Microbiology

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Neisseria, Spirochetes, and Intracellular Pathogens

- This lecture focuses on various bacterial genera that are responsible for sexually transmitted diseases (STDs), many of which are intracellular. Some are transmitted by ticks, while others are unique. Including gram-negative cocci. that usually infect the genital tract, CNS, or cause bloodstream infections.These include:
  1. **Neisseria species** – *Neisseria gonorrhoeae* and *Neisseria meningitidis*
  2. **Spirochetes** – *Treponema pallidum* and *Borrelia burgdorferi*
  3. **Intracellular Pathogens** – *Rickettsia* and *Chlamydia*

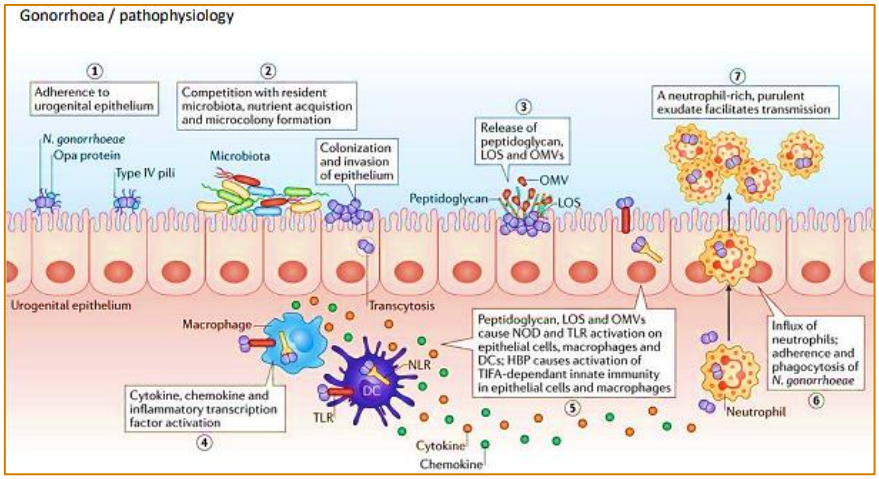
- **Neisseria**
  - Neisseria species are gram-negative, aerobic, coccoid bacteria, typically in pairs (diplococci), and range from 0.6 to 1.0 µm in diameter.
  - Neisseria gonorrhoeae and Neisseria meningitidis are strictly human pathogens, both oxidase positive and most produce catalase properties that combined with the Gram stain morphology allow a rapid, presumptive identification of a clinical isolate.
  - The presence of *N. gonorrhoeae* in a clinical specimen is always considered significant. In contrast, strains of *N. meningitidis* can colonize the nasopharynx of healthy people without producing disease.
  - Neisseria gonorrhoeae is a fastidious pathogen that grows only on enriched media such as chocolate agar.

1) Neisseria gonorrhoeae

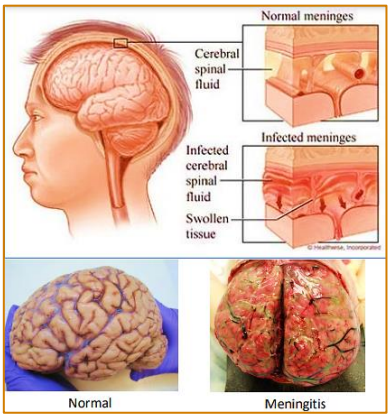
- Causes gonorrhea, one of the most common STDs after chlamydia in the United States.
- Gonococcemia (disseminated infection) with septicemia and infection of skin and joints affects 1 3% of infected women and even fewer men.
- Symptoms:
  - ✓ Men usually develop acute symptoms like urethral discharge and dysuria within 2–5 days incubation period.
  - ✓ Women often have asymptomatic or mild infections, but complications like pelvic inflammatory disease (PID) can occur if left untreated.
- Pathogenesis:

Table 23-2 Virulence Factors in *Neisseria gonorrhoeae*

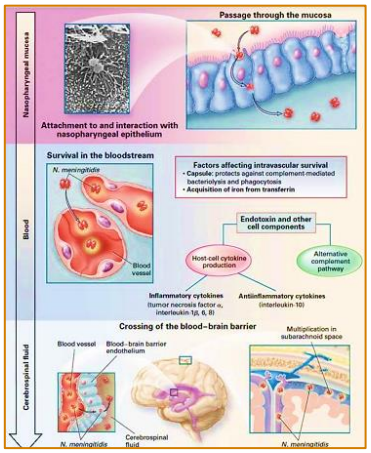
Virulence Factor	Biological Effect
Pilin	Protein that mediates initial attachment to nonciliated human cells (e.g., epithelium of vagina, fallopian tube, and buccal cavity); interferes with neutrophil killing
Por protein	Porin protein: promotes intracellular survival by preventing phagolysosome fusion in neutrophils
Opa protein	Opacity protein: mediates firm attachment to eukaryotic cells
Rmp protein	Reduction-modifiable protein: protects other surface antigens (Por protein, lipooligosaccharide) from bactericidal antibodies
Transferrin-, lactoferrin-, and hemoglobin-binding proteins	Mediate acquisition of iron for bacterial metabolism
LOS	Lipooligosaccharide: has endotoxin activity
IgA1 protease	Destroys immunoglobulin A1 (role in virulence is unknown)
β-Lactamase	Hydrolyzes the β-lactam ring in penicillin



2) Neisseria meningitidis



- Causes meningitis, the disease usually begins abruptly with headache, meningeal signs, and fever; however, very young children may have only nonspecific signs such as fever and vomiting. Mortality approaches 100% in untreated patients.
- Can also cause meningococcemia (septicemia), a life-threatening infection.
- Pathogenesis involves attachment to mucosal cells, penetration, and replication in the subepithelial space where infection is established. Specific differences in the bacterial polysaccharide capsule contribute to disease severity.



- High-risk groups:
  - ✓ Meningococcal disease occurs in patients who lack specific antibodies directed against the polysaccharide capsule and other expressed bacterial antigens.
  - ✓ Disease is greatest in children younger than 2 years (antibodies from the mother are disappearing). Patients with deficiencies in C5, C6, C7, or C8 of the complement system are estimated to be at a 6000-fold greater risk for meningococcal disease. Post-splenectomy patients are at risk as well.

• Spirochetes

- Spirochetes are bacteria characterized by their long, helically coiled shape (corkscrew-shaped). They include:
  - ✓ Treponema: *Treponema pallidum*, the causative agent of syphilis.
  - ✓ Borrelia: Includes *Borrelia burgdorferi*, the agent responsible for Lyme disease.

1) Treponema pallidum

- These spirochetes are thin, helical (0.1 to 0.5 × 5 to 20 μm), gram-negative bacteria.
- Causes syphilis, a sexually transmitted disease.
- Diagnosis:
  - ✓ Traditional diagnostic tests such as gram stain and microscopy are of little value because the spirochetes are too thin to be seen with light microscopy.
  - ✓ T. pallidum has not been cultured regularly in vitro because they are dependent on host cells for many metabolites (e.g. purines, pyrimidines, amino acids). Moreover, they're extremely sensitive to oxygen (microaerophilic or anaerobic
  - ✓ Relies on specialized techniques like darkfield microscopy or immunofluorescent stains due to the spirochete's small size and sensitivity to oxygen.
- Transmission:
  - ✓ Syphilis is found worldwide and is a common sexually transmitted bacterial disease
  - ✓ Between 2000 and 2012, the incidence of newly acquired disease has increased each year.
  - ✓ Patients infected with syphilis are at increased risk for transmitting and acquiring HIV when genital lesions are present
  - ✓ Syphilis cannot be spread through contact with inanimate objects such as toilet seats (since the bacteria is very labile to drying and disinfectants). The most common route of spread is by direct sexual contact.

- ✓ Other routes include congenitally (from an infected mother) or by transfusion with contaminated blood.
- ✓ The two general types of tests used are biologically nonspecific (nontreponemal) tests and specific treponemal tests. The nontreponemal tests are used as screening tests because they are rapid to perform and inexpensive. Positive reactivity with one of these tests is confirmed with a treponemal test.

