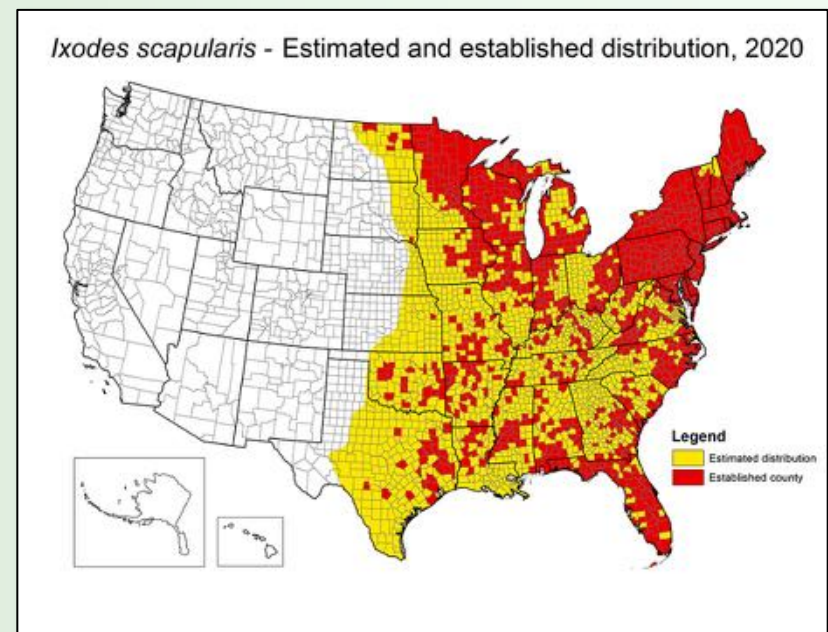
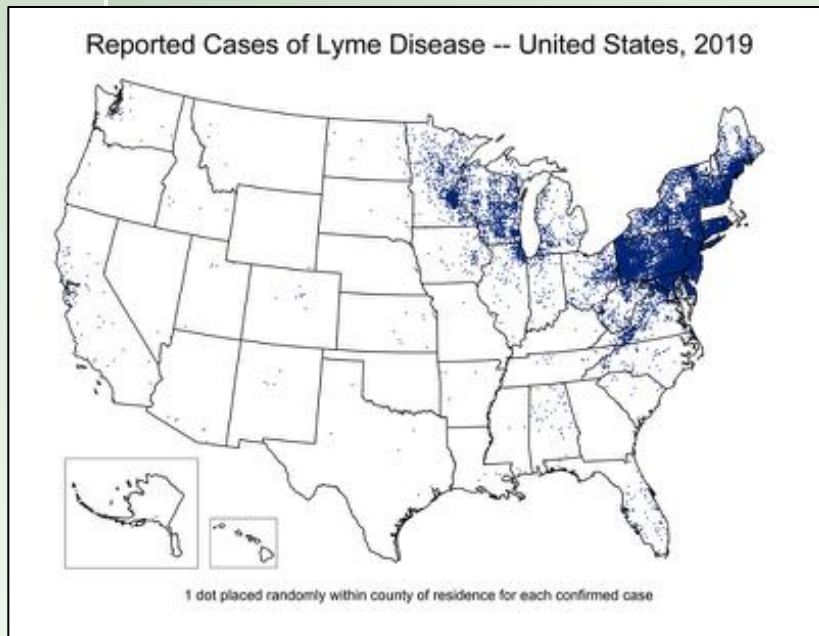


Source:
CDC

- Increase in reported cases in 1990s; stable since
 - Increased incidence
 - More **contact** with reservoirs and vectors
 - Increased reporting
 - Laboratory and clinician requirements
 - Increased awareness
 - Popular press and medical literature



Lyme Disease Geography



Source: CDC



Lyme Disease

Epidemiology

- Peak ages: **Bimodal**: children 5-9 and adults 20-54
- Peak months: **May-Oct**
- *Borrelia lonestarii* spread by the Lone Star tick in SE US causes similar illness, but with negative serology
- Europe: *Ixodes ricinus* vector
 - Different *Borrelia* strains; *B. afzelii*, *B. garinii*, *B. lusitaniae*, *B. bissettii*,
 - Different presentation; more neurologic disease, chronic skin lesions



Lyme Disease Reservoirs



- White-footed mouse and other small animals.
- On the West coast and in the SE US, human-feeding species of *Ixodes* nymphs primarily feed on reptiles, and are rarely infected with *B. burgdorferi* even though it is found in rodents in those areas.
- The white-tailed deer is not competent as a host, but is critical to the ecology of the vector.



