# Lecture 3

# Chlamydia, Gonorrhea & Syphilis

## *Microbiology team 430*

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— Syphilis, Chlamydia and Gonorrhea are the main STDs, caused by delicate organisms, cannot survive outside the body. Humans are the only reservoirs.

# CHLAMYDIA

- An obligate intracellular bacterium with elements of bacteria but no rigid cell wall.
- Fail to grow on artificial media.
- Uses host cell metabolism for growth and replication. (Can't produce its own energy→ needs a living cell to grow).

No rigid cell wall →can't be stained with routine gram stain and can't be treated by B-lactam antibiotics.

## Life cycle

EB invade host cell ( infective stage) →differentiate into RB → replicate in epithelial cell forming inclusions →differentiate into EB → cell burses → EB invade adjacent cells or distant cells if carried in lymph or blood.

EB: elementary body, adapted for extracellular survival and initiation of infection.
RB: reticulate body, adapted for intracellular multiplication.

## Pathogen

| Species | Disease |
|---|---|
| *C. trachomatis* A,B,C | Trachoma |
| ***C. trachomatis* D – K** | **Inclusion conjunctivitis**<br>**Genital infection** |
| *C. trachomatis* L1, L2, L3 | Lymphogranulomavenerum (LGV) |
| *C.psittaci* | Psittacosis |
| *C.pneumoniae* | Respiratory infections |

## Epidemiology

- *C.trachomatis* is a common cause of sexually transmitted disease (STD).
- Spread by genital secretions, anal or oral sex.
- Wide spread, 5-20 % among STD clinic in USA.
- Human are the sole reservoir.
- 1/3 of male sexual contacts of women with *C.trachomatis* cervicitis develop urethritis after 2-6 w incubation period.

## Pathogenesis

- Chlamydia has**tropism** for epithelial cells of endocervixe and upper genital tract of women, urethra, rectum and conjunctiva of both sexes.
- LGV can enter through skin or mucosal breaks.
- Release of pro-inflammatory cytokines, leads to tissue infiltration by inflammatory cells, progress to necrosis, fibrosis then scaring.

LGV: sexually transmitted disease characterized by enlargement of inguinal lymph node.

## Clinical features

**Genital infections caused by *C.trachomatis***

- **In men**: non gonococcalurethritis, epididymitis & proctitis.
- **In women**: cervicitis, salpingitis, urethral syndrome, endometritis & proctitis.
- Urethritis present as dysuria and thin urethral discharge in 50 % of men.
- Uterine cervix infection may produce vaginal discharge but is asymptomatic in 50-70% of women.
- If not treated it can progress to salpingitis and pelvic inflammatory disease causing sterility and ectopic pregnancy.
- **In infants:** 50% of infants born to mothers excreting *C.trachomatis* during labor show evidence of infection during the first year of life. Most develop inclusion conjunctivitis, 5-10% develop infant pneumonia syndrome.
- LGV caused by *C.trachomatis* strains L1,L2,L3
- LGV presents as papule and inguinal lymphadenopathy.

## Diagnosis

- Polymerase chain reaction (PCR) is the most sensitive method of diagnosis, performed on vaginal, cervical, urethral swabs, or urine.
- Isolation on tissue culture ( McCoy cell line) but *rarely done*.
- *C.tracomatis* inclusions can be seen by iodine or Giemsa stained smear.

## Treatment & Prevention

- Azithromycin single dose for non- LGV infection.
- Erythromycin for pregnant women.
- Doxycycline for LGV.

Use **Macrolides** or **Tetracycline** antibiotics.

- Prevention and control through early detection of asymptomatic cases, screening women under 25 years of age to reduce transmission to the sexual partner.

# GONORRHEA

— A- STD disease acquired by direct genital contact. It is localized to mucosal surfaces with infrequent spread to blood or deep tissues.

## Pathogen

- ***Neisseria gonorrheae***: Gram negative diplococcic grows on chocolate agar and on selective enriched media and CO2 required. Not a normal flora.
- **Pathogenesis**: mainly a localized infection of epithelium, leads to intense inflammation.
- Possespili and outer membrane proteins that mediate attachment to non-ciliated epithelium.