➢ Phases of syphilis:

- ✓ The clinical course of syphilis evolves through three phases. If the patient is not treated, syphilis cause systemic devastating damage.
  - Primary phase: Characterized by painless skin lesions (chancres).
  - Secondary phase: Systemic spread leads to fever, skin rashes, and other symptoms.
  - Late syphilis: Severe damage to organs like the heart and brain, leading to complications like neurosyphilis and cardiovascular syphilis.

primary phase is characterized by skin lesions **(chancres)** at the site where the spirochete penetrated

In the **secondary phase,** the clinical signs of disseminated disease appear, (e.g. **skin lesions** over the entire body, fever, headache). Symptoms resolve within weeks.

- Late syphilis severely damages organs involved (e.g., **neurosyphilis**, cardiovascular syphilis) leading to various symptoms (e.g. **dementia** or **blindness**.)

➢ Syphilis be controlled only through the practice of safe-sex techniques and adequate treatment with antibiotics.

- **Borrelia:**
  - ➢ Members of the genus Borrelia cause two important human diseases: Lyme disease and relapsing fever.
  - ➢ Because culture is generally unsuccessful, diagnosis of diseases caused by borreliae is by serology or microscopy

Infection	Reservoir	Vector
Relapsing fever epidemic (louse-borne)	Humans	Body louse
Relapsing fever endemic (tick-borne)	Rodents, soft ticks	Soft tick
Lyme disease	Rodents, deer, domestic pets, hard ticks	Hard tick

2) Borrelia burgdorferi (Lyme Disease)

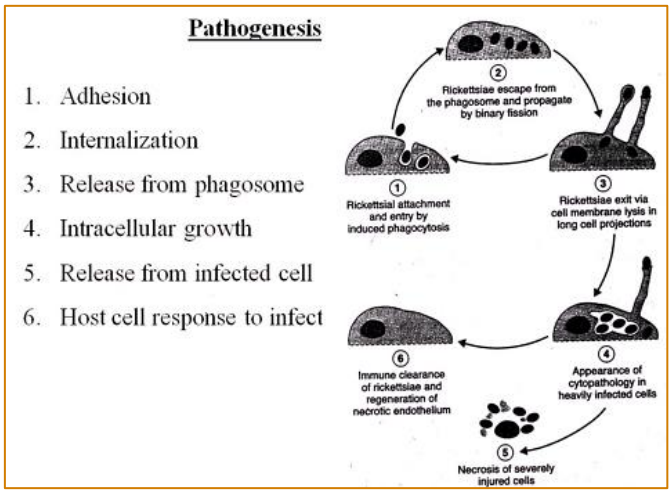
- ➢ Transmitted by hard ticks.
- ➢ Hematogenous dissemination will occur in untreated patients within days to weeks of the primary infection. This stage is characterized by systemic signs of disease (e.g., severe fatigue, headache, fever, malaise).
- ➢ Approximately 60% of patients with untreated Lyme disease will develop arthritis
- ➢ Symptoms include a characteristic "bull's-eye" rash at the site of a tick bite, fatigue, headache, fever, and swollen joints.

- ➢ If untreated, it can cause long-term symptoms like arthritis and neurological disorders.

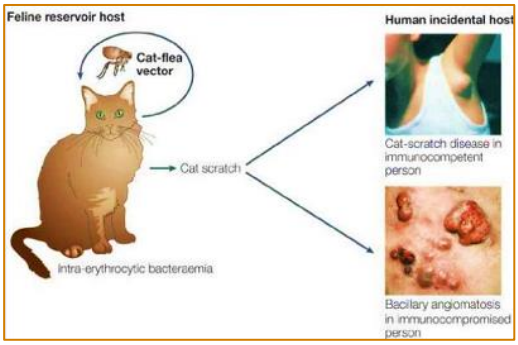
- Tick-born disease
  - ✓ Tick-borne pathogens can be passed to humans by the bite of infected ticks. Ticks can be infected with bacteria, viruses, or parasites
  - ✓ Because individual ticks can harbor more than one disease causing agent, patients can be infected with more than one pathogen at the same time, compounding the difficulty in diagnosis and treatment

- **Intracellular Pathogens**
  - Intracellular pathogens are bacteria that can only replicate within host cells. These include:

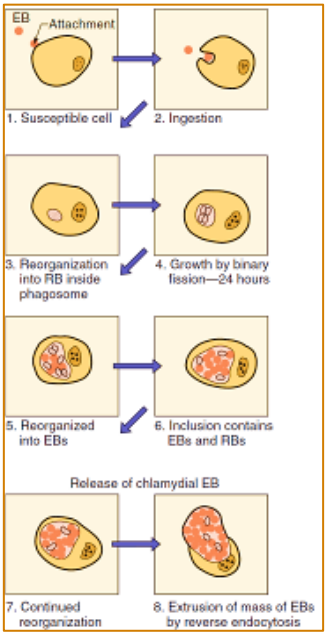
1) Rickettsia
   - Obligate intracellular, aerobic, gram-negative rods, and grow only in the cytoplasm of eukaryotic cells. Seen best with Giemsa stain. subdivided into:
     - ✓ Spotted fever group: Includes *R. rickettsii* (Rocky Mountain spotted fever).
     - ✓ Typhus group: Includes *R. prowazekii* (epidemic typhus).
   - Transmission: Rickettsiae are transmitted by ectoparasites such as fleas, lice, and ticks. The diseases they cause are often linked to the arthropod distribution.
   - The distribution of rickettsial diseases is determined by the distribution of the arthropod host/vector.
   - The primary clinical manifestations appear to result from the replication of bacteria in endothelial cells, with subsequent damage to the cells and leakage of the blood vessels.



2) Bartonella
   - Bartonella species are gram-negative, coccobacillary rods with fastidious growth requirements, requiring prolonged incubation (2 to 6 weeks).
   - They are typically facultative intracellular pathogens.
   - Bartonella species are transmitted by vectors such as ticks, fleas, sand flies, and mosquitoes
   - *Bartonella henselae* is responsible for cat-scratch disease, which follows exposure to cat scratches or bites.
     - ✓ Symptoms include a non-painful bump or blister at the site of injury and painful and swollen lymph nodes.



3) Chlamydia



- Chlamydia species are obligate intracellular parasites with 0.3 microm in diameter, a unique life cycle.
  - ✓ Unlike other bacteria, the Chlamydia have a unique developmental cycle, forming metabolically inactive infectious forms (elementary bodies [EBs]) and metabolically active noninfectious forms (reticulate bodies [RBs]).
  - ✓ They have both elementary bodies (EBs) (infectious) and reticulate bodies (RBs) (noninfectious but metabolically active).
- Are they viruses? the organisms have the following properties of bacteria: they (1) possess inner and outer membranes similar to those of gram-negative bacteria, (2) contain both deoxyribonucleic acid (DNA) and ribonucleic acid (RNA), (3) possess prokaryotic ribosomes, (4) synthesize their own proteins, nucleic acids, and lipids, and (5) are susceptible to numerous antibacterial antibiotics.
- Infects epithelial cells, which are found on the mucous membranes of the urethra, endocervix, endometrium, fallopian tubes, anorectum, respiratory tract, and conjunctivae.
- Damage is thought to be caused by intracellular replication and destruction of infected cells upon release.
- Chlamydia infections are the most common bacterial sexually transmitted diseases in humans and are the leading cause of infectious blindness worldwide.
- *C. trachomatis* is responsible for a variety of infections, including genital infections and trachoma (the leading cause of preventable blindness).
- Trachoma transmission occurs via direct contact with infected eye secretions or through flies that transfer bacteria, is the leading cause of preventable blindness.
- Infections in the genital tract can be asymptomatic in women (up to 80%) and symptomatic in men, leading to urethritis and other complications.
- *C. trachomatis* infection can be diagnosed
  (1) Cytological, serologic, or culture findings
  (2) The direct detection of antigen in clinical specimens
  (3) The use of nucleic acid–based tests.

- **Clinical Considerations**
  - Gonorrhea and syphilis are major STDs with differing symptoms in men and women.
  - Neisseria meningitidis can cause deadly infections, especially in high-risk populations, such as infants and individuals with immune system defects.
  - Lyme disease requires prompt treatment with antibiotics to prevent long-term effects.
  - Rickettsial infections can be serious and are often associated with travel to endemic regions.
  - Chlamydia infections are the most common bacterial STDs and are often asymptomatic, particularly in women, but can lead to severe complications such as infertility if untreated.
    - ✓ Proper diagnosis and early treatment with appropriate antibiotics (like penicillin, doxycycline, or azithromycin) are critical in managing these infections and preventing complications.

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