Lyme Disease Vectors



- Ixodes ticks
- Larval tick prefers small mammals
- Nymph prefers white-footed mice; **humans incidental**
- Adult prefers white-tailed deer; **humans incidental**



Lyme Disease

Pathogenesis

- Early disease
 - local multiplication and erythema migrans rash
 - A few days after bite
 - Disseminated disease with musculoskeletal, cardiac, or neurological involvement
 - Days to weeks
 - Neurological disease after weeks to months
 - tissue injury due to presence of organism
- Later disease
 - tissue injury both organism and immune-mediated
 - Relapsing arthritis wanes in frequency as immunity slowly eliminates spirochetes
 - chronic arthritis associated with HLA-DRB1*0401 and DRB1*0101
 - Months to years after initial infection; rare



Lyme Disease Pathogenesis

- Genome sequence
 - Minimal metabolic suite
 - Lots of lipoproteins
- Physiology
 - Adapted to insect and mammalian hosts; relies on host for substrates
 - Differential expression of surface lipoproteins depending on host location



Lyme Disease

Clinical Features: Early



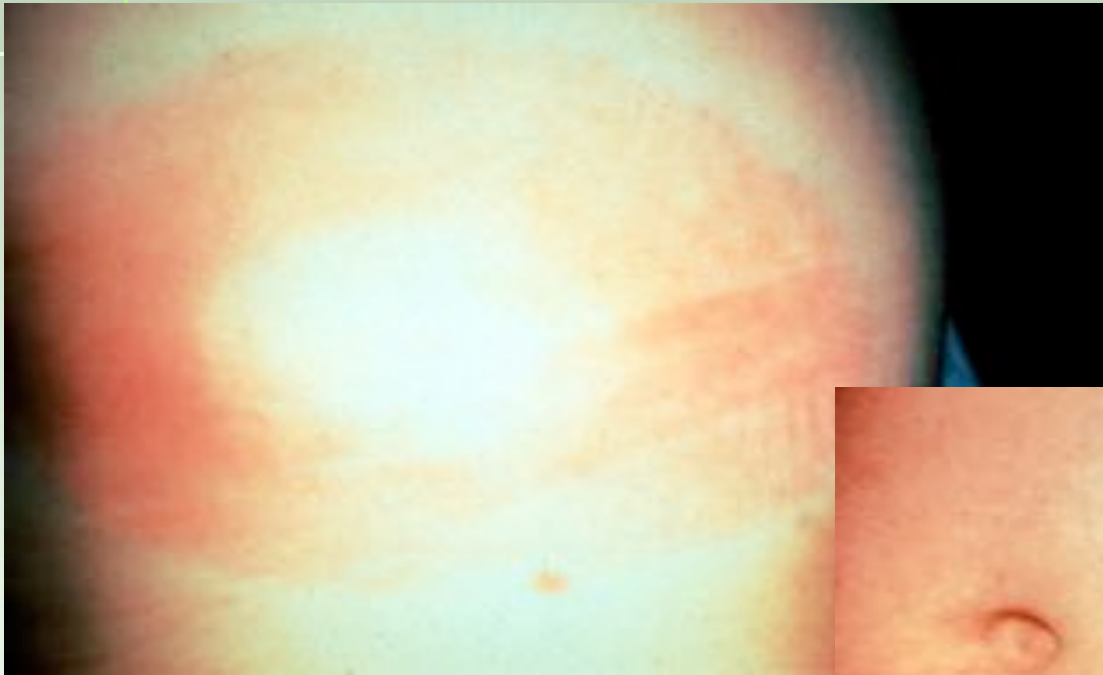
Large, red, slowly spreading rash characteristic of Lyme Disease called erythema migrans (EM) rash



- Erythema migrans
 - Doesn't always clear in center
 - Can be pleiomorphic; plaque-like lesions or scattered.
 - Present in 70-80% of patients.
- Fever, HA, chills, myalgias, arthralgias, and fatigue



