Introduction to Microbiology

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Lecture 24

Overview

Bacterial genera that will be discussed this lecture mostly cause sexually transmitted diseases, many are intracellular, some are transmitted by ticks, and some are unique.

Including gram-negative cocci. that usually infect the genital tract, CNS, or cause bloodstream infections:

- ***Neisseria gonorrhoeae***
- ***Neisseria meningitidis***

We will also discuss spirochetes

- ***Treponema***
- **Borrelia**

We will also discuss **intracellular pathogens**

- ***Rickettsiaceae***
- ***Chlamydia***

Neisseria

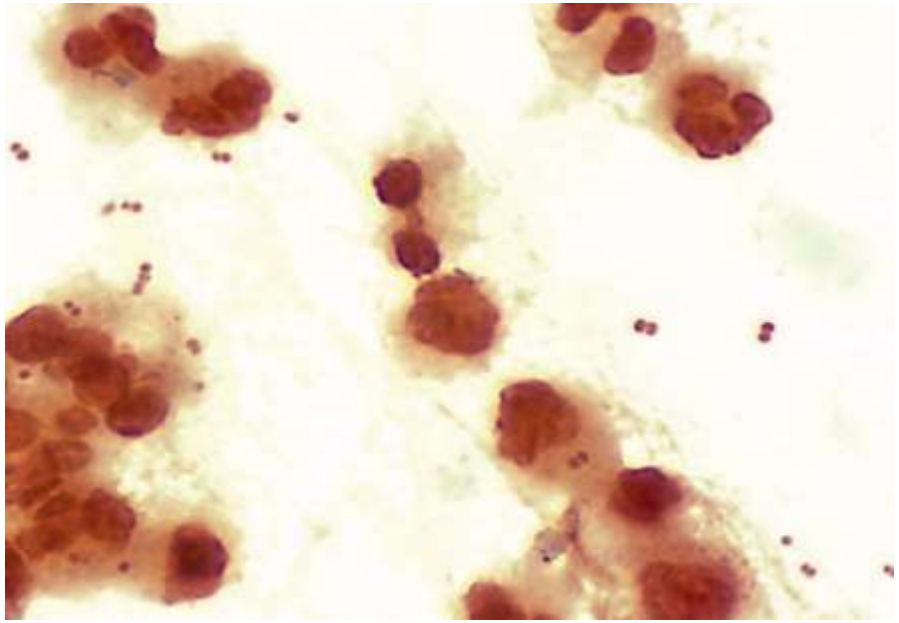
- *Neisseria* species are aerobic **gram-negative** bacteria, typically coccoid shaped (0.6 to 1.0 µm in diameter) and arranged in pairs **(diplococci)**

- ***Neisseria gonorrhoeae*** and ***Neisseria meningitidis,*** strictly human pathogens.

- All species are **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.

- *N. gonorrhoeae is fastidious and* only grows on enriched **chocolate agar** and other supplemented media.



Neisseria gonorrhoeae

- ***Gonorrhea*** is second only to chlamydia as the most commonly reported sexually transmitted disease in the United States.

- ***Gonococcemia :*** Disseminated infections with **septicemia** and **infection of skin and joints** occur in 1% to 3% of infected women and in a much lower percentage of infected men.

Neisseria gonorrhoeae

Gonorrhea: characterized by purulent discharge for involved site (e.g., urethra, cervix, epididymis, prostate, rectum) after 2- to 5-day incubation period

Disseminated infections: spread of infection from genitourinary tract through blood to skin or joints; characterized by pustular rash with erythematous base and suppurative arthritis in involved joints

