

1. Case of the Unknown Spirochete

## Case of the Unknown Spirochete

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A 40 yo male presents with a 5 day history of fevers, chills, sore throat and diffuse myalgias. Two days prior to presenting, the patient developed a diffuse erythematous rash covering his chest and abdomen. In the emergency room, the patient was given amoxicillin for presumed pharyngitis and discharged.

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2. Case of the Unknown Spirochete

## Case of the Unknown Spirochete

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One hour after taking his first dose of amoxicillin, he developed high fevers, chills, headache and light-headedness. He returned to the ER where his blood pressure was noted to be 80/50.

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3. Spirochetes

## Spirochetes

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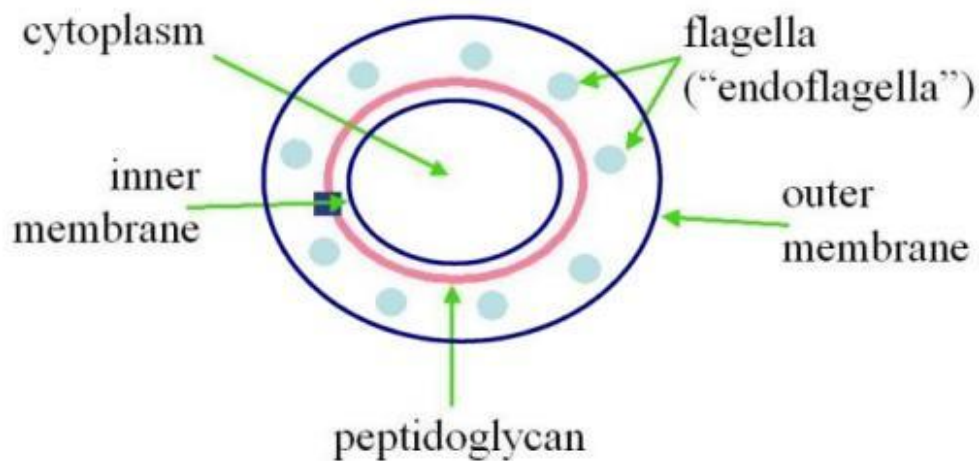
### 3 Genera Causing Human Disease

- *Leptospira*
- *Borrelia*
- *Treponema*
- Common: LONG, THIN, SPIRAL

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4. Spirochete Cell Structure, Cross Section

### Spirochete Cell Structure, Cross Section



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## 5. Leptospirosis

### Leptospirosis

- most common zoonotic infection world-wide
- most prevalent in tropics, subtropics
- caused by *Leptospira interrogans*
- severity of disease varies with serovar

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## 6. Leptospirosis (cont.)

### Leptospirosis

- contact: fresh water contaminated with animal urine
- OR animal urine, blood, tissue
- entry: mucous membranes, skin

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7. Leptospirosis (cont.)

## Leptospirosis

- 2 forms, vary with serovar: icteric and anicteric
- 2 stages: “septicemic” and “immune” both febrile
- early or septicemic phase: high fever, headache, myalgias, conjunctival suffusion and/or hemorrhage, abdominal pain, vomiting

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8. Leptospirosis (cont.)

## Leptospirosis

- “anicteric” ~90% of patients:  
less severe, with lower fever, meningitis, uveitis, rash
- “icteric” ~10% of patients:  
more severe, with hepatitis and jaundice, renal failure, pulmonary and visceral hemorrhage, carditis  
often fatal if untreated  
“Weil’s disease”

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9.

## Lyme Disease

# Lyme Disease

- Contact and Entry: tick bite
- wide distribution in Northern hemisphere
- caused by *Borrelia burgdorferi* (US and Eurasia), *Borrelia garinii* (Eurasia), *Borrelia afzelii* (Eurasia)
- bacteria cause persistent infection in immunocompetent hosts
- 3 clinical stages

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## Early Localized Lyme Disease

# Early Localized Lyme Disease

- days to a couple of weeks after tick bite
- erythema migrans skin rash reflects migration of spirochetes from tick bite through skin
- can also have regional lymphadenopathy

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11. Early Disseminated Lyme Disease

## Early Disseminated Lyme Disease

- days to months after tick bite
- fever, malaise, migratory arthralgias, arthritis
- secondary erythema migrans skin lesions
- neuroborreliosis, especially facial palsy, radiculoneuropathy
- pancarditis, AV nodal block

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12. Late Lyme Disease

## Late Lyme Disease

- months to years after tick bite
- arthritis (most common with *B. burgdorferi*)
- polyradiculopathy  
(neurologic manifestations worst with *B. garinii*)
- encephalopathy
- acrodermatitis chronicum atrophicans (skin lesion with *B. afzelii*)

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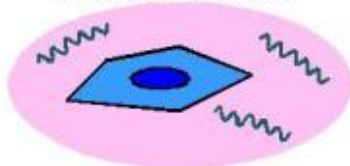
13.