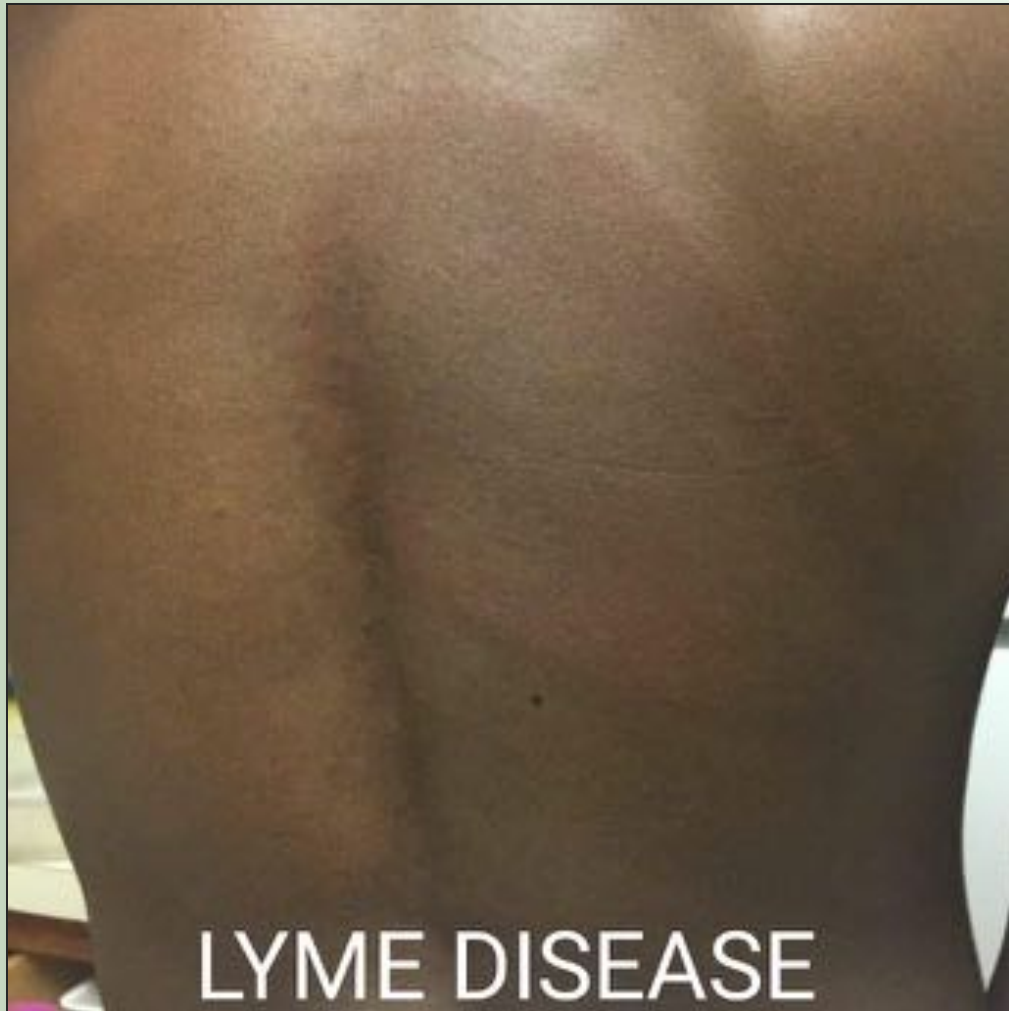
More EM Rashes



EM Rash images courtesy
Dr. Eugene Shapiro



EM on Darker Skin



- From @brownskinmatters
- <https://twitter.com/brownskinmatters/status/1276505449362337793?lang=en>



An Unusual EM



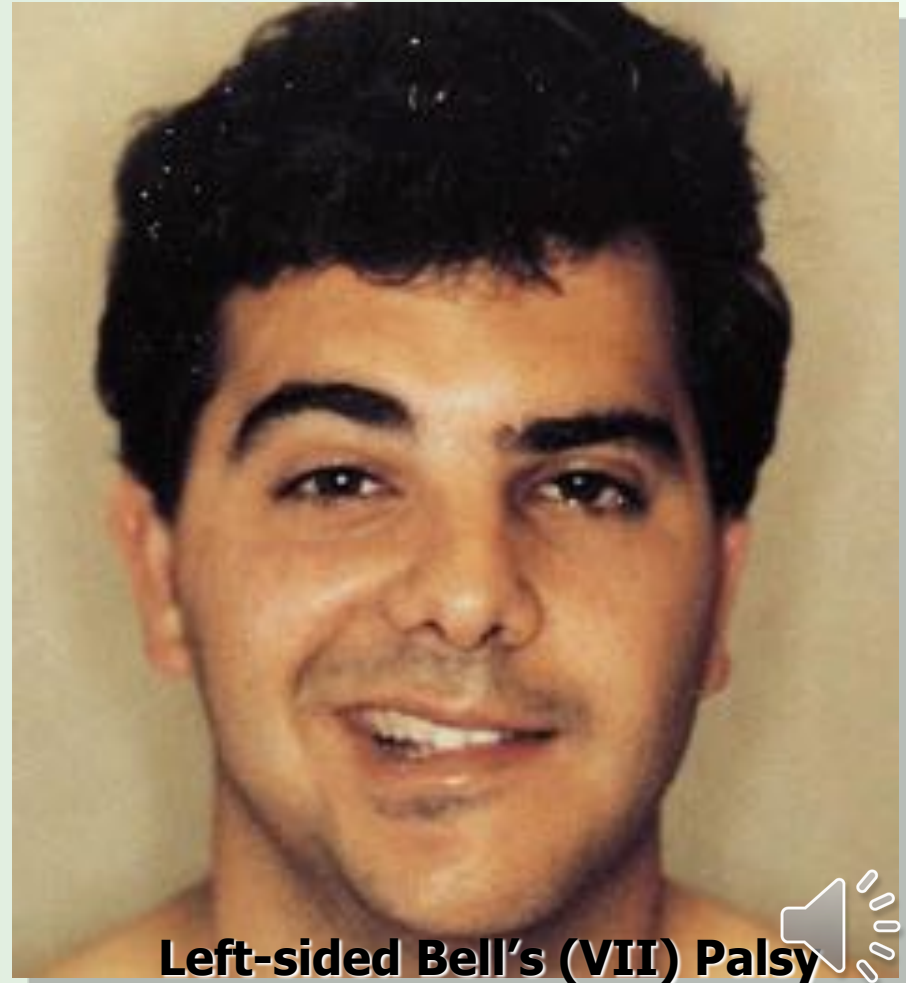
This unusual vesicular EM was mistaken for shingles, but the wide area of erythema is unusual. Patient developed Bell's palsy the next day and seroconverted to Lyme. Courtesy Dr. Eugene Shapiro