Ophthalmia neonatorum: purulent ocular infection acquired by neonate at birth

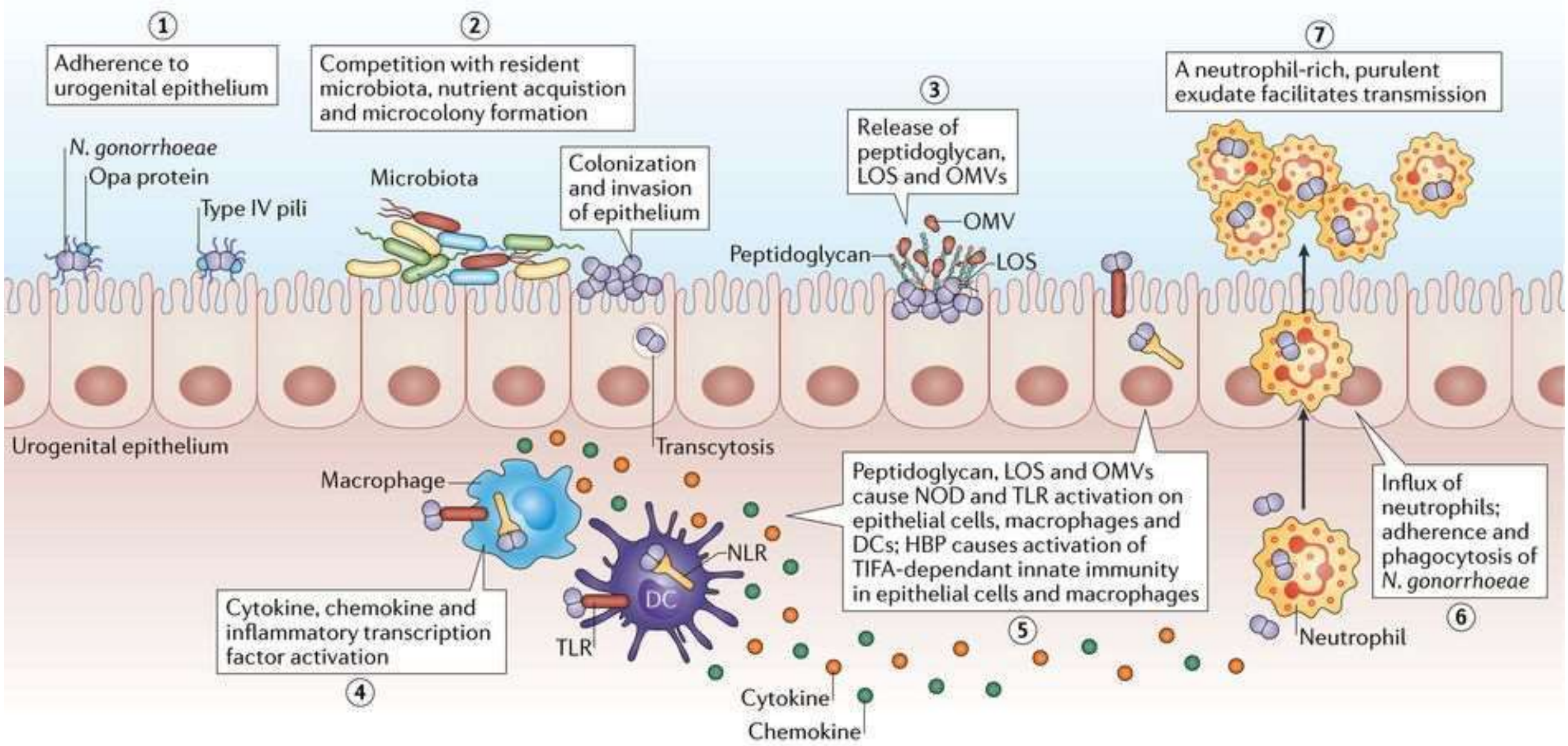
Neisseria gonorrhoeae

- A purulent urethral discharge and dysuria develop after a 2- to 5-day incubation period.
- **Virtually all infected men have acute symptoms**.
- As many as half of all infected women have mild or **asymptomatic** infections.

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

Gonorrhoea / pathophysiology



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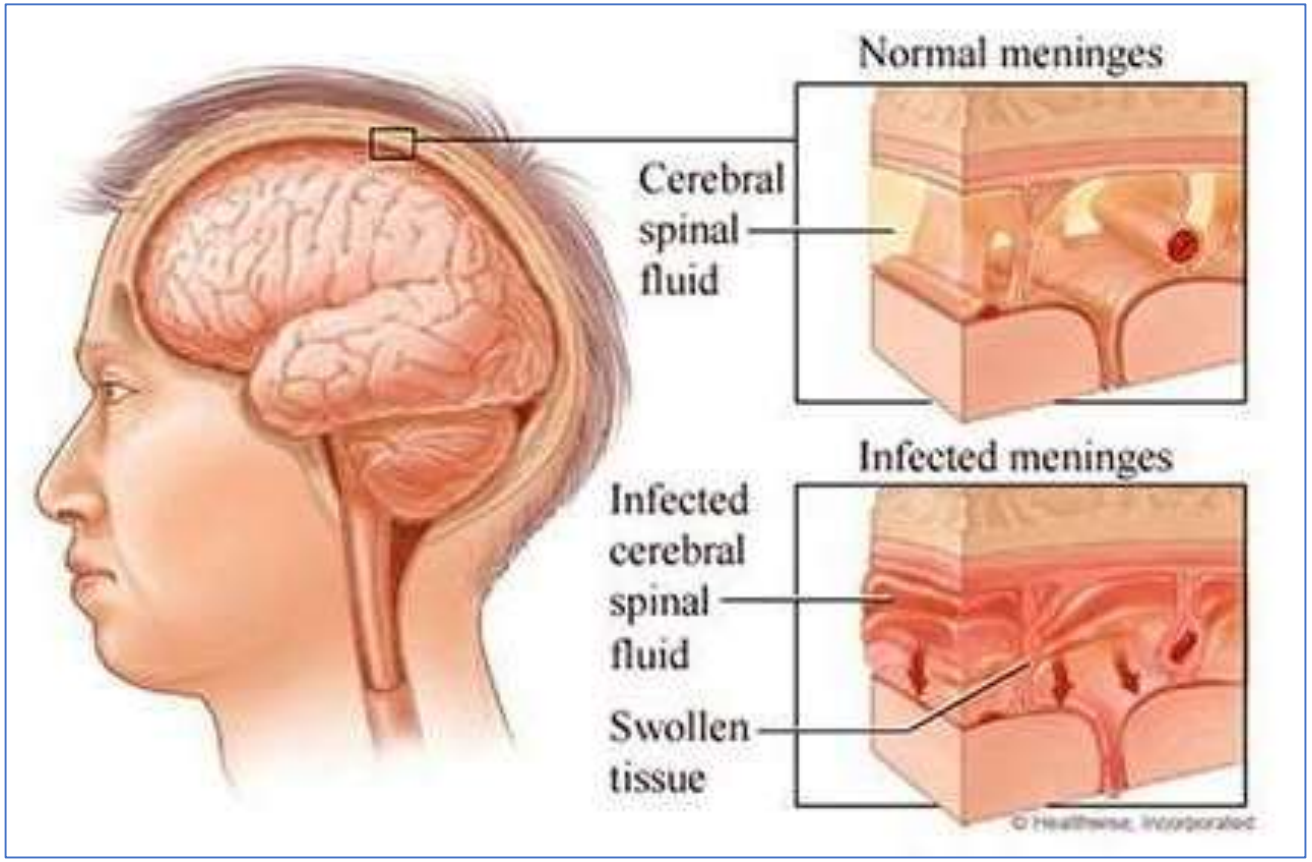
Neisseria meningitidis