Spirochetes: Slide 29

### ADHESION PATHWAYS USED BY *BORRELIA*

#### EXTRACELLULAR MATRIX

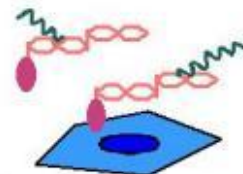
multiple components



decorin-binding proteins (Dbp),  
fibronectin-binding protein,  
unknowns?

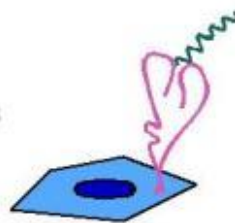
#### PROTEOGLYCAN

protein core + glycosaminoglycan  
chains, cell-associated and matrix



*Borrelia* glycosaminoglycan-binding  
protein (Bgp), Dbp, unknowns?

#### INTEGRINS



protein heterodimers,  
cell-associated

P66, unknowns?

At least some of these binding pathways are also present in *RF Borrelia*.

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14.

Immune Evasion by *B. burgdorferi*

## Immune Evasion by *B. burgdorferi*

- Few Integral Outer Membrane Proteins
- Antigenic Variation
  - Vls locus in Lyme disease *Borrelia*
    - small changes in multiple portions can generate over  $10^{30}$  variants in the VlsE protein
  - Vsp and Vlp loci in relapsing fever *Borrelia*
    - change entire protein, with about 15 possible variants (together termed Vmp)
- Binding of Complement Factor H

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15. Relapsing Fever

## Relapsing Fever

- Contact and Entry: tick- or louse-borne (tick=endemic, louse=epidemic)
- episodes of high fever separated by afebrile periods
- peaks of fever coincide with peaks of spirochetemia
- other clinical findings: thrombocytopenia, hepatomegaly, splenomegaly

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16. Relapsing Fever (cont.)

## Relapsing Fever

- recurrent spirochetemia and fever due to emergence of subpopulations of bacteria expressing a different major surface antigen, Vsp or Vlp, together known as Vmp
- spirochetes expressing original antigen are cleared by immune response
- major antigen switching due to recombination of silent gene into single expression site

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17. Relapsing Fever vs. Lyme Disease

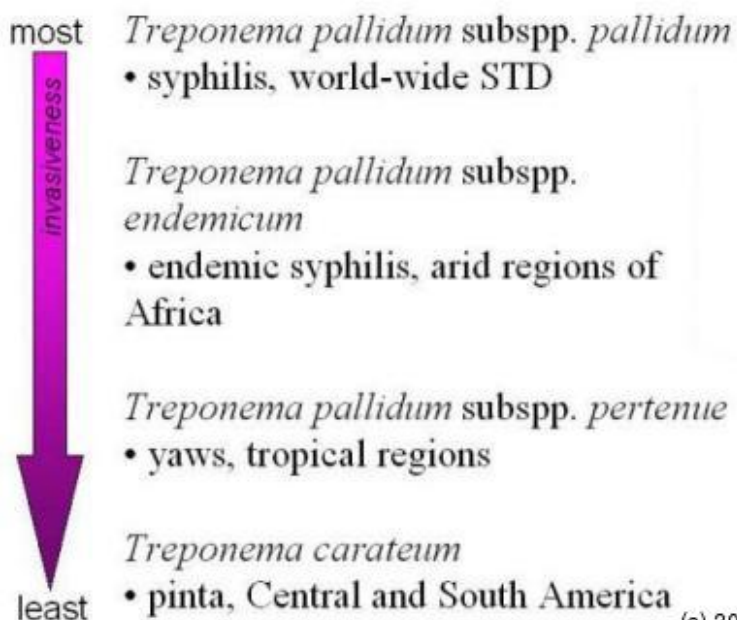
## Relapsing Fever vs. Lyme Disease

- Relapsing fever: agents reach high titers in blood  
Lyme disease: agents do not
- Relapsing fever: episodes of high fever separated by afebrile episodes are common  
Lyme disease: not
- Relapsing fever: thrombocytopenia is frequent  
Lyme disease: not
- Relapsing fever can be fatal, Lyme disease is not

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18. Treponemal Diseases

## Treponemal Diseases



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19.

## Syphilis

### Syphilis

- Contact and Entry: STD, skin or mucous membrane contact with infectious lesion, or congenital
- 3 stage disease
- >36,000 cases in US in 1999,  
INCREASING PREVALENCE
- agent, *T. pallidum* subspp. *pallidum*, has not yet been propagated in laboratory culture
- essentially nothing known of virulence mechanisms

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## Primary Syphilis

### Primary Syphilis

- 10-90 days after encounter
- painless lesion (chancre) at site of inoculation
- regional lymphadenopathy

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## Secondary Syphilis

### Secondary Syphilis

- 6 weeks-6 months after primary, lasts 4-12 weeks
- diffuse, non-itchy rash all over, including palms and soles
- fever
- myalgias and arthralgias

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## Latent Syphilis

Then comes latent syphilis...