Lyme Disease

Clinical Features: Early

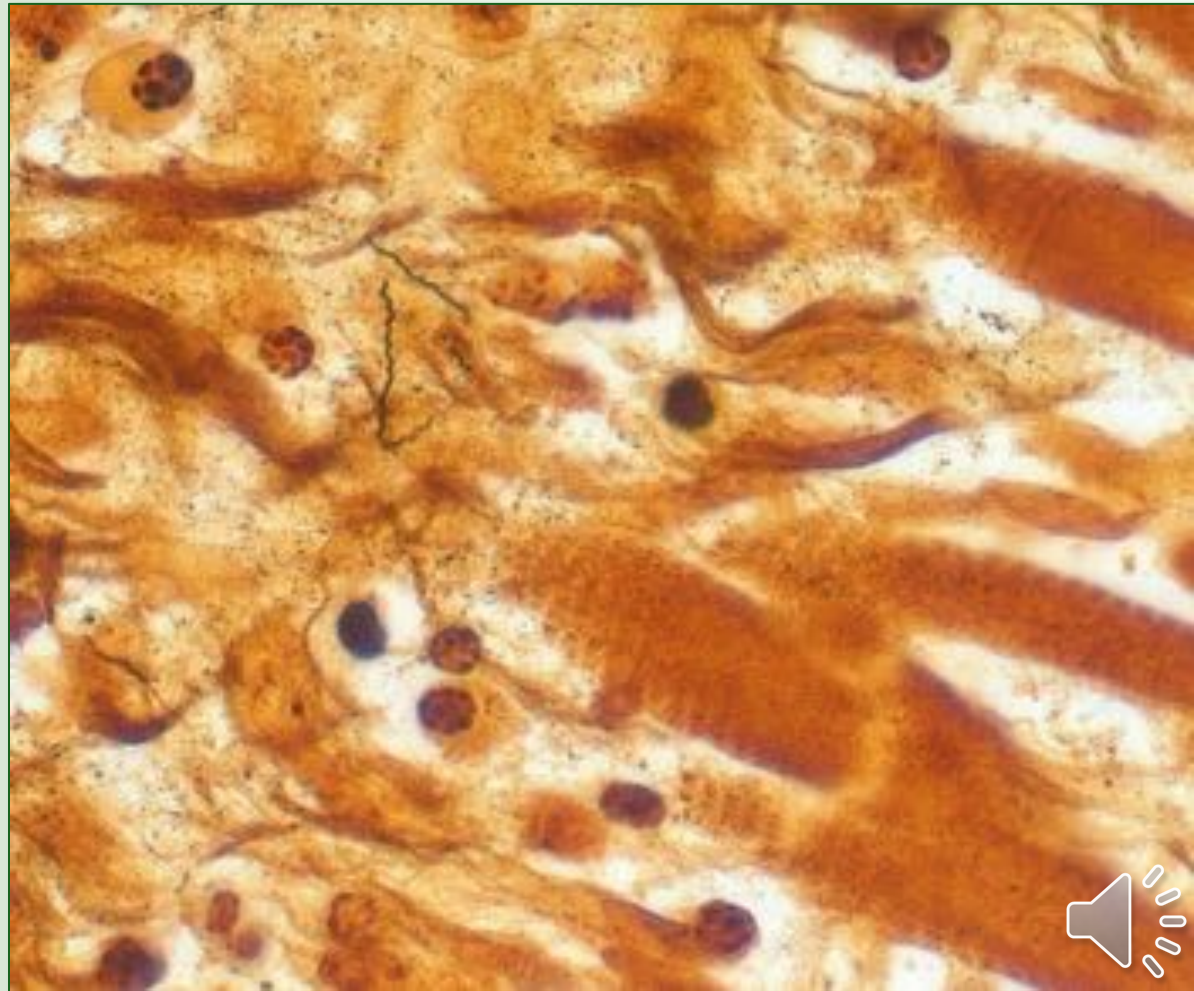
- Disseminated disease can occur early
 - **Cutaneous:** secondary EM lesions, tend to spare palms and soles
 - **Musculoskeletal:** joint pain, arthritis, myositis
 - **Neurologic:** 'aseptic' meningitis resulting in cranial neuritis, **Bell's palsy**, peripheral neuropathy (~15% of patients)
 - **Cardiac:** conduction disturbances (AV block), myocarditis (~5%)
 - **Other:** hepatitis, conjunctivitis, pharyngitis, hematuria, malaise, and fatigue



Left-sided Bell's (VII) Palsy

Lyme Carditis

- Warthin-Starry stained photomicrograph of a heart tissue specimen revealed the presence of a number of *Borrelia burgdorferi* spirochete s. At this stage, after having infected the heart muscle, the disease is more specifically referred to as Lyme carditis.
- https://phil.cdc.gov/details_linked.aspx?pid=16517