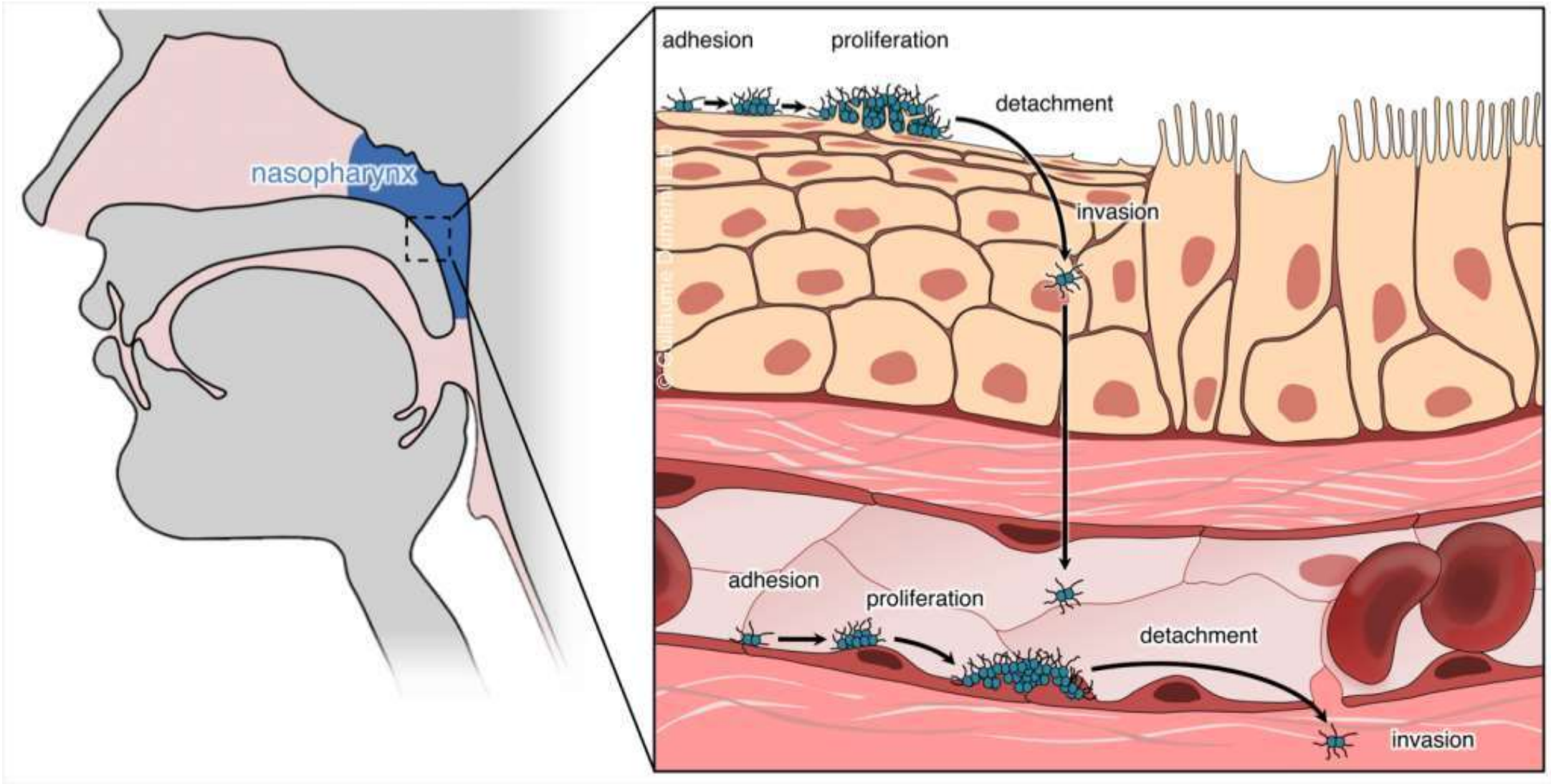
- ***Meningitis*** The disease usually begins abruptly with headache, meningeal signs, and fever; however, very young children may have only nonspecific signs such as fever and vomiting. Mortality approaches 100% in untreated patients

- ***Meningococcemia*** *(*Septicemia) with or without meningitis is a life-threatening disease



Normal

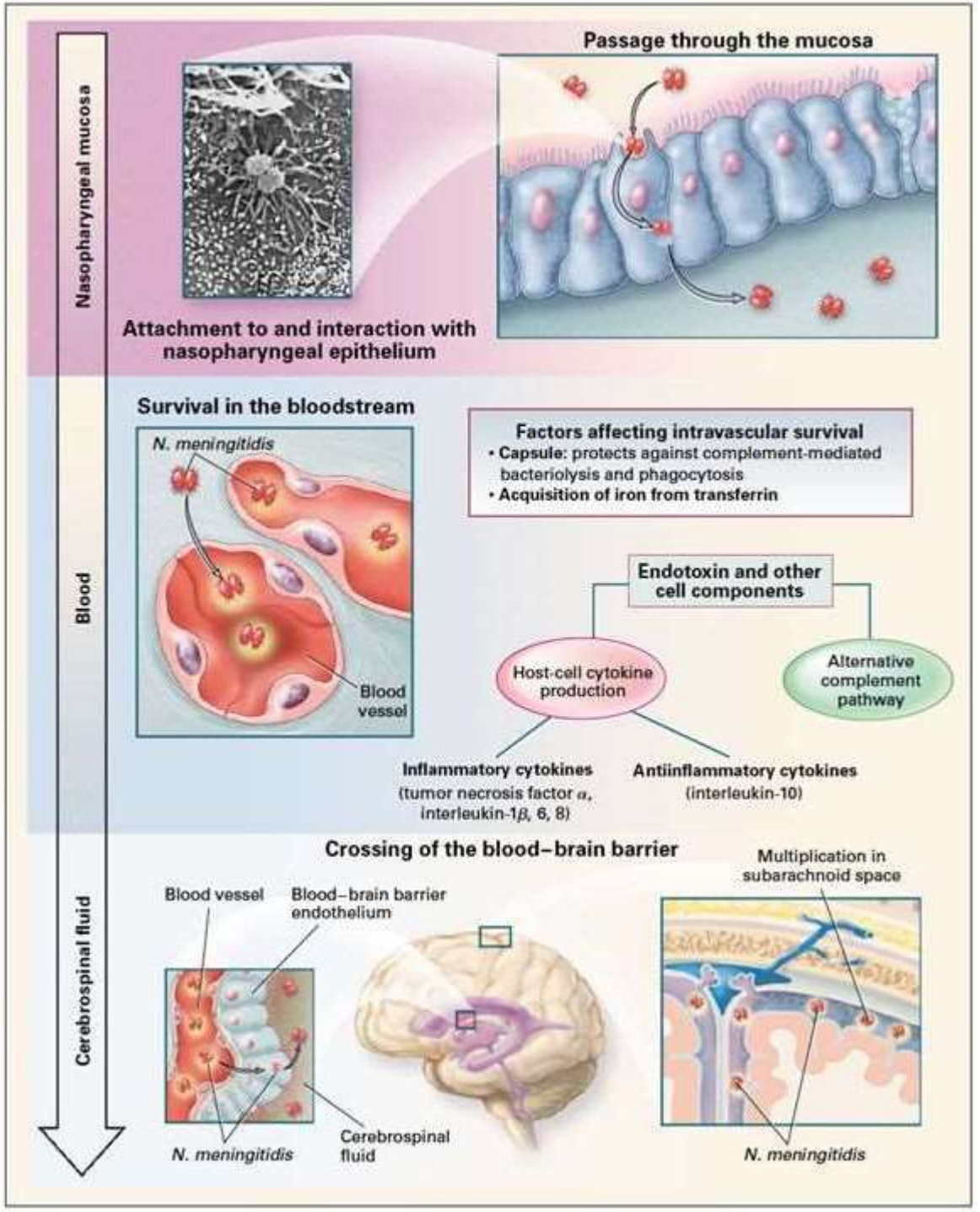
Meningitis



Carriage and pathogenesis of N. meningitidis

- Meningococci attach to mucosal cells, penetrate into the cells and multiply, and then pass through the cells into the subepithelial space where infection is established.

- Antigenic differences in the **polysaccharide capsule** of *N. meningitidis,* determine if an individual strain will cause disease .



