Chlamydia
Family: *Chlamydiaceae*

- **Genus: *Chlamydia***
  - *C. trachomatis* - Urogenital infections, trachoma, conjunctivitis, pneumonia and lymphogranuloma venerium (LGV)

- **Genus: *Chlamydophilina***
  - *C. psittaci* - Pneumonia (psittacosis)
  - *C. pneumoniae* - Bronchitis, sinusitis, pneumonia and possibly atherosclerosis

*N.B. New taxonomy, previously three species in one genus - *Chlamydia***
Chlamydia - Microbiology

- Small obligate intracellular parasites
- Contain DNA, RNA and ribosomes
- Inner and outer membrane
- LPS but no peptidoglycan
  - Cell wall not well characterized
- Energy parasites
  - Can’t make ATP
Physiology and Structure

• Elementary bodies (EB)
  – Small (0.3 - 0.4 µm)
  – Extracellular form
  – Rigid outer membrane
    • Disulfide linked proteins
  – Resistant to harsh conditions
  – Non-replicating, non-metabolically active form
  – Infectious form
    • Bind to columnar epithelial cells (macrophages)
Physiology and Structure

• Reticulate bodies (RB)
  – Larger (0.8 - 1 µm)
  – Intracellular form
  – Fragile membrane
    • Fewer disulfide bonds
  – Metabolically active form
  – Replicating form
  – Non-infectious
Developmental Cycle of Chlamydia

- EB bind to host cells
  - Epithelial
  - Macrophage
- Internalization
  - Endocytosis
  - Phagocytosis
- Inhibition of phagosome-lysosome fusion
- Reorganization into RB
  - Breakdown of disulfide bonds
- Growth of RB
Developmental Cycle of Chlamydia

- Reorganization into EB
- Inclusion bodies
- Release of EB
  - Lysis - *C. psittaci*
  - Extrusion - *C. trachomatis* and *C. pneumoniae*
Chlamydia trachomatis

- Trachoma
- Inclusion conjunctivitis
- Infant pneumonia
- Ocular lymphogranuloma venerium
- Urogenital infections
- Reiter’s syndrome
- Lymphogranuloma venerium
C. trachomatis

• Biovars - biological variants
  – Trachoma
  – LGV
  – Mouse pneumonitis

• Serovars - serological variants
  – Major outer membrane proteins
  – A through L
### Clinical Spectrum of C. trachomatis Infections

<table>
<thead>
<tr>
<th>SEROVARS</th>
<th>DISEASES</th>
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<tbody>
<tr>
<td>A, B, Ba, C</td>
<td>Trachoma</td>
</tr>
<tr>
<td>B, Ba, D to K</td>
<td>Oculogenital disease (conjunctivitis, urethritis, proctitis, cervicitis); infant pneumonia</td>
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<td>L&lt;sub&gt;1&lt;/sub&gt;, L&lt;sub&gt;2&lt;/sub&gt;, L&lt;sub&gt;3&lt;/sub&gt;</td>
<td>LGV</td>
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C. trachomatis-Pathogenesis and Immunity

• Infects nonciliated columnar epithelial cells (macrophages)
• Downregulation of Class I MHC
• Infiltration of PMNs and lymphocytes
• Lymphoid follicle formation
• Fibrosis
• Disease results from destruction of cells and host immune response
• No long lasting immunity; reinfection results in inflammatory response
**C. trachomatis - Epidemiology**

- Ocular infections - Biovar: trachoma
  - Worldwide
  - Poverty and overcrowding
  - Endemic in Africa, Middle East, India, SE Asia
  - United States - American Indians
  - Infection of children
  - Transmission: droplets, hands, contaminated clothing, flies, contaminated birth canal
C. trachomatis - Epidemiology

• Genital tract infections
  – Biovar: trachoma
    • Most common STD in US
      – 2006: USA = 1,030,911; SC = 22,351
      – 2007: USA = 1,025,208; SC = 31,086
      – 2008: USA = 757,740; SC = 18,263 (through 9/15)
    • 50 million new cases/year worldwide
  – Biovar: LGV
    • Humans are only natural host
    • Prevalent in Africa, Asia and South America
    • Sporadic in USA
      – 300 -500 cases/year
      – Male homosexuals are major reservoir
Clinical Syndrome - *Trachoma*  
 (*C. trachomatis* biovar: trachoma)

- Chronic or repeated infection
  - Follicle formation on conjunctiva
  - Scarring of the conjunctiva
Clinical Syndrome - *Trachoma*

- Eyelids turn in and abrade cornea
  - Ulceration
  - Scarring
  - Blood vessel formation
Clinical Syndrome - Trachoma

- Flow of tears impeded
  - Secondary infections
Clinical Syndrome - *Trachoma*

From: G. Wistreich, Microbiology Perspectives, Prentice Hall
Clinical Syndrome - Inclusion Conjunctivitis (\textit{C.trachomatis} biovar: trachoma)

- Associated with genital chlamydia
- Mucopurulent discharge
- Corneal infiltrates, vascularization and scarring can occur
- In neonates infection results from infected birth canal
  - Apparent 5-12 days after birth
  - Ear infection and rhinitis often accompany ocular disease
Clinical Syndrome - Infant Pneumonia

\(C.\text{trachomatis\ biovar: trachoma}\)