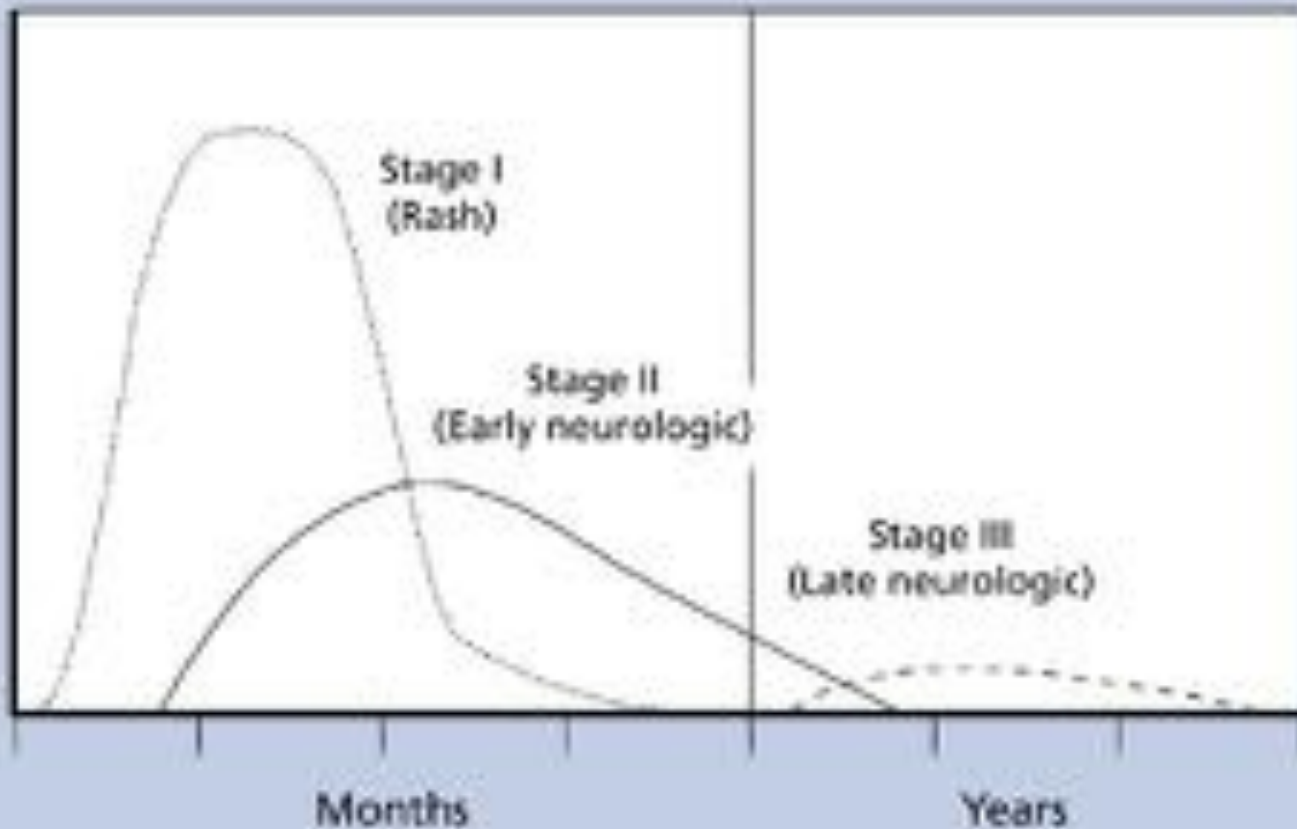
Lyme Disease

Clinical Features: Late/Persistent

- Skin
 - acrodermatitis chronica atrophicans (Europe)
- Musculoskeletal
 - 60% of untreated patients may experience relapsing or chronic **arthritis**, most commonly of knees; 1 or a few joints affected.
- Neurologic
 - Polyneuropathy, ataxia, spastic paraparesis,
 - More questionable: encephalopathy, cognitive defects, dementia, headache

