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Third stage

THE SPIROCHETES

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Th e spirochetes

- A group of large number of spiral and motile bacteria
- They are divided into two main families:
  1. Spirochaetaceae involve two genera : Borrelia and Treponema (pathogenes for human) .
  2. Leptospiraceae : includes three genera: Leptospira, Leptonema , and Turneriella .

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Th e spirochetes

- The spirochetes bacteria share many structural characteristics that are common among them.
- The typical organism is characterized as long, slender, helically coiled, spiral or cork screw shaped bacilli.

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The spirochetes

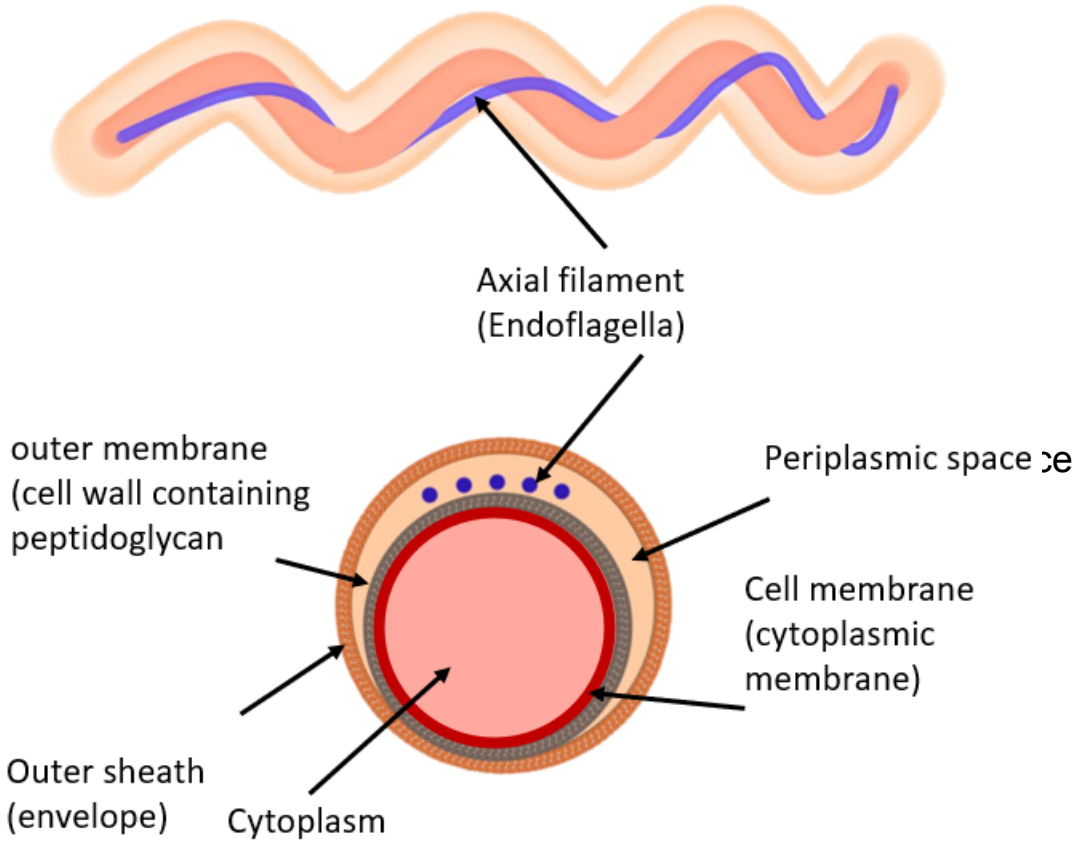
- **The cross section of *T pallidum* as a typical spirochetes shows that the bacteria has:**

  1. An outer envelope or sheath (glycosaminoglycan coating).
  2. the outer membrane (under the sheath) containing the peptidoglycan and maintains the structural integrity of the organisms.
  3. Periplasmic space
  4. Axial filaments (Endoflagella) in the periplasmic space encased by the outer membrane.

- Th endoflagella begin at each end of the organism and wind around it, extending to and overlapping at the midpoint.

  5. The inner membrane (cytoplasmic membrane) that provides osmotic stability and covers the protoplasmic cylinder.

- Treponemes reproduce by transverse fission.



Cross section of typical spirochete

spirochete

TREPONEMA PALLIDUM

A. Morphology and identification

- The bacteria are slender spirals measuring about 0.2 μm in width and 5–15 μm in length.
- They are actively motile,
- The motility involve the rotation of the bacterium around their endoflagella even after attaching to cells by their tapered ends.
- The organism is so thin and cannot be seen without using immunofluorescent or dark-field illumination techniques
- The spirals can be seen in tissues after staining with a silver impregnation method

Pathogenesis, Pathology, and Clinical Findings

1. Acquired Syphilis

- The infection caused by this organism is restricted to human
- Infection is usually transmitted by sexual contact (via the infectious lesions on the skin and mucosa of genital)
- *The* pathogens can penetrate the intact mucous membranes, or through breaks in the epidermis.
- infectious dose is extremely low, as few as four to eight organisms may cause infection.
- After their entrance, the bacteria multiply locally at the site of entry, and some organisms can spread to nearby lymph nodes and then reach the bloodstream.

