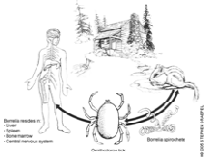
Borrelia

Borrelia recurrentis and others: relapsing fever

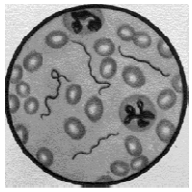
Borrelia burgdorferi: Lyme disease

Borrelia recurrentis

Typical organism:
-10-30 x0.3 µm
-irregular, flexible spirals (spirochete)
-motile: rotation, twisting



Culture:
-Fluid media containing blood, serum or tissue
-chorioallantoic membrane of the chick embrio



Antigenic switching

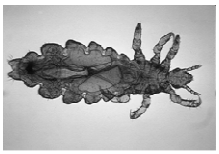
- During antigenic switching, the expressed gene is displaced by an achieved copies of variable antigen genes, residing on linear plasmids
- Antibodies against *Borrelia* appear during the febrile stage, and attack is terminated by their agglutinating and lytic effects

Relapsing fever

Species	Transmission	Distribution
B. recurrentis	Louse-borne	Worldwide
B. latychevi	Tick-borne	Iran
B. persica	Tick-borne	Asia
B. hispanica	Tick-borne	Spain
B. parkeri, *B. turicate* *B. hermsii*	Tick-borne	N. America
B. venezuelensis	Tick-borne	S. America

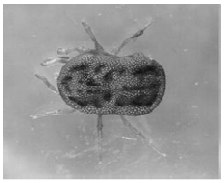
Louse-born relapsing fever

- is a disease of war and starvation
- Occurs as epidemics wherever people are clothed but impoverished
- transmitted by human body louse (bacteria not transmitted to the next generation)
- humans are the only hosts



Tick-born relapsing fever

- Zoonosis
- transmitted by ticks (bacteria are passed transovarially)
- rodents are the main reservoirs
- Endemic foci exist in Asia, Africa, the Americas, the Middle-East and Spain



Pathogenesis, clinical findings

arthropod bites introduce spirochetes into the blood circulation, multiply in many tissues

• incubation: 8 (3-32) days

• fever, chills, headaches for 3-5 day, then fever declines (if untreated)

• afebrile period: 4-10 days; but the antigenic structure of the organisms changes, hence second attack of chills, fever, headache, malaise occurs

• 3 (louse born)-10 (tick-borne) such recurrences (terminates as antibodies arise against the new variant)

✓Clinical Signs	Percentage
✓Fever	100
✓Tachycardia	98
✓Headache	95
✓Myalgia	92
✓Arthralgia	92
✓Hepatosplenomegaly	70
✓Epistaxis	30
✓Peticheal rash	8
✓Other*	3
✓Jaundice	1

*Other symptoms included pneumonia; still-birth; and unconsciousness.

Diagnosis:

• specimen: blood (taken during the rise of the fever)

•GlpQ gene product can be detect by serology

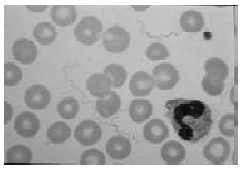
• thin and thick smear stained by Giemsa

• culturing is generally not used

Treatment: tetracycline, erythromycin

Prior to exposure or shortly after tick exposure:

prophylactic: doxycycline



Mother delousing her child in Ethiopia.

Borrelia burgdorferi

• Three genospecies of *B. burgdorferi* cause most human disease: *B. burgdorferi* sensu stricto, *B. garinii*, and *B. afzelii*.

•spiral bacterium,

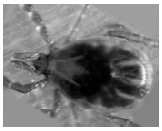
•linear chromosome and multiple linear and circular plasmids

• flexible, motile (endoflagella: enclosed between the outer and inner membranes)

• trasmitted by tick bite

  • Ixodes scapularis, Ixodes pacificus

• reservoirs: small mammals, large mammals (deer)



