Chlamydiae

- Are obligate intracellular organisms

\[ \Downarrow \]

Grow only within cells

Including →

1. Chlamydia trachomatis → eye, respiratory and genital tract infections.
2. Chlamydia pneumoniae → atypical pneumonia
3. Chlamydia psittaci → psittacosis

Important properties

- They lack the ability to produce sufficient energy to grow independently.
- They have a rigid cell wall (but not a typical peptidoglycan layer)
- Have a replicative cycle different from that of all bacteria

begin when extra cellular, metabolically inert (elementary body)

enter the cell

\[ \Downarrow \]

Reorganize into larger metabolically active (reticulate body)

\[ \Downarrow \]

release daughter repeated binary fission

repeated binary fission

↑

appear as inclusions useful in diagnosis

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- All chlamydiae share a group-specific lipopolysacharide antigen (detected by CFT)
- They also possess species-specific and immunotype-specific antigens (proteins) (detected by IF)
- C.psittaci and C.pneumoniae each have 1 immunotype, whereas C.trachomatic has at least 15.

**Transmission & Epidemiology**
- C.trachomatis infects only humans and transmitted by close personal contact (sexually or by passage through the birth canal)
- Individuals with asymptomatic genital tract infections are important reservoir.
- In trachoma, the microorganisms is transmitted by finger-to eye contact.
- C.pneumoniae → human ← by aerosol
- C.psittaci → birds → dry feces of bird → humans

**Pathogenesis & clinical finding**
- Chlamydiae infect primarily epithelial cell & rarely invasive
- C.psittaci infect lungs primarily → asymptomatic
  ↓
  or produce high fever & pneumonia
- C.pneumoniae causes upper & lower respiratory tract infections (bronchitis & pneumonia, in young adults)
- C. trachomatis, types A, B and C → trachoma and chronic conjunctivitis and may lead to blindness.
  • Types D-K → genital tract infections
  In men → non gonococcal urethritis → epididymitis or proctitis.
  In women → cervicitis → salpingitis → infertility
  • Infants born to infected mothers → mucopurulent eye infections 7-12 days after labour.
    → or develop (chlamydial pneumonitis) 2-12 weeks
  • Patient with genital tract infection may develop autoimmune disease caused by antibodies against C.trachomatis → cross reacting with antigens on cells of
the urethra, joints and uveal tract, this so called (Reiter's syndrome).

- Chlamydia trachomatis L1-L3 immunotypes cause lymphogranuloma venereum ← a sexually transmitted disease with lesions on genitalia and in lymph nodes.

**Laboratory diagnosis**

- Cytoplasmic inclusion seen with Giemsa's stain or by immunofluorescence.
- Organisms can be identified in exudates by fluorescent antibody staining, ELISA, or by use of DNA probe (hybridization).
- Chlamydiae can be grown in cell culture or embryonated egg
- Chlamydial antigens can be detected by ELISA.
- Serologic tests reliable in diagnosis of chlamydial infection but not for C.trachomatis because the frequency of infection is so high that many people already have antibodies.

**Treatment**

- All Chlamydia are susceptible to tetracycline and erythromycin.
- C.psittaci & C.pneumoniae ← tetracycline
- C.trachomatis → sexual infection ← azithromycin
- There is no vaccine available against any chlamydial disease.
**Rickettsiae**

They are the agents of:

Typhus $\leftarrow$ R. prowazekii  
R. typhi  
R. tsutsugamoshi

Rocky Mountain spotted fever $\leftarrow$ R. rickettsii

Q fever $\leftarrow$ Coxiella burnetii

**Important properties**

- Are very short rods, their cell wall resemble that of Gram's negative but stained poorly.
- Are obligate intracellular parasites
- Rickettsiae devide by binary fission inside host cell but by a distinctive intracellular cycle.
- Several rickettsiae (R. prowazekii, tsutsugamoshi & rickettsii) posses antigens that cross-react with antigens of the OX strains of Proteus vulgaris  
  $\rightarrow$ The Weil-Felix test $\leftarrow$ anti-rickettsial antibodies in serum will agglutinate Proteus vulgaris.

**Pathogenesis**

- The life cycle of rickettsiae maintained in nature in certain arthropods (ticks, fleas and lice) $\rightarrow$ transmitted to human by bite of arthropod, except C. burnetti which is transmitted by aerosol.
- All rickettsial infections are zoonotic only for epidemic typhus which occur only in humans.
- The typical lesion caused by rickettsiae is a vasculitis particularly in the endothelial lining.
- Damage of vessels of skin → characteristic rash, edema and hemorrhage.
- Endotoxin is involved in pathogenesis but no exotoxin or cytolytic enzymes.

Typhus begins with the sudden onset of chills, fever, headache and other influenza like symptoms 1-3 weeks after the louse bite. A maculopapular rash appear on the trunk 5th-9th days of the onset. Signs of sever meningo-encephalitis. In untreated cases death may occurs from peripheral vascular collapse or from bacterial pneumonia.

- Epidemic typhus ← R.prowazekii (louse transmit infection from person to person)
- Endemic typhus ← R.typhi (by flea).

**Laboratory diagnosis**
- Based on serologic analysis rather than isolation of the organism
- Rickettsiae can be grown in cell culture or embryonated egg but hazardous.
- CFT provides more specific data.
- Weil-Felix reaction (microagglutination test) based on cross reaction of antigens in rickittsial disease and with O antigen (polysaccharide) found in Proteus vulgaris strains OX-2, O-19 & OX-k. but the test is of limited value.
**Yersinia**

- Short pleomorphic Gram's negative rods, can exhibit bipolar staining.
- Mainly microaerophilic, catalase positive and oxidase negative.
- All are animal pathogens but some can cause bacterial zoonoses and human infected accidently mainly through vectors.