The stages of syphilis

- The disease divided into three main stages:
- **Primary syphilis**
- Within 2–10 weeks after infection, a papule develops at the site of infection and breaks down to form an ulcer with a clean, hard base (“hard chancre”).
- **Secondary syphilis**
- This “primary lesion” always heals spontaneously, but 2–10 weeks later, the “secondary” lesions appear.
- These consist of a red maculopapular rash anywhere on the body, including the hands and feet, and moist, pale papules (condylomas) in the anogenital region, axillae, and mouth.

- The patient may also have syphilitic meningitis, chorioretinitis, hepatitis, nephritis (immune complex type), or periostitis.
- The secondary lesions also subside spontaneously.
- Syphilitic infection may remain subclinical, and the patient may pass through the primary or secondary stage (or both) without symptoms or signs yet develop tertiary lesions.
- **Latent syphilis**
- In 30% of cases, the untreated infection remains latent without any symptoms and signs (principally evident by positive serologic test results).

- **Tertiary syphilis**
- In the remain untreated cases, the disease progresses to the “tertiary stage” characterized by the development of granulomatous lesions (gummas) in the skin, bones, and liver; degenerative changes in the central nervous system (meningovascular syphilis, paresis, tabes); or cardiovascular lesions (aortitis, aortic aneurysm, aortic valve insufficiency).
- treponemes can occasionally be found in the eye or central nervous system in late syphilis.

2. Congenital Syphilis

- A pregnant woman with syphilis can transmit ***T. pallidum*** to the fetus through the placenta beginning in the 10th–15th weeks of gestation.
- Some of the infected fetuses die, and miscarriages result; others are stillborn at term.
- Others are born live but develop the signs of congenital syphilis in childhood, including interstitial keratitis, Hutchinson's teeth, saddle nose, periostitis, and a variety of central nervous system anomalies

Treatment

- Penicillin is the drug of choice for treating syphilis
- The spirochete did not showed resistance to penicillin yet.
- For patients with primary, secondary or early latent syphilis, a single dose of benzathine penicillin G administered intramuscularly is enough for cure
- Patients with late latent syphilis or latent syphilis of unknown duration, benzathine penicillin G intramuscularly is given three times at weekly intervals.
- Patients with central nervous system (neurosyphilis) should receive high dose intravenous penicillin for 10 to 14 days
- Penicillin-allergic, nonpregnant patients with early syphilis can be treated with tetracycline.
- Penicillin-allergic, pregnant patients and patients with neurosyphilis must be desensitized to penicillin because of the lack of effective alternative therapies

Borrelia

- the bacteria can be cultured in bacteriologic media containing serum or tissue extracts, but their doubling time is very slow (24 -48 hrs)
- Two main disease caused by these bacteria include , Lyme disease and relapsing fever.

BORRELIA BURGDORFERI AND LYME DISEASE

- Lyme disease is named after the town of Lyme, Connecticut, where clusters of cases in children were identified.
- The spirochete *B. burgdorferi* is transmitted to humans by the bite of a small Ixodes tick.
- The disease has early manifestations with a characteristic skin lesion, erythema migrans, along with flulike symptoms, and late manifestations often with arthralgia and arthritis

Borrelia burgdorferi under darkfield microscope

Ixodes scapularis, the tick that transmits Lyme disease causing bacteria , *Borrelia burgdorferi*, to humans and animals

Lyme disease

- Similar to other diseases caused by spirochetes, Lyme disease occurs in different stages with early and late manifestations.
- stage 1.
- A unique skin lesion that begins 3 days to 4 weeks after a tick bite often marks
- The lesion, erythema migrans, begins as a flat reddened area near the tick bite and slowly expands, with central clearing. With the skin lesion, there is often a flulike illness with fever, chills, myalgia, and headache.
- Stage 2
- occurs weeks to months later and includes arthralgia and arthritis; neurologic manifestations with meningitis, facial nerve palsy, and painful radiculopathy; and cardiac disease with conduction defects and myopericarditis.