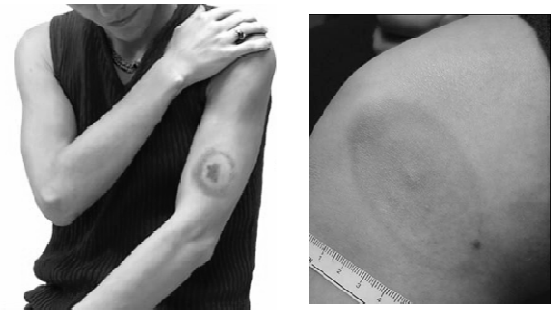
- Eggs into larvae during the late summer. Larvae feed on small animals (usually mice)
- Larvae ⟶ nymphs, (following spring to early summer)
- Nymphs ⟶ ticks in mid-October and early-November, when the adult female ticks feed again, mainly on large animals.
- Small mammals are asymptomatic and therefore serve as reservoirs for the organism.
- Deer are the principal hosts for the adult ticks
- Most Lyme-disease cases result from bites by infected nymphs, as their small size (about the size of a poppy seed) allow them to easily go unnoticed.

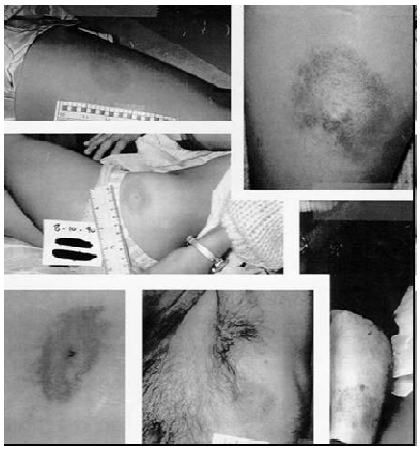
Virulence factors

- Outer surface protein A (OspA)
- OspB
- OspC, for the transmission of the spirochete from tick to mammal
- Lipoprotein variable major protein-like sequence: is needed for the persistence in the host and have a role in immune evasion

Lyme disease is divided into early and late disease

- 1. Erythema migrans : characteristic skin lesion, at the site of the tick bite.
- Incubation period: 7-14 days (but may be as short as a day and as long as 30 days).
- Classically, erythema migrans starts as a red papule at the site of the bite, which gradually expands to an annular lesion with red borders and partial central clearing
- Arthralgias, myalgias, severe fatigue, regional lymphadenopathy.
- Erythema migrans may be absent in about 10% of patients with early Lyme disease





Stage 2 (early disseminated LD)

- After several days or weeks (after the original tick byte), the spirochete may **spread hematogenously**, and patients may develop multiple erythema migrans lesions.
- Fever, headache (flu-like symptoms), mild neck stiffness, migratory musculoskeletal pain, arthralgias, and profound malaise and fatigue
- Neurologic abnormalities (15-20%) of untreated patients: cranial neuropathy, particularly **facial palsy** (which **may be bilateral**), **lymphocytic meningitis**, and motor or sensory **radiculoneuritis.**
- Cardiac involvement (4-8 % of untreated patients): fluctuating **atrioventricular block, pericarditis**.
- *Borrelia* **lymphocytoma** (in Europe) is a firm, painless, bluish-red nodular lesion usually localized on the **earlobe or nipple**.
- **Both stage 2 and 3: arthritis** which affect 60% of the patients. Arthrits is usually **recurrent monoarthritis or asymmetric oligoarticular arthritis**
- Antibiotic-refractory Lyme arthritis ⟶(after antibiotic treatment) associated with certain HLA-DR molecules and T-cell reactivity against OspA

Stage 3 (late persistent LD)

- Arthritis
- subacute mild **encephalopathy** affecting memory and concentration
- chronic mild axonal **polyneuropathy** manifested as distal paresthesias or as radicular pain
- Rarely, **encephalomyelitis or leukoencephalitis**
- autoimmune mechanism may play a role in certain cases of chronic neurologic disease
- **Acrodermatitis chronica atrophicans** found on the extensor surfaces of the extremities: begin insidiously with reddish violaceous discoloration and progress to atrophy of the skin over a period of years. Patients may have an associated sensory neuropathy

Diagnosis

- **Erythema migrans (clinically)**
- Culture: Barbour-Stoenner-Kelly or modified Kelly-Pettenkofer, as well as a prolonged period of observation (up to 12 weeks)
- PCR: from skin, blood, CSF, and synovial fluid
- Serology: a sensitive ELISA or IFA assay, followed by Western blotting when results are indeterminate or positive. IgM Western blot is used only within the first 4 weeks of the illness
- The C6 peptide ELISA has excellent sensitivity and specificity for acute-, convalescent-, and late-phase specimens

Therapy

Oral agents		Comments
Preferred	Doxycycline	Contraindicated in pregnancy, lactation, and children younger than 8 y
	Amoxicillin	–
	Cefuroxime axetil	Useful when cellulitis cannot be ruled out. More expensive.
Alternative	Azithromycin	Patients treated with macrolides should be observed closely because of the risk of failure. .