Neisseria meningitidis

- 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.

Neisseria

A 22-year-old woman was admitted to the hospital with a 1-day history of high fever, chills, and an erythematous maculopapular rash over her chest, arms, and legs. She had an elevated leukocyte count and sedimentation rate. Blood cultures drawn at the time of admission were positive 10 hours later with gram-negative diplococci. This patient most likely has an infection with either *Neisseria gonorrhoeae* or *Neisseria meningitidis*, because no other gram-negative bacteria will look like this. Additional tests will be required to determine which bacterium is responsible for this infection.

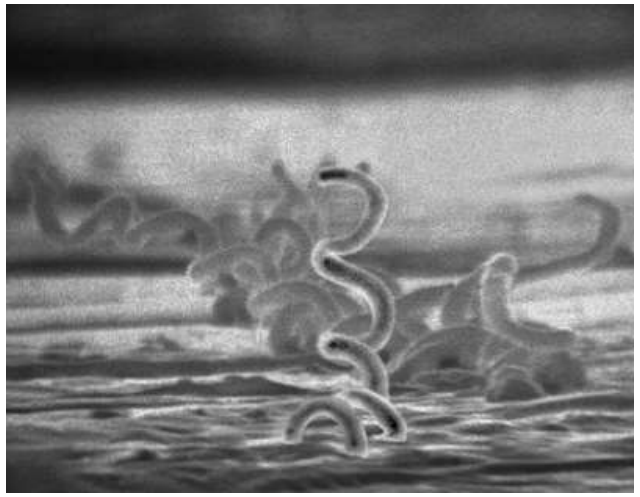
FIGURE 23-5 Skin lesions in a patient with meningococcemia. Note that the petechial lesions have coalesced and formed hemorrhagic bullae.

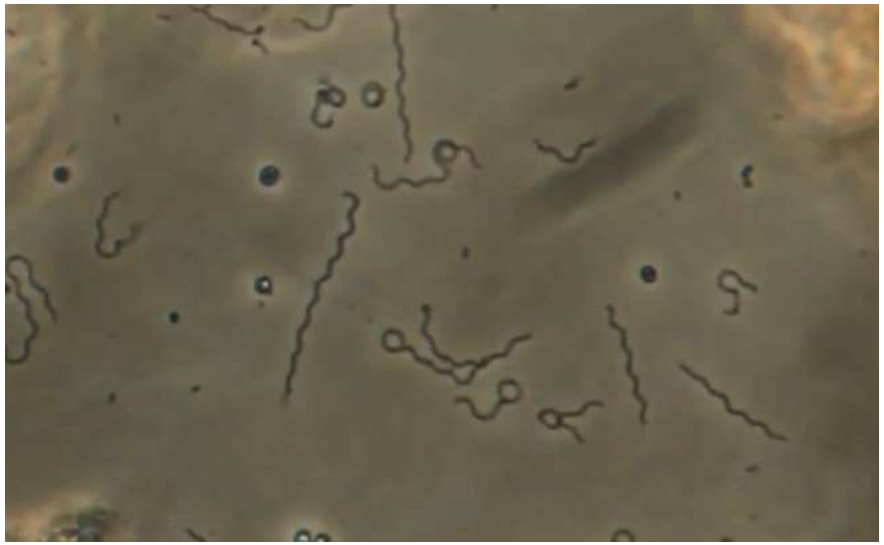
Spirochetes

- Spirochete are bacteria with distinctive diderm (double-membrane), most of which have long, helically coiled (corkscrew-shaped or spiraled, hence the name) cells.

Important pathogens include :

- ***Treponema palladium***
- ***Borrelia Burgdorferi***





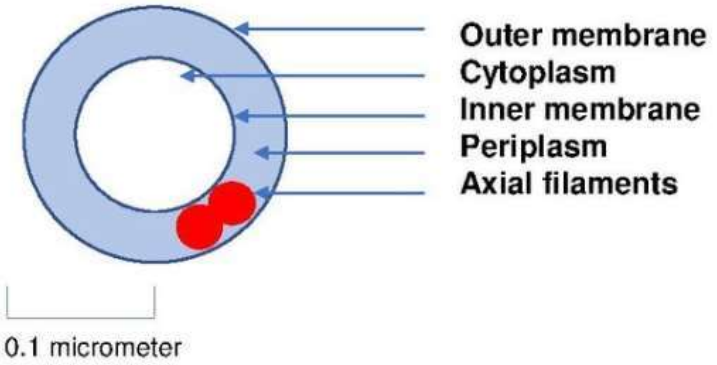


Fig. 1 Sectional view of a spirochete cell

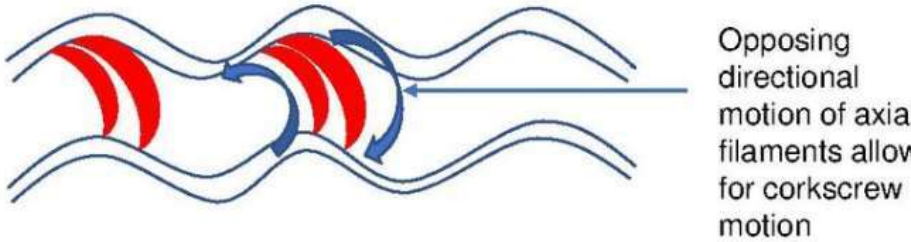


Fig. 2 Axial filament mechanics

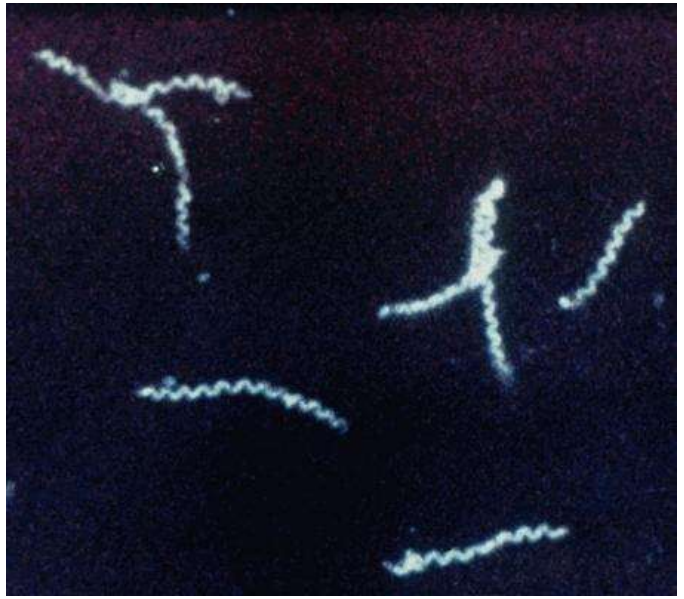
Treponema

- These spirochetes are **thin**, helical (**0.1 to 0.5** × 5 to 20 µm), **gram-negative** bacteria. The most important treponemal species that causes human disease is ***Treponema pallidum, the causative agent for*** **Syphilis**

- 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**).