**Yersinia pestis**

Is the cause of plaque (black death)

**Antigenic structure & virulence factors**

1. Lipopolysaccharide capsule or envelope protein (fraction 1, F-1) with endotoxic activity and antiphagocytosis, loss of capsule is accompanied by a loss of virulence.
2. V-W antigens-2 proteins encoded by genes on plasmid.
3. Exotoxins that are lethal to animal but with unknown role in humans.
   - Two additional correlates of virulence are the formation of pigmented colonies on certain media and the ability to synthesize purines.

**Pathogenesis & Epidemiology**

The zoonotic cycle consist of transmission among wild rodents by fleas, most rodents are asymptomatic, humans are accidental hosts. This cycle predominate during time of poor sanitation.
The flea ingests the bacteria while taking blood from bacteremic rodent → organisms inoculated with the bite → spread to the regional lymph nodes ← swollen and tender (buboes) → bubonic plaque → high concentration in blood → disseminated → form abscess in many organs.

The endotoxin-related symptoms including → disseminated intravascular coagulation and cutaneous hemorrhages (black death).

Primary pneumonic plaque may occur by respiratory droplet transmission of the organisms from patients with pneumonic plaque or secondary pneumonic plaque from septic emboli that can reach the lungs.

**Laboratory diagnosis**

- Specimens may be stool, blood, pus or material obtained from bubo. Sputum in pneumonic plaque.
- Staining of smear by Giemsa's stain reveal typical safety pin appearance also fluorescent antibody staining can be used.
- Culture is the best diagnostic method where they usually increase the small amount of micro-organisms by cold enrichment (buffer saline at 4°C for 2-4 weeks), then placed on MacConkey.
- Serology-at or after two weeks → rise of agglutinating antibodies (against envelope antigens) → can be detected but cross reaction may confuse the results.
Treatment
- The choice is usually combination of Streptomycin and tetracycline.
- No significant antibiotic resistance.
- Treatment should not wait for the results of bacteriologic culture.

Prevention
1. Controlling the spread.
2. Isolation of suspected cases
3. Treatment of contacts with tetracycline.
4. A vaccine of formalin-killed organisms provides partial protection against bubonic plaque (not pneumonic).

Yersinia enterocolitica
Yersinia pseudotuberculosis
Those are domestic animal pathogens but can cause human diarrheal disease by accidental ingestion of micro-organisms.
**Francisella tularensis**
Are animal pathogens, transmissible to humans by arthropods bites and direct contact with infected animal tissues, inhalation of aerosols or ingestion of contaminated food or water → Tularemia.

**Pasteurella multocida**
Causes wound infection associated with cat and dog bites (organisms are normal flora of mouth of many animals) → rapid cellulitis.
Osteomyelitis ← cat sharp teeth implant micro-organisms under the periosteum.
Cat bite should not be sutured and prophylactic Ampicillin must be given.

**Bacteroids species**
- Very important anaerobic Gram's negative bacilli
- Normal flora of the bowel and genital tract.
- Usually associated with intra-abdominal suppuration in association with anaerobic cocci and bacilli as Peptostreptococcus and Clostridia.
- Isolated under anaerobic conditions.
- Treated by Clindamycin and Metronidazole.
Mycoplasmas
Are a group of small, wall-less organisms of which Mycoplasma pneumoniae is the major pathogen.

Mycoplasma pneumoniae → atypical pneumonia

Important properties
- Mycoplasma are the smallest free-living organisms (≥ 0.3/μm)
- Absence of a cell wall → stain poorly with Gram's stain. And antibiotics that inhibit cell wall synthesis are ineffective.
- Pleomorphic ← a flexible 3-layer cell membrane
- Mycoplasmas can grow on artificial media (including several lipids) → grow slowly (1 week) → visible colony "fried egg" shape.

Pathogenesis & Epidemiology
- Only human pathogen transmitted by respiratory droplets.
- In the lungs, the organism is rod-shaped with a tapered tip that contains specific proteins attached to the respiratory epithelium. The mucosa not invaded but ciliary motion is inhibited → necrosis of epithelium.
- M.pneumonia has one serotype but immunity is incomplete, auto-antibodies produced during infection (cold agglutinins) against red blood cells and brain, lung and liver cells → extra pulmonary manifestations.
Infections occur worldwide, increasing in winter effect mostly young adults, outbreaks occur in groups of close contact. 10% of infected individuals develop pneumonia.

**Clinical findings**

Most common cause of atypical pneumonia, (causative bacterium can not be isolated on routine lab media and the disease does not resemble pneumococcal pneumonia)

- The onset is gradual, begins with non-productive cough, sore throat, or earache → then produce whitish, non-bloody sputum.
- Constitutional symptoms (fever, headache, malaise and myalgias) are pronounced.
- The disease resolves spontaneously in 10-14 days.

**Laboratory Diagnosis**

- Culturing sputum sample may take at least 1 week and need special media.
- Serological test → cold agglutinin titer ≥ 1:128 ← recent infection

IgM auto antibodies against type O RBC ← agglutination at 4°C (Non specific)← false positive ← influenza virus

↑_ adenovirus

- Infection can be confirmed by 4-fold rise in specific antibody titer in CFT.
Treatment

- Usually erythromycin or tetracycline

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Shorten the duration

- Disease resolve by it self

- Penicillins and Cephalosporins are inactive

Other mycoplasmas

- M.hominis → infrequent cause of pelvic inflammatory disease
- Ureaplasma urealyticum → one of several causes of non gonococcal urethritis.