Intravenous agents		Comments
Preferred	Ceftriaxone	Easy to administer and largest experience in Lyme disease.
Alternative	Cefotaxime	Requires more frequent administration than cefriaxone.
	Penicillin G	More frequent administration. May be less effective than ceftriaxone.

Leptospira

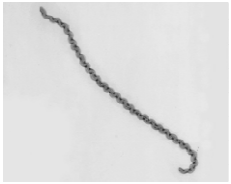
• tigthly coiled spirochetes (darkfield microscope)

•Leptospires are obligate aerobes with an optimum growth temperature of 28 to 30°C. They produce both catalase and oxidase

• Culture: liquid media containing rabbit serum (Fletcher, Korthoff)

• *Leptospira interrogans*: leptospirosis

- zoonosis
- reservoirs: rodents, domestic livestock, pets
- animals excrete the bateria by urine
- humans are infected during swimming or consuming the bacteria
- human to human infection is rare



electron microscopy

Serogroups and some serovars of L. interrogans sensu lato

Serogroup	Serovar(s)
icterohaemorrhagiae,	Icterohaemorrhagiae, copenhageni, zimbabwe
Autumnalis	autumnalis, fortbragg, bim, weerasinghe
Pyrogenes	pyrogenes
Grippotyphosa	grippotyphosa, canalzonae, ratnapura
Canicola	canicola
Australis	australis, bratislava, lora
Pomona	pomona

Virulence factors

- Outer membrane proteins/lipoprotens (fibronectin-binding protein: adhesion)
- Motility (endoflagellum)
- Chemotaxis
- LPS (low endotoxic activity) triggers innate system through TLR2
- Secretory proteins (hemolysine, protease and collagenase) are expressed

Pathogenesis, clinical findings

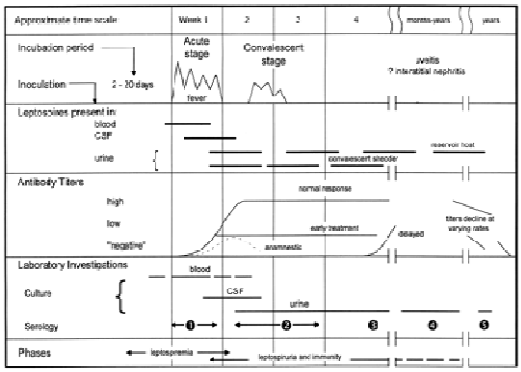
- The disease is maintained in nature by chronic infection of the renal tubules of maintenance hosts
- Ingested water or food or pass through mucous membranes
- The **great majority** of infections caused by leptospires are either **subclinical or of very mild** severity
- Enter into the blood
- Extensive damage to capillary endothelial cells, **vasculitis, petechial hemorrhages**
- Aseptic meningitis
- In **severe cases** widespread **visceral haemorrhages, renal failure (uremia) and hepatocellular failure (jaundice)**

Classicaly: biphasic illness

- The clinical presentation of leptospirosis is biphasic with the acute or septicemic phase lasting about a week, followed by the immune phase, characterized by antibody production and excretion of leptospires in the urine (Weil-disease)
- Complications are associated with localization of leptospires within the tissues during the immune phase and thus occur during the second week of the illness (jaundice, renal failure, widespread hemorrhages, myocarditis, shock and confusion).

Clinical symptoms

Jaundice	Arthralgia
Anorexia	Abdominal pain
Headache	Nausea
Conjunctival suffusion	Cough
Vomiting	Hemoptysis
Myalgia	Hepatomegaly



Diagnosis

- Clinical symptoms
- Microscopic agglutination test: gold standard
- Isolation from urine, blood or tissues (culture or PCR)
- liquid media containing rabbit serum (Fletcher, Korthoff)

Treatment

- - penicillin / doxycycline
- Chemoprophylaxis: -doxycycline
- Vaccine: used in some countries