## Clinical manifestations

- Incubation period [IP] 2-5 days.
- **Men**: acute urethritis and acute profuse **purulent**urethral discharge,

- **Women**: mucopurulent cervicitis, urethritis with discharge.
- **In both sexes**: Urethritis, proctitis.
- Symptoms similar to *Chlamydia* infection.
- Women usually are asymptomatic.
- Pharyngitis may occur.
- Complications include :
  - **Pelvic Inflammatory Disease (PID)**in women
    - PID occurs in 10-20% of cases, including fever, lower abdominal pain, adnexal tenderness, leukocytosis with or without signs of local infection.
    - Salpingitis and pelvic peritonitis cause scarring and infertility.
  - **Disseminated Gonococcal Infection (DGI)**
    - Due to spread of the bacteria to the bloodstream.
    - Clinically: Fever, migratory arthralgia and arthritis. Purulent arthritis involving large joints. Petechial, maculopapular rash.
    - Metastatic infection such as Endocarditis, Meningitis & Perihepatitis may develop.

### Epidemiology

- Rates among adolescents are high, about 10% increase per year in USA.
- Inability to detect asymptomatic cases such as women and patient fail to seek medical care hampers control.
- Major reservoirs for continued spread are asymptomatic cases.

### Diagnosis

- Direct smear for Gram stain of urethra and cervical specimens to see under the microscope **gram negative intracellular diplococci and pus cells.**
- **Co-agglutination test.**
- Isolates identified by sugar fermentation of **glucose** only ( *does not ferment maltose or sucrose*)
- Culture on Thayer-Martin or other selective medium.

Microscopic examination doesn't differentiate between N.meningitidis and N.gonorrhea.
Useco-agglutination test and sugar fermentation test to confirm N.gonorrhea.

### Treatment

- **Ceftriaxone** IM (or oral Cefixime recommended).
- Ciprofloxacin or Ofloxacin
- Patients suspected to be co-infected with gonorrhea and chlamydia →give azithromycin or doxycycline both cover *C.trachomatis & N.gonorrhea*.

## SYPHILIS

A chronic systemic infection caused by a spiral organism called *Treponemapallidum*

### Epidemiology

- An exclusively human pathogen.

- Transmission by contact with mucosal surfaces or blood, less commonly by non-genital contacts with a lesion, sharing needles by IV drug users, or transplacental transmission to fetus.
- **Early disease is infectious**, late disease is not infectious.

## Pathogenesis

- Bacteria access through in-apparent skin or mucosal breaks.
- Slow multiplication produces **endarteritis &granulomas.**
- **Ulcer heals but spirochete disseminate.**

## Clinical Manifestations

**Stages of Syphilis**

1) **Primary syphilis**:
   - **Chancre** is a painless, indurated ulcer with firm base and raised margins on external genitalia or cervix, anal or oral site appear after an IP of about 2-6 weeks.
   - Enlarged inguinal lymph nodes may persist for months.
   - Lesion heals spontaneously after 4-6 weeks.

2) **Secondary Syphilis**
   - Develops 2-8 weeks after primary lesion healed.
   - Characterized by symmetric mucocutaneousrash, mouth lesions ( *snail track ulcers*) and generalized non-tender lymph nodes enlargement ( *full of spirochete*) with **bacteremia** causing fever, malaise and other systemic manifestations.
   - Skin lesion distributed on trunk and extremities often palms, soles and face.
   - 1/3 develop **condylomatalata**: which are painless mucosal warty erosions on genital area and **perineum**.
   - Secondary lesion resolve after few days to many weeks but disease continue in 1/3 of patients. Disease enters into a latent state.

**Latent syphilis**: a stage where there is no clinical manifestations but **infection evident by serologic tests**.
**Risk of blood-borne transmission or from relapsing infection or mother to fetus continue.**

3) **Tertiary syphilis**:
in 1/3 of untreated cases. Manifestations may appear after 15-20 years or may be asymptomatic but serological tests positive.
   - **Neurosyphilis**: chronic meningitis, with increased cells and protein in CSF, leads to degenerative changes and psychosis. Demyelination causes peripheral neuropathies. Most advanced cases result in **paresis** (***p****ersonality*, ***a****ffect*, ***r****eflexes*, ***e****yes*, ***s****enorium*, ***i****ntellect*, ***s****peech)* due to the effect on the brain parenchyma and posterior columns of spinal cord and dorsal roots.
   - **Cardiovascular Syphilis**
     - Due to **arteritis** leads to aneurysm of aorta and aortic valve incompetence.

Effect on the brain parenchyma (especially frontal lobe) →affect behavior →generalized paralysis of insane (GPI).
Posterior columns of spinal cord →tabesdorsalis→high-stepping gait.

- Localized granulomatous reaction called **gumma** on skin, bones, joints or other organs leads to local destruction.

**Congenital syphilis:** develop if the mother not treated, fetus susceptible **after 4th month** of gestation. Fetal loss or congenital syphilis result. Rhinitis, rashandbone changes ( *saddle nose, saber shine*) ,anemia thrombocytopenia, and liver failure.