- Associated with genital chlamydia
- Infection arises from contaminated birth canal
- Wheezing cough and pneumonia but no fever
- Often preceded by conjunctivitis
Clinical Syndrome - Ocular
Lymphogranuloma Venereum
\((C.\textit{trachomatis} \text{ biovar: LGV})\)

- Associated with LGV serovars
- Conjunctivitis and associated lymphadenopathy
Clinical Syndrome - Urogenital Infections

\(C. trachomatis\) biovar: trachoma

• Females
  – Asymptomatic (80%)
  – Cervicitis, urethritis and salpingitis
  – Postpartum fever
  – Increased rate
    • Premature delivery
    • Ectopic pregnancy
Clinical Syndrome - Urogenital Infections

(C. trachomatis biovar: trachoma)

• Males
  – Symptomatic (75%)
  – Urethritis, dysuria and pyuria
  – Cause of nongonococcal urethritis (35 - 50%)
  – Common cause of postgonococcal urethritis
Time Course of Untreated Chlamydial Urethritis in Males

Symptomatic infection: urethral discharge, dysuria, pyuria

Percent of infected men

Week after infection

Asymptomatic infection
Clinical Syndrome - Reiter’s Syndrome

- Conjunctivitis, polyarthritis and genital or gastrointestinal inflammation
- Associated with HLA-B27
- 50 - 65 % have *C. trachomatis* infection
- 80% have antibodies to *C. trachomatis*
Clinical Syndrome - Lymphogranuloma Venereum

*C. trachomatis* (biovar: LGV)

- **First stage**
  - Small painless vesicular lesion at infection site
  - Fever, headache and myalgia
- **Second stage**
  - Inflammation of draining lymph nodes
  - Fever, headache and myalgia
  - Buboes (rupture and drain)
  - Proctitis
  - Ulcers or Elephantiasis
Patient with LGV

Bilateral inguinal buboes (arrows)
C. trachomatis - Diagnosis

- **Cytology**
  - Iodine-staining inclusions
  - Not sensitive

- **Culture**
  - Iodine staining inclusions
  - Most specific

Iodine-stained inclusion bodies
C. trachomatis - Diagnosis

- Antigen detection (ELISA or IF)
  - Group specific LPS
  - Strain specific outer membrane proteins
- Serology
  - Can’t distinguish between current or past infection
  - Detection of high titer IgM antibodies can be helpful
- Nucleic acid probes
  - Several kits available
  - May eventually replace culture
C. trachomatis - Treatment and Prevention

- Tetracycline, erythromycin and sulfonamides
- Vaccines are of little value
- Treatment coupled with improved sanitation
- Safe sexual practices
- Treatment of patients and their sexual partners
Chlamydophilia (Chlamydia) psittaci

- Psittacosis (Parrot fever)
- Ornithosis
Pathogenesis - *C. psittaci*

- Inhalation of organisms in bird droppings
  - Person to person transmission is rare
- Hematogenous spread to spleen and liver
  - Local necrosis of tissue
- Hematogenous spread to lungs and other organs
- Lymphocytic inflammatory response
  - Edema, infiltration of macrophages, necrosis and occasionally hemorrhage
  - Mucus plugs may develop in alveoli
- Cyanosis and anoxia
Epidemiology - *C. psittaci*

- 50 - 100 cases per year in USA
- Organisms present in birds (symptomatic or asymptomatic)
  - Tissue, feces, feathers
- Primarily an occupational disease
  - Veterinarians, poultry workers, zoo keepers, pet shop workers
Clinical Syndrome - Ornithosis
Uncomplicated Infection

• Incubation period
  – 1-2 weeks
• Fever, chills, headache, nonproductive cough, mild pneumonitis
• Recovery
  – 5-6 weeks
Clinical Syndrome - Ornithosis
Complicated Infection

- Incubation period
  - 1-2 weeks
- Fever, chills, headache, nonproductive cough, mental confusion, pneumonitis, cyanosis, jaundice
- Prolonged Recovery
  - 7-8 weeks
Laboratory Diagnosis - *C. psittaci*

- Serology (Complement fixation test)
  - Fourfold rise in titer
Treatment and Prevention - *C. psittaci*

- Tetracycline or erythromycin
- Quarantine of imported birds
- Control of bird infection
  - Antibiotic supplementation of food
Chlamydomphilia (Chlamydia) pneumoniae

• TWAR agent
  – Taiwan (TW-183) and acute respiratory isolate (AR-39)
• Atypical pneumonia
• Atherosclerosis ?
Pathogenesis - *C. pneumoniae*

- Person to person spread
  - Respiratory droplets
- Bronchitis, sinusitis and pneumonia
Epidemiology - *C. pneumoniae*

- Common infection (200,000 - 300,000 cases per year)
- Primarily in adults
- Most infections are asymptomatic
- Associated with crowded conditions
  - Schools, military bases *etc.*
- Association with atherosclerosis
  - Organisms in diseased arteries
  - Antibodies
Clinical Syndrome - *C. pneumoniae*

- Mild or asymptomatic disease
- Pharyngitis, bronchitis, persistent cough and malaise
- Pneumonia may develop
  - Usually a single lobe
Laboratory Diagnosis - *C. pneumoniae*

- Serology
  - Fourfold rise in titer
Treatment and Prevention - *C. pneumoniae*

- Tetracycline or erythromycin
- Difficult to prevent transmission
- No vaccine