- **darkfield microscopy** or **immuno-fluorescent stains** must be used for visualization and diagnosis.



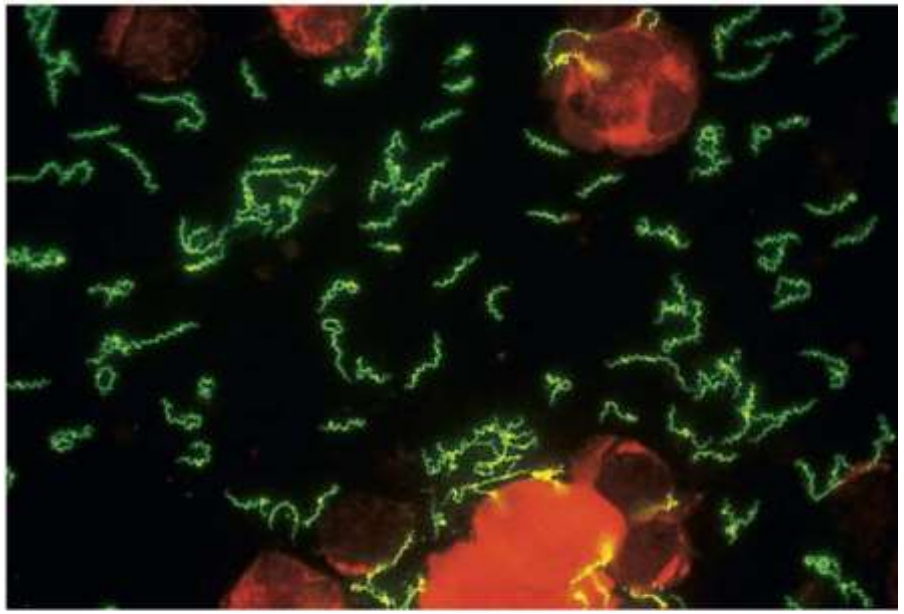


FIGURE 32-3 *Treponema pallidum* in the direct fluorescent antibody test for *T. pallidum*. (From Morse SA, Ballard RC, Holmes KK

Treponema

- 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.

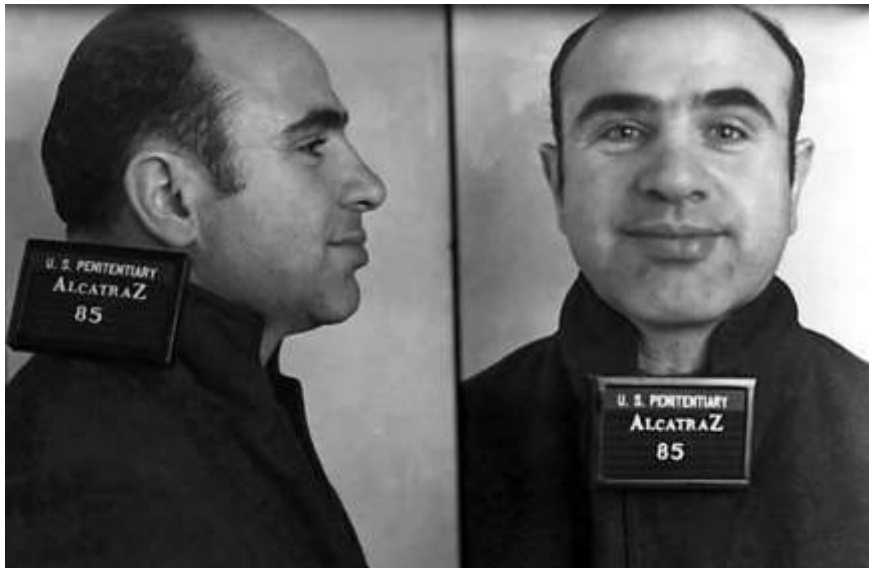
Treponema

- The clinical course of syphilis evolves through three phases. If the patient is not treated, syphilis cause **systemic devastating damage**.

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

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**.)

Borrelia

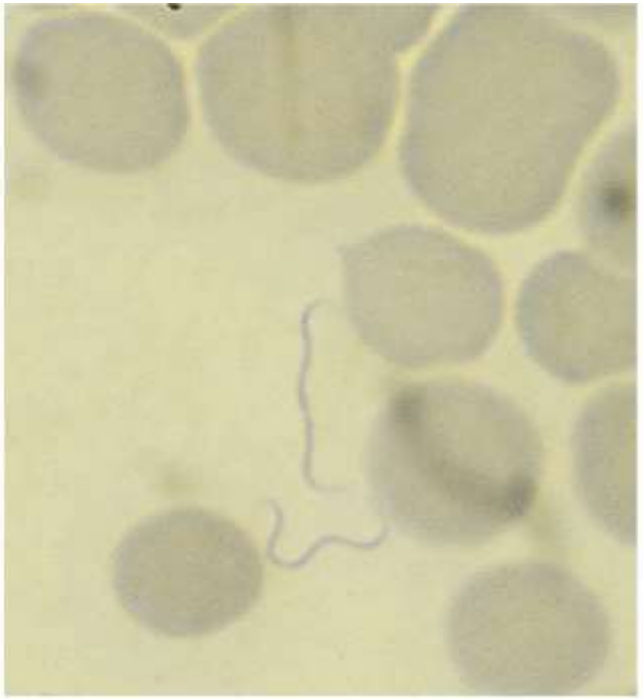
- **Spirochetes** (0.2 to 0.5 × 8 to 30 µm), stain well with dyes such as Giemsa and stain poorly with gram stain, but have an outer membrane similar to **gram-negative** bacteria.

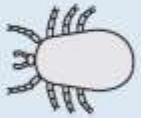
- Members of the genus *Borrelia* cause two important human diseases: **Lyme disease** and **relapsing fever.**

- Because culture is generally unsuccessful, diagnosis of diseases caused by borreliae is by serology or microscopy

- **Hard ticks are the major vectors for lyme disease.**

- The ticks contaminate the bite wound with borreliae present in saliva or feces.