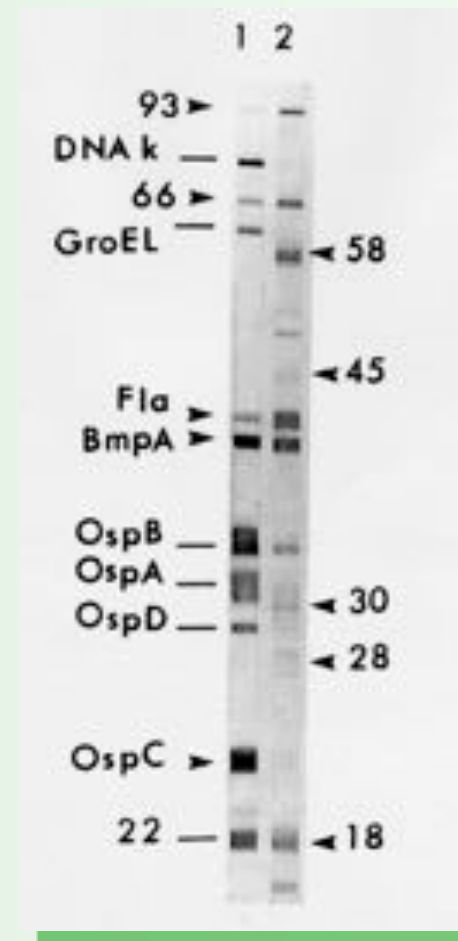


Lyme Disease – Clinical Time Course



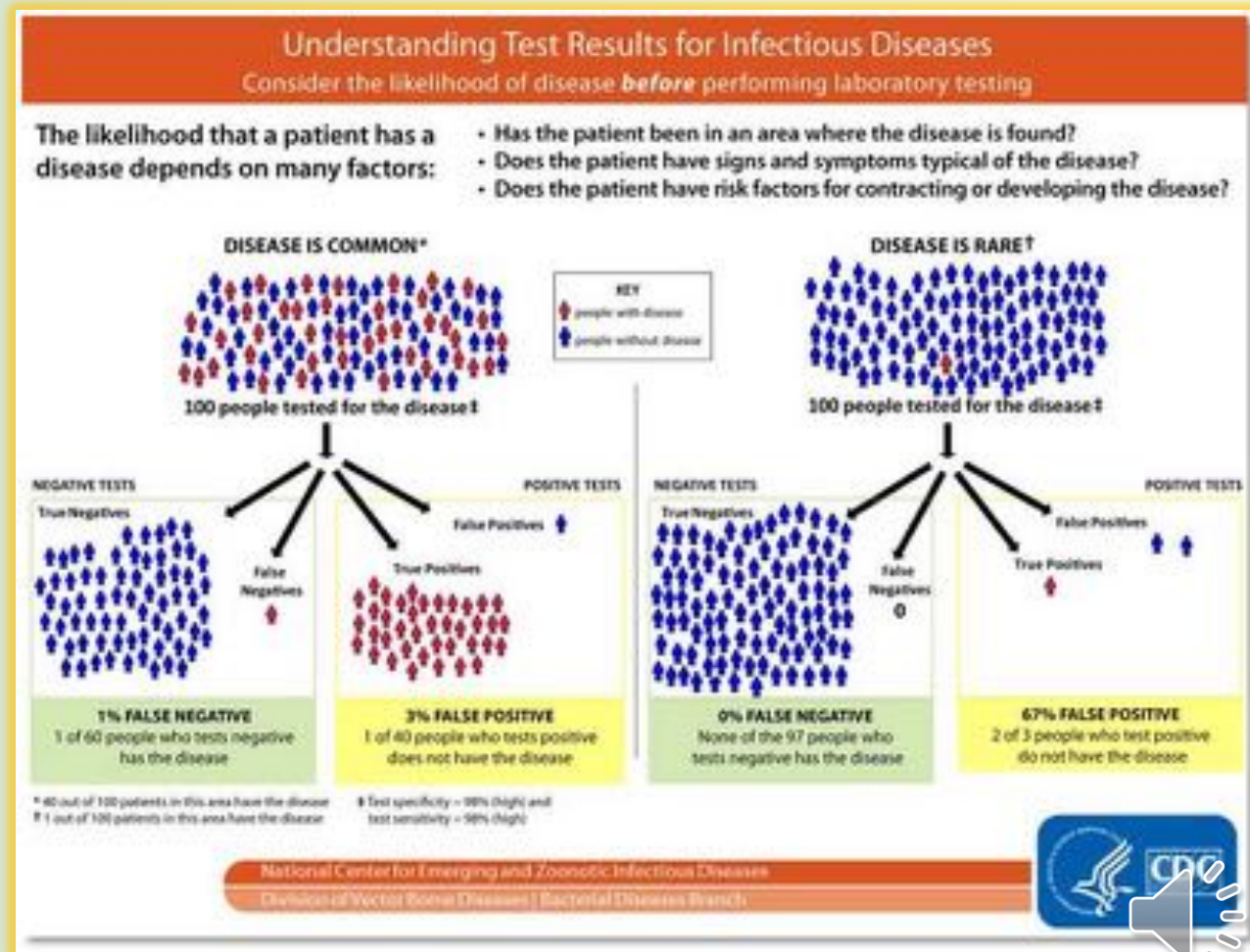
Lyme Disease Diagnosis

- Early disease: clinical diagnosis; requires up to 4-6 weeks for IgM response to appear
 - An isolated IgM that doesn't convert to an IgG **is a false-positive.**
- Lyme serology and Western blot
- DNA probes and PCR investigational
- CSF titers in late CNS disease



Lyme Disease – Don't Test Everyone!!

- Test only at-risk patients with compatible clinical syndromes.
- Consider geography, disease.
- Lyme is **overtested** and **overtreated**.



Lyme Disease

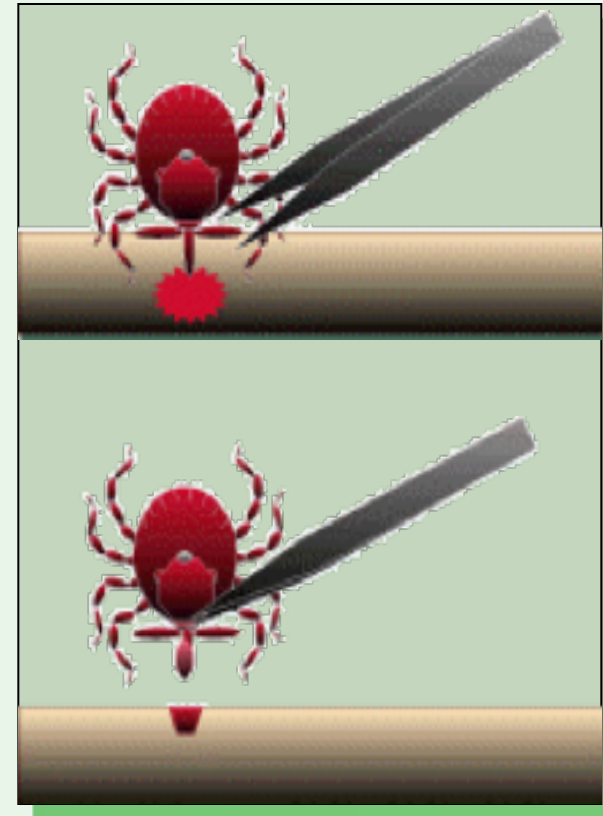
Treatment

- **Early disease:** amoxicillin or doxycycline for 10-21 days
- **Cardiac disease:** oral doxycycline for mild cases: IV PCN or ceftriaxone for 10 days otherwise
- **Neurologic disease:** IV ceftriaxone or PCN or doxycycline (oral; in patients without severe parenchymal disease)
- **Arthritis:** doxycycline or amoxicillin for 1 month, IV therapy for non-responders.