Congenital syphilis is completely preventable if women are screened serologically early in pregnancy (<3months) and those who are positive are treated with penicillin.

## Diagnosis

The organism grow on cultured mammalian cells **only**, not stained by Gram stain but readily seen only by immunoflurescence (IF), dark filed microscopy or silver impregnation histology technique.

1) **Dark field microscopy**ofsmearfrom primaryor secondary lesions.
2) **Serologic tests**: commonly used.
   A. **Non-treponemaltests (non-specific)**: antibody to cardiolipin (*lipid complex extracted from beef heart*) called **reagin**. The tests are called rapid plasma regain (**RPR**) and venereal disease research laboratory ( **VDRL**). Become positive during the primary stage, antibody peak in secondary syphilis. Slowly wane in later stages.
   Used for **screening** and titer used to **follow up therapy**.

   B. **Treponemaltests (specific)**: treponemal antigen used.
   Detects specific antibody to *T.pallidum**:***
   - Fluorescent treponemal antibody ( **FTA-ABS**) .
   - Microhemagglutination test(**MHA-TP**) (*antigen attached to erythrocytes*)
   - **Positive results confirm RPR and VDRL.**
   - **IgM** used to diagnose congenital syphilis.

## Treatment and Prevention

- Treponema is sensitive to Penicillin.
- Hypersensitive patients treated with Tetracycline, Erythromycin or Cephalosporins.
- Prevention: counseling

# Summary

- Syphilis, Chlamydia and Gonorrhea are the main STDs, caused by delicate organisms, cannot survive outside the body, humans are the only reservoirs.

- Chlamydia is an obligate intracellular bacteria with elements of bacteria but no rigid cell wall.
- Chlamydia fail to grow on artificial media→ needs living cell.
- Pathogen:

| | |
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| ***C. trachomatis*** **D – K** | **Inclusion conjunctivitis**<br>**Genital infection** |
| *C. trachomatis* L1, L2, L3 | Lymphogranulomavenerum (LGV) |

- Chlamydia has tropism for epithelial cells of endocervixe and upper genital tract of women, urethra, rectum and conjunctiva of both sexes.
- Genital infections caused by *C.trachomatis, serotypes D-K:*
  - **In men**: non gonococcal urethritis, epididymitis &proctitis.
  - **In women**: cervicitis, urethritis, salpingitis, urethral syndrome, endometritis & proctitis.
  - **In neonates**: inclusion conjunctivitis.
- Genital tract infection with serotype D-K is asymptomatic in most women, but usually symptomatic in men.
- LGV presents as papule and inguinal lymphadenopathy.
- Polymerase chain reaction (PCR) is the most sensitive method for the diagnosis of chlamydial genital infections.
- Chlamydial infection is treated with doxycycline, azithromycin, and erythromycin.
- Gonorrhea is caused by the gram-negative coccus, Neisseria gonorrhoeae.
- Women are usually asymptomatic therefore considered the major reservoir of infection.
- Women may not be alerted to their infection until complications arise such as PID or infertility.
- Symptoms of gonorrhea includeacute urethritis and acute profuse **purulent** urethral discharge in men.
- Diagnosis of gonorrhea is done by microscopic examination showing intracellular gram-negative diploccoci and pus cells and the test is confirmed by Co-agglutination test and glucose fermentation test.
- Treatment is by giving single dose of Ceftriaxone IM.
- Syphilis is a chronic systemic infection , sexually transmitted , caused by a spiral organism called *Treponemapallidum*

| | **Primary stage** | **Secondary stage** | **Tertiary stage** |
|---|---|---|---|
| **Clinical manifestation** | Chancre (painless ulcer). | ▪ Bacteremia<br>▪ Symmetric mucocutaneous rash<br>▪ Snail track ulcers<br>▪ condylomatalata. | ▪ CNS →generalizes paralysis of insane & tabesdorsalis.<br>▪ CVS→ arteritis, aortic aneurysm, aortic valve incompetence & endarteritis.<br>▪ Gumma |
| **Diagnosis** | Dark field microscopy | Serology | Serology |

- Syphilis serology:

| Test | Stage |
|---|---|
| — **Non-treponemal tests**<br>— **(RPR & VDRL )** | — **POSITIVE** during primary stage,screening, follow up therapy |
| — **Treponemal tests**<br>— **( FTA-ABS)&( MHA-TP )** | — **POSITIVE** at all stages , confirm RPR & VDRL |
| — **IgM antibody** | — Congenital syphilis |

- Penicillin is the drug of choice for treating people with syphilis.
- Patients who present with an STD need to be screened for other STDs especially HIV.