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 

Borrelia/ Lyme disease

- 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**

Box 32-2 Definition of Lyme Disease

Clinical Case Definition

Either of the Following:

Erythema migrans (≈5 cm in diameter)

At least one late manifestation (i.e., musculoskeletal, nervous system, or cardiovascular involvement) and laboratory confirmation of infection

Laboratory Criteria for Diagnosis

At Least One of the Following:

Isolation of *Borrelia burgdorferi*

Demonstration of diagnostic levels of immunoglobulin (Ig)M or IgG antibodies to the spirochetes

Significant increase in antibody titer between acute and convalescent serum samples

Tick-born diseaes

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.

Many tickborne diseases can have similar signs and symptoms. If you have been bitten by a tick and develop the symptoms below within a few weeks, a health care provider should evaluate the following before deciding on a course of treatment:

- Your symptoms
- The geographic region in which you were bitten
- Diagnostic tests, if indicated by the symptoms and the region where you were bitten

The most common symptoms of tick-related illnesses are:

- Fever/chills: With all tickborne diseases, patients can experience fever at varying degrees and time of onset.
- Aches and pains: Tickborne disease symptoms include headache, fatigue, and muscle aches. With Lyme disease you may also experience joint pain. The severity and time of onset of these symptoms can depend on the disease and the patient's personal tolerance level.
- Rash: Lyme disease, southern tick-associated rash illness (STARI), Rocky Mountain spotted fever (RMSF), ehrlichiosis, and tularemia can result in distinctive rashes:

Rickettsiaceae

- **Obligate intracellular**, **aerobic**, **gram-negative rods**, and grow **only in the cytoplasm of eukaryotic cells.** Seen best with **Giemsa stain**.
- *Rickettsia* is subdivided into the **spotted fever group** and the **typhus group**
- Most rickettsial pathogens are transmitted by ectoparasites such as **fleas, lice, mites, and ticks**. All age groups are at risk for rickettsial infections during travel to endemic areas.
- 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.

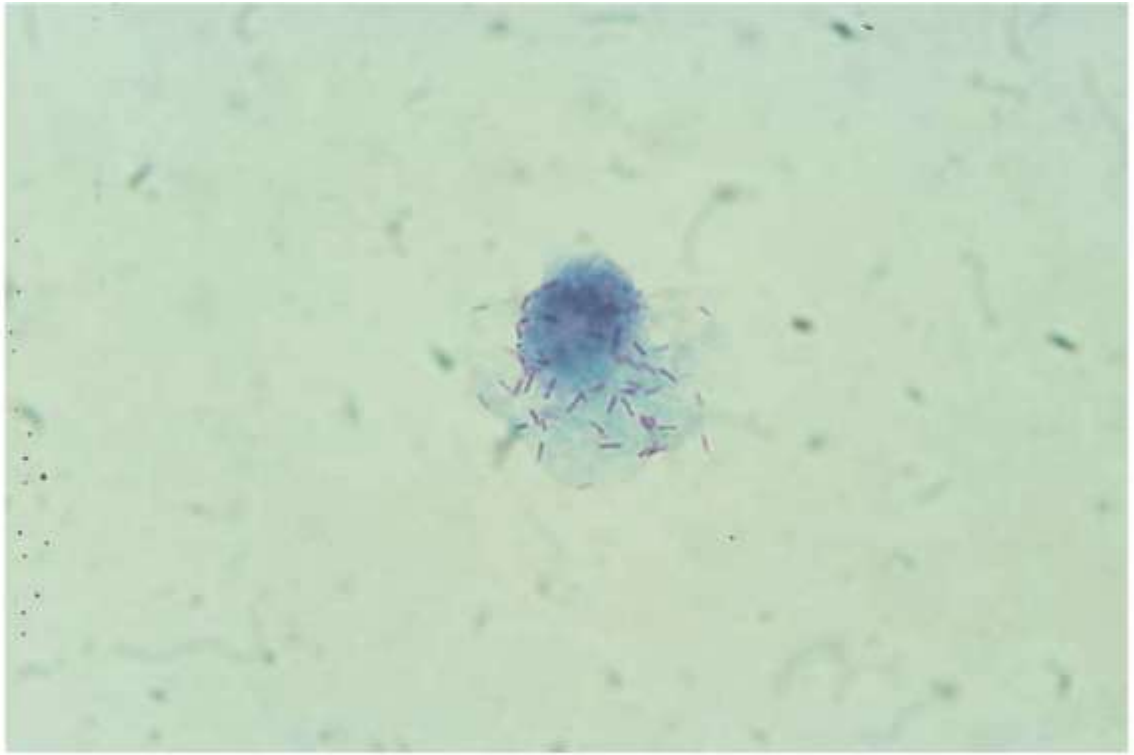
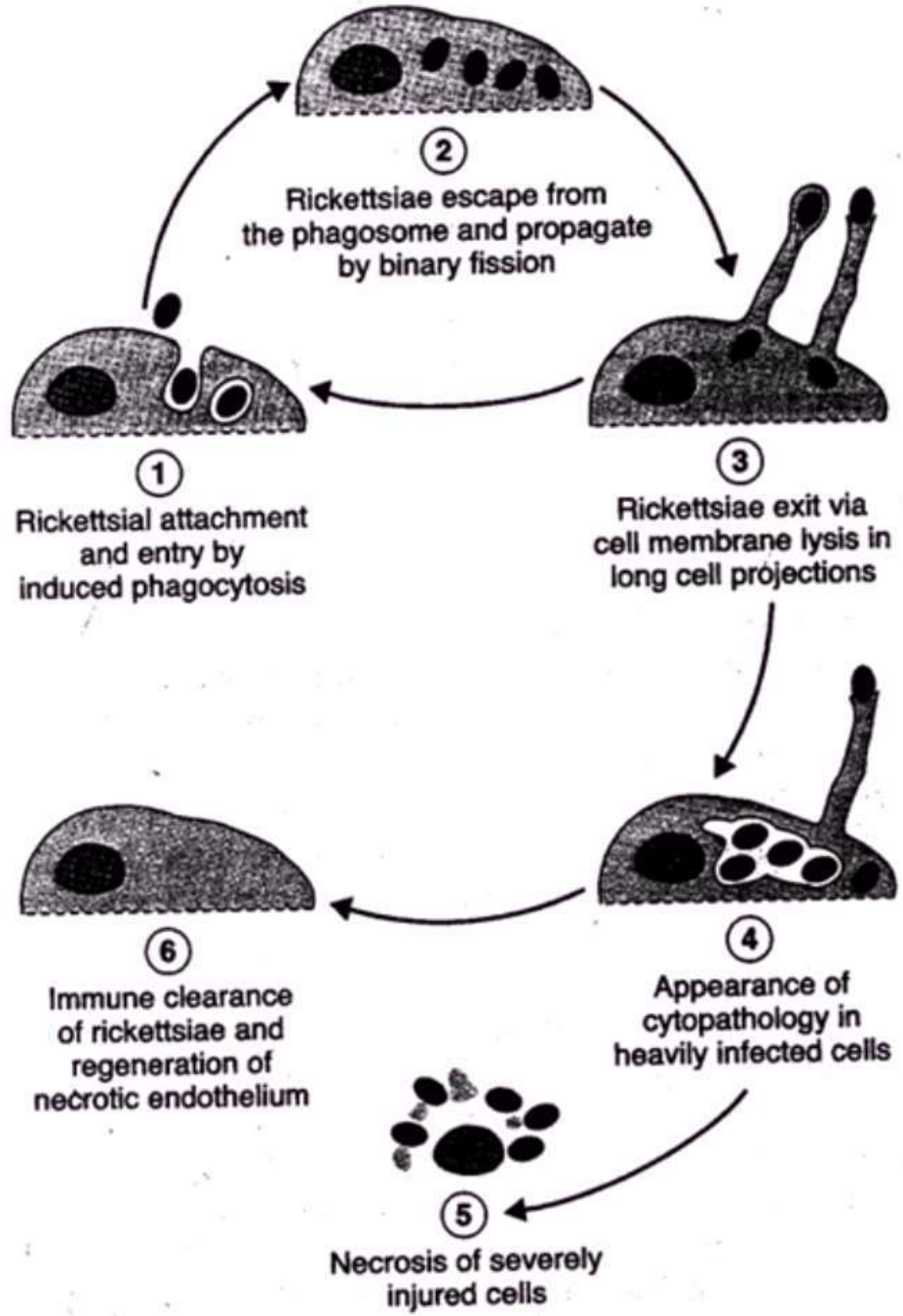