Erythema migrans

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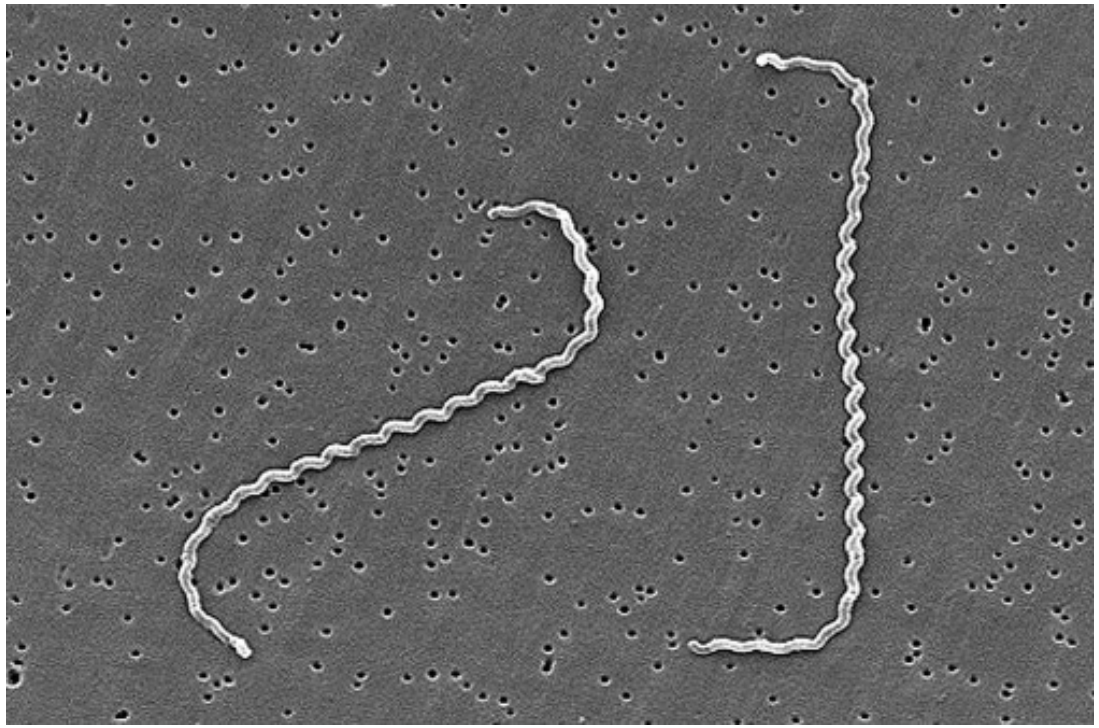
Treatment

- Early infection (local or disseminated) : should be treated with doxycycline, amoxicillin, or cefuroxime axetil for 14–21 days.
  - Treatment relieves early symptoms and promotes resolution of skin lesions.
  - Doxycycline may be effective than amoxicillin in preventing late manifestations.
- Established arthritis may respond to prolonged therapy with doxycycline or amoxicillin orally or penicillin G or ceftriaxone intravenously.
- In refractory cases, ceftriaxone has been effective.
- Nearly 50% of patients treated with doxycycline or amoxicillin early in the course of Lyme disease develop minor late complications (eg, headache, joint pains)

Leptospira

- Leptospiras is the causative agents of leptospirosis which is a zoonosis that occurs worldwide
- They are thin and tightly coiled spirochetes and one of their ends is forming a hook
- It is very fine and does not stain readily with dye and then cannot be seen by light microscope, but they are seen by dark field microscopy.
- It can also be impregnated with silver
- The bacteria is also actively motile using endoflagella
- It can be cultivated in culture media that contain serum



- the species *Leptospira interrogans* is the causative agents of leptospirosis.
- The organism infect a wide range of animals including rats and other rodents, domestic livestock, and pets.
- Such animals excrete the pathogen in their urine.
- The bacteria transmit to human due to exposue to contaminated water and soil, either by swimming or by eating contaminated food (ingestion is less common to cause the infection).

- Upon contact, leptospirae penetrate through breaks in the skin (cuts and abrasions) and mucous membranes (mouth, nose, conjunctivae) and then disseminated hematogenously and multiply in various organs especially liver, kidney and lungs.
- This resulting in hemorrhage and necrosis of tissue and dysfunction of the liver (jaundice), kidneys (uremia), lungs (hemorrhage),
- As well as central nervous system (aseptic meningitis).

- The disease is often biphasic
- the first phase or early phase is characterized with fever chills and intense headache
- the second phase is called immune phase, which is often characterized by the manifestation of aseptic meningitis with an intense headache, stiff neck, and pleocytosis of the CSF.
- In sever cases, liver damage (jaundice) and impaired kidney function can develop.
- The infection is accompanied with serovarspecific immunity development

Treatment

- The treatment of choice is penicillin G.
- The bacteria does not show significant antibiotic resistance.
- Prevention primarily involves avoiding contact with the contaminated environment.
- Chemoprophylaxis with Doxycycline is effective in preventing the disease in exposed persons

THANK YOU