Lyme Disease Prevention: Tick exposure

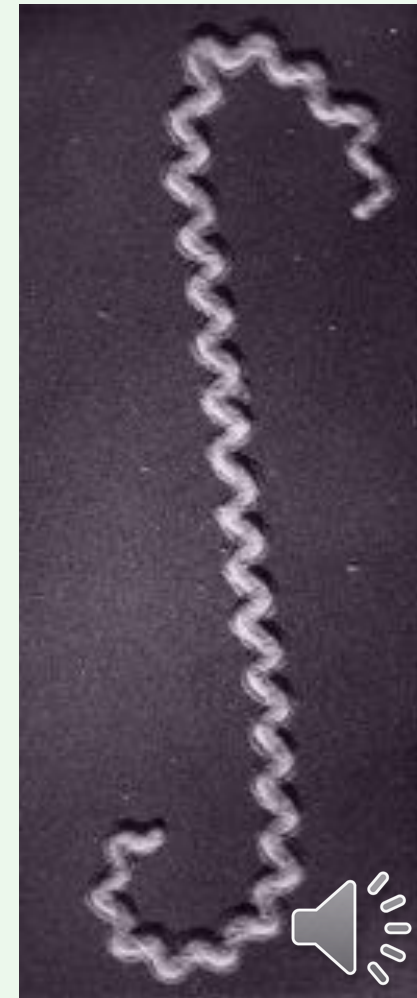
- Tick avoidance and rapid removal
 - light colored clothing
 - daily inspection
 - prompt removal
 - 20-fold increase in likelihood of infection if tick attached >72h
 - repellants with DEET or permethrins
- Antibiotic prophylaxis not recommended
 - possibly useful in high-prevalence areas with *Ixodes* bites



Leptospira spp.

Leptospirosis

- Caused by *L. interrogans*
- A zoonosis: domestic animals and rodents
 - Spirochetes shed in urine, enter skin
- Occurs in a benign and a severe (Weil's disease) form
- Diagnosed by culture or serology
- **Increasing incidence** in the US over the past 20 years.
 - Seen in persons with occupational exposure
 - Urban children
 - And in freshwater recreation; kayaking, rafting, swimming, triathletes; occasional outbreaks.



Leptospira spp.

Clinical forms

- Mild form: flu-like illness
- Weil's disease (~10%)
 - damage to vascular endothelium
 - 2-28d incubation period then...
 - **Septicemic** phase, up to 1 week
 - fever, chills, HA, stiff neck,
 - 'Immune' phase
 - HA, **meningitis**,
 - **hepatic** and **renal** dysfunction,
 - thrombocytopenia, hemorrhage, hypotension
 - 10-15% mortality
 - Survivors usually recover fully



Leptospira spp.

Diagnosis and therapy

- Diagnosis
 - Microscopy & DFA
 - insensitive
 - Culture
 - 2 weeks or more to positive
 - Serology
 - Most common approach, but not 100% sensitive
 - CDC microscopic agglutination (MAT)
 - Molecular (not FDA approved, but useful)
- Therapy
 - A penicillin or tetracycline; IV in severe disease



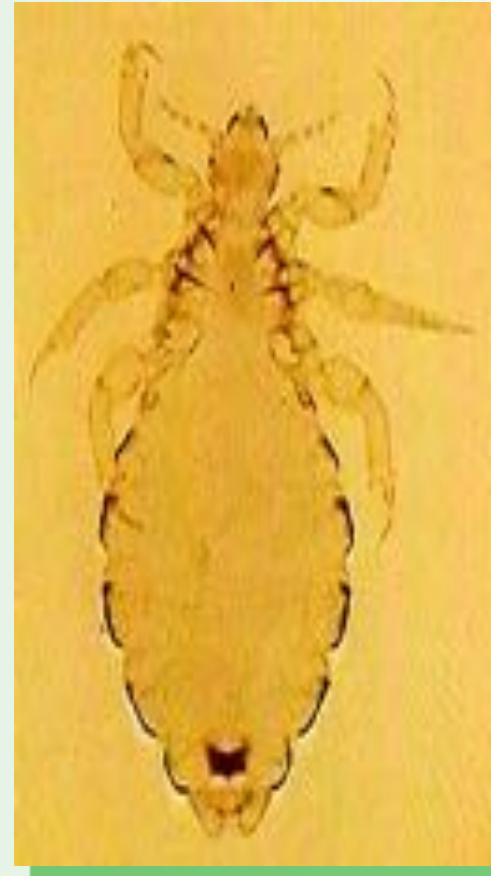
***Borrelia*: Relapsing fever, General Aspects**

- Caused by *B. recurrentis* (louse-borne relapsing fever), or up to 15 endemic species (tick-borne (endemic) relapsing fever)
- Both forms manifested by:
 - 1 week incubation, abrupt onset
 - fever, headache, myalgias, hepatosplenomegaly
 - neurologic complications
 - possible death from pneumonia, myocarditis, hemorrhage or shock
- Relapses of declining severity at 7-10 day intervals
- *Borrelia miyamotoi* seen rarely in NE, upper Midwest, mid-Atlantic states.



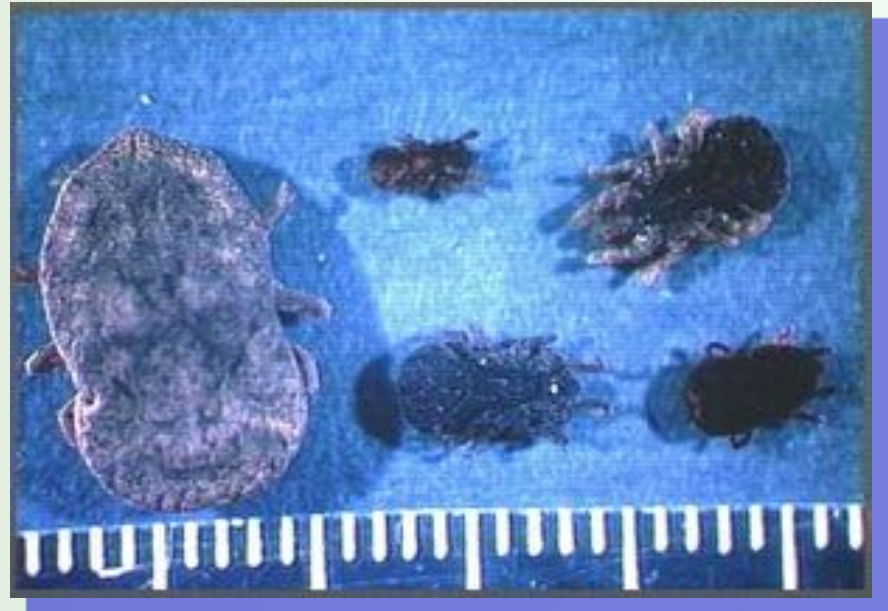
***Borrelia*: Relapsing Fever Epidemic (louse-borne)**

- Spread by human body louse (*Pediculus humanus*)
- 4-40% case-mortality
- Endemic in Central & East Africa, Andes
- Only 1 relapse, usually



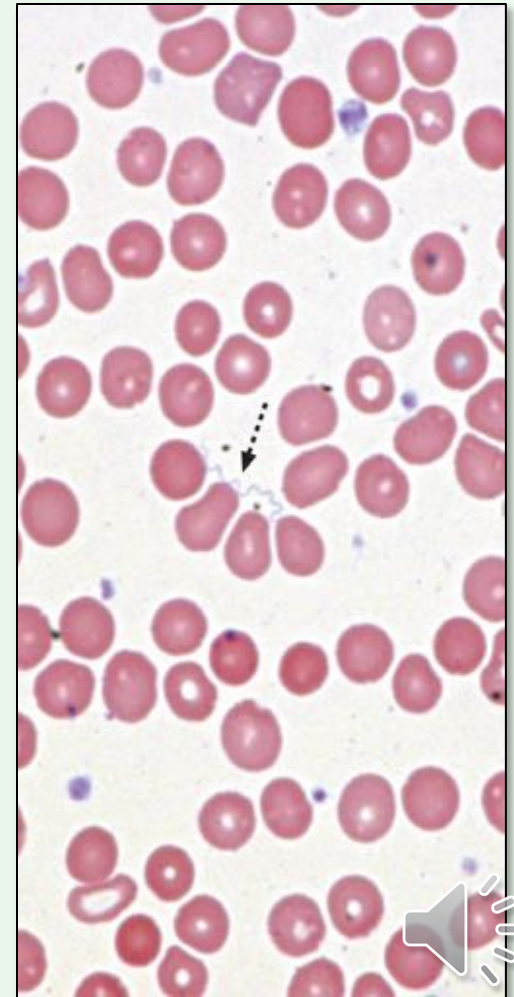
***Borrelia*: Relapsing Fever Endemic (tick-borne)**

- Spread by soft ticks (*Ornithodoros* spp.)
- 2-5% case mortality
- Endemic worldwide
- Multiple relapses common



Borrelia: Relapsing Fever Diagnosis and Therapy

- Diagnosis
 - **Visualization of organisms** in peripheral blood - 70% of patients
 - Serology of limited value
- Therapy
 - Tetracycline, chloramphenicol, penicillin, or erythromycin
 - Typically causes a *severe* Jarisch-Herxheimer type reaction; fever and prostration upon treatment.



Treponema spp

Yaws, Bejel

- Both caused by subspecies of *Treponema pallidum*
 - Bejel
 - Bejel is also called 'endemic syphilis'
 - Present in Africa, Asia, Australia
 - Spread orally by cooking and eating utensils
 - Yaws
 - Nodular skin disease followed by destructive lesions of bone and lymph nodes
 - Present in Central and South America
 - Spread by direct contact



Treponema spp

Pinta

- Caused by *Treponema carateum*
 - predominantly cutaneous; pruritic papules persist for months-years
 - Present in Central and South America
 - Spread by direct contact