FIGURE 34-1 Gimenez stain of tissue culture cells infected with spotted fever group *Rickettsia*. (From Cohen J, Powderly WG: *Infec-*

Pathogenesis

1. Adhesion
2. Internalization
3. Release from phagosome
4. Intracellular growth
5. Release from infected cell
6. Host cell response to infect



Organism	Disease	Reservoir	Vector	Distribution
Rickettsia rickettsii	Rocky Mountain spotted fever	Ticks, wild rodents	Hard ticks (dog tick, wood tick)	Western Canada, continental US, Mexico, Panama, Argentina, Brazil, Bolivia, Colombia, Costa Rica
R. akari	Rickettsialpox	Mites (chiggers), wild rodents	Mites	North America (particularly urban areas of Northeastern US), Mexico, Europe (e.g., Croatia, Ukraine, Turkey), Asia (e.g., Korea), Africa
R. prowazekii	Epidemic (louse-borne) typhus	Humans	Human body louse	Mountainous regions of Central and Eastern Africa (Burundi, Rwanda, Ethiopia), Central and South America, Asia
	Recrudescent typhus	Humans	Relapse disease	Worldwide
	Sporadic typhus	Flying squirrels, squirrel fleas and lice	Possibly squirrel fleas	United States

Disease	Average Incubation Period (Days)	Clinical Presentation	Rash	Eschar	Mortality without Treatment (%)
Rocky Mountain spotted fever	7	Abrupt onset; fever, headache, malaise, myalgias, nausea, vomiting, abdominal pain	>90%; macular; centripetal spread	No	10-25
Rickettsialpox	9-14	Abrupt onset; fever, headache, chills, myalgias, photophobia	100%; papulovesicular; generalized	Yes	Low
Epidemic typhus	8	Abrupt onset; fever, headache, chills, myalgias, arthralgia	20%-80%; macular; centrifugal spread	No	20

Epidemic typhus caused by *R. prowazekii* infection is rarely reported among tourists but can occur in impoverished communities and refugee populations where body lice are prevalent.

Tickborne spotted fever rickettsioses are the most frequently reported travel-associated rickettsial infections.

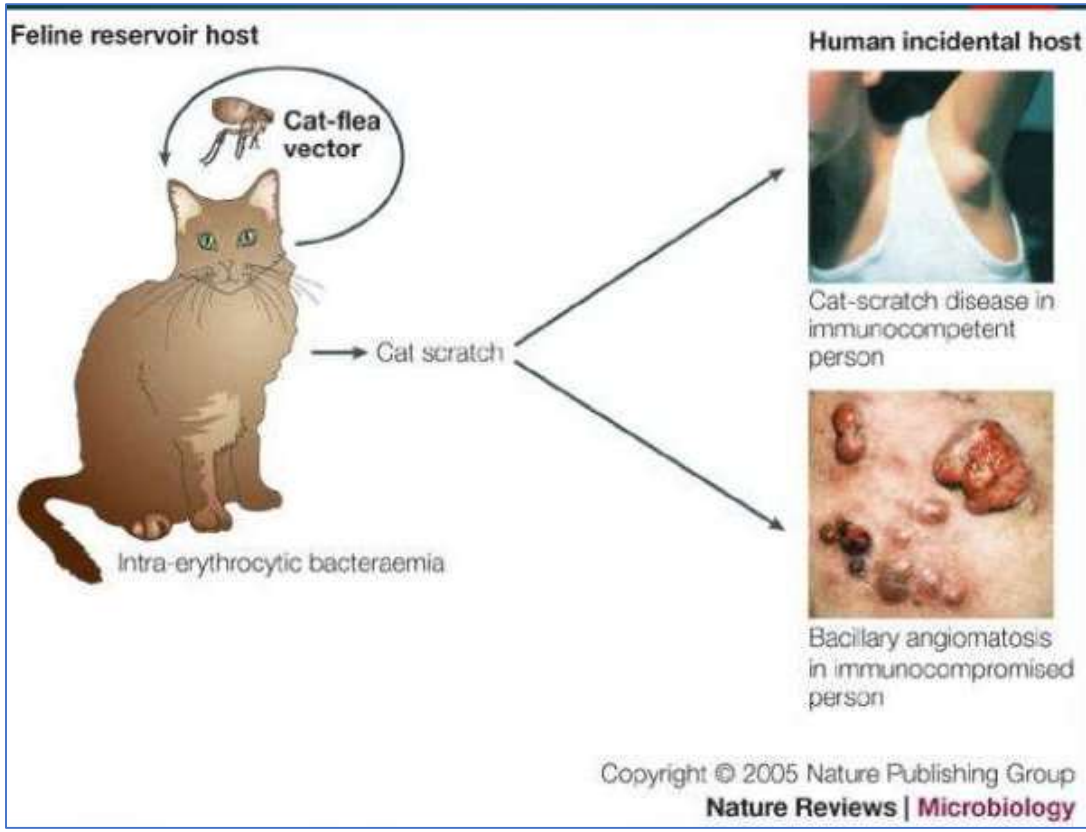
Bartonella

- *Bartonella* are **gram-negative, coccobacillary** or bacillary rods with **fastidious** growth requirements, requiring prolonged incubation (2 to 6 weeks). usually **facultative intracellular bacteria.**