- Patient is asymptomatic
- Can last years to decades

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## Tertiary Syphilis

### Tertiary Syphilis

- dementia
- loss of sensory & motor neuron function
- seizures
- arthritis
- heart failure
- tissue destruction

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24.

## Case of the Unknown Spirochete (cont.)

### Case of the Unknown Spirochete

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One hour after taking his first dose of amoxicillin, he developed high fevers, chills, headache and light-headedness. He returned to the ER where his blood pressure was noted to be 80/50.

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25.

Spirochetes: Questions to Ask

## Case of the Unknown Spirochete

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Questions to ask:

Where are the lesions?

What do the lesions look like?

When did the lesions develop?

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Spirochetes: Questions to Ask (cont.)

## Case of the Unknown Spirochete

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Questions to ask:

Where has the patient been?

What has the patient been doing?

Who has he/she been doing it with?

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27. Diagnosis of Spirochetal Diseases

## Diagnosis of Spirochetal Diseases

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Isolation is futile!!

Diagnosis relies on direct visualization  
(relapsing fever, leptospirosis), PCR or  
serologic testing

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28. Diagnosis of Spirochetal Diseases (cont.)

## Diagnosis of Spirochetal Diseases

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Syphilis

Non-specific

Rapid Plasma Reagin (RPR)

Venereal Disease Research Laboratory  
(VDRL)

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29. Diagnosis of Spirochetal Diseases (cont.)

## Diagnosis of Spirochetal Diseases

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### Syphilis: RPR and VDRL

Anti-cardiolipin tests

Must be confirmed by a specific anti-treponemal test

Useful for following response to therapy

No cross reaction with other spirochetes

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30. Diagnosis of Spirochetal Diseases (cont.)

## Diagnosis of Spirochetal Diseases

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### Syphilis: Specific tests

Fluorescent antibody absorbed test (FTA-ABS)

*T. Pallidum* hemagglutination assay (MHA-TP)

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31. Diagnosis of Spirochetal Diseases (cont.)

## Diagnosis of Spirochetal Diseases

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Syphilis: FTA-ABS, MHA-TP

Remain positive for life (not useful for following response to therapy)

Can cross react with other spirochetes (e.g. *Borrelia*)

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32. Diagnosis of Spirochetal Diseases (cont.)

## Diagnosis of Spirochetal Diseases

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Lyme Disease  
Modalities

- Histopathology
- Culture
- Serology
- Polymerase chain reaction

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33. Diagnosis of Spirochetal Diseases (cont.)

## Diagnosis of Spirochetal Diseases

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### Serology

Two step testing for both IgM  
(early) and IgG (late)  
antibody response

- ELISA
- Western blot

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34. Diagnosis of Spirochetal Diseases (cont.)

## Diagnosis of Spirochetal Diseases

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### Lyme Disease Serology

- IgM- typically becomes positive 1-3 weeks  
IgG- typically becomes positive 3-6 weeks
- Both IgM and IgG may remain positive for years  
after treatment of infection
- **DO NOT USE IF THERE IS A CLINICAL  
DIAGNOSIS OF LYME DISEASE!!**

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35. Diagnosis of Spirochetal Diseases (cont.)

## Diagnosis of Spirochetal Diseases

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### Leptospirosis and Relapsing fever

- PCR
- Serologic tests: hemagglutination, ELISA
- Direct visualization (from CSF for *Leptospira*; from blood for Relapsing fever)

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36. Treatment of Spirochetal Diseases

## Treatment of Spirochetal Diseases

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Only 4 drugs to know:

- Penicillin (or Amoxicillin)
- 3<sup>rd</sup> Generation Cephalosporins (eg Ceftriaxone)
- Tetracyclines (e.g. doxycycline)
- Macrolides

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37. Treatment of Spirochetal Diseases (cont.)

## Treatment of Spirochetal Diseases

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Syphilis	Lyme	Relapsing fever & Leptospirosis
PCN	Amoxicillin or Doxycycline	any
Ceftriaxone Erythromycin Doxycycline	Ceftriaxone for neurologic or severe cardiac disease	
	Macrolides for allergic patients	

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38. Spirochetal Diseases: Take home

## Spirochetal Diseases: Take home

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Human spirochetal diseases are largely similar!!

All :

Enter through skin

Cause disseminated disease involving  
multiple organ systems including CNS

Are able to avoid the initial host immune  
response to cause relapses or late disease

Are susceptible to similar antibiotics

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