- Bartonella species are **transmitted by vectors** such as ticks, fleas, sand flies, and mosquitoes

- ***B. henselae*** is responsible for a disease acquired after exposure to cats (e.g., scratches, bites, contact with the contaminated feces of cat fleas): **cat-scratch disease,** 1–3 weeks after inoculation**.**

- Symptoms typically include a **non-painful bump or blister at the site of injury** and painful and **swollen lymph nodes**

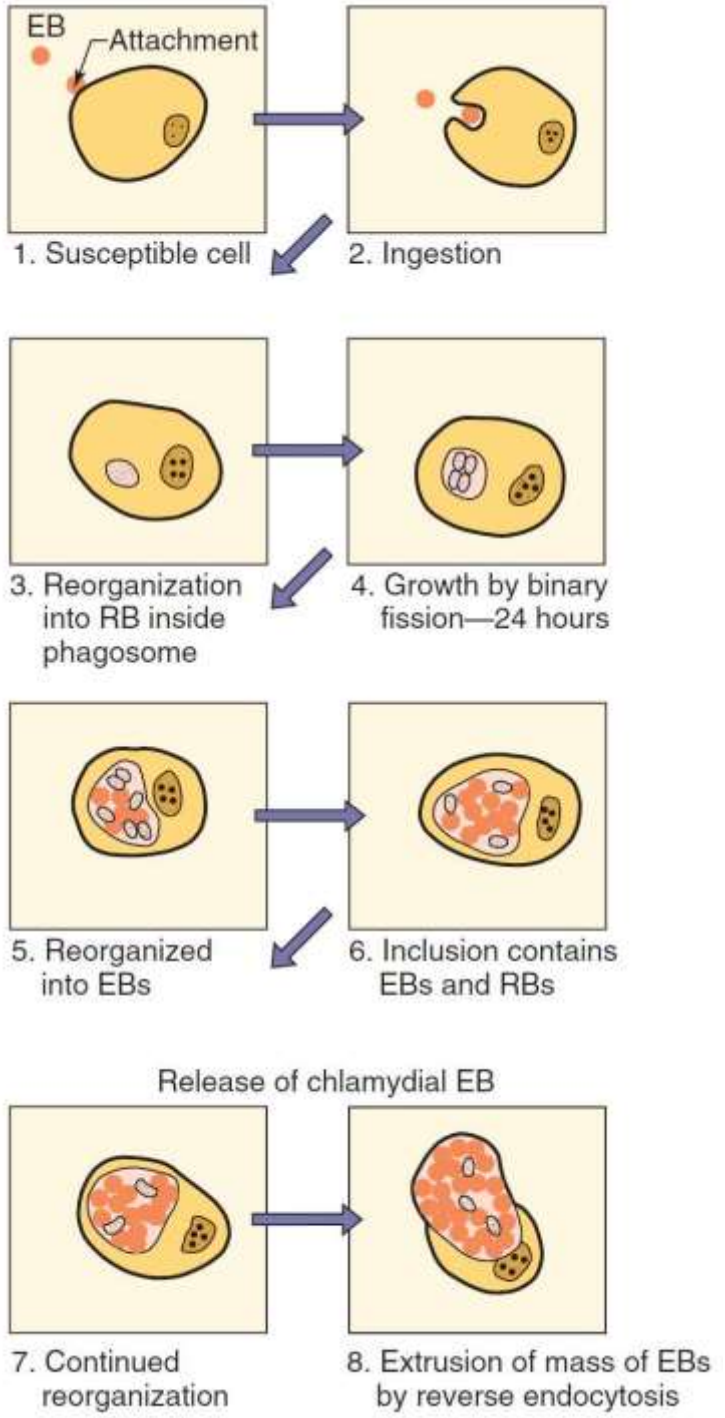


Chlamydia

- **Obligate intracellular parasites (**they use host cell ATP for their energy requirements) **, 0.3 microm in diameter, with a unique life cycle.**

- **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.

- 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]).**



Chlamydia

- 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 disease**s in humans and are **the leading cause of infectious blindness** worldwide.

- *C. trachomatis* infection can be diagnosed (1) on the basis of cytologic, serologic, or **culture** findings, (2) through the direct **detection of antigen** in clinical specimens, and (3) through the use of **nucleic acid–based** tests.

Chlamydia / clinical picture

- **Trachoma** is the **leading cause of preventable blindness.** Infections occur predominantly in children, who are the chief reservoir of ***C. trachomatis*** in endemic areas.

- Eye-to-eye transmission of trachoma is by **droplet, hands, contaminated clothing**, and flies that transmit ocular discharges from the eyes of infected children to the eyes of uninfected children.

- Most genital tract infections in **women** are **asymptomatic** (as many as 80%)

- Most *C. trachomatis* genital infections in **men** are **symptomatic**, as many as 25% of the infections will be inapparent.

- It can cause **cervicitis** in women and **urethritis** and **proctitis** in both men and women.

Chlamydia trachomatis

Trachoma: chronic inflammatory granulomatous process of eye surface, leading to corneal ulceration, scarring, pannus formation, and blindness

Adult inclusion conjunctivitis: acute process with mucopurulent discharge, dermatitis, corneal infiltrates, and corneal vascularization in chronic disease

Neonatal conjunctivitis: acute process characterized by a mucopurulent discharge

Infant pneumonia: after a 2- to 3-week incubation period, the infant develops rhinitis, followed by bronchitis with a characteristic dry cough

Urogenital infections: acute process involving the genitourinary tract with characteristic mucopurulent discharge; asymptomatic infections common in women

Lymphogranuloma venereum: a painless ulcer develops at the site of infection that spontaneously heals, followed by inflammation and swelling of lymph nodes draining the area, then progression to systemic symptoms

Further reading:

- Murray - Medical Microbiology 8th Edition
  Section 4: Bacteriology
  Chapter 23:
  Chapter 32:
  Chapter 35: