Chlamydia, syphilis & gonorrhea

Lecture 3

- Additional Notes
- Important
- Explanation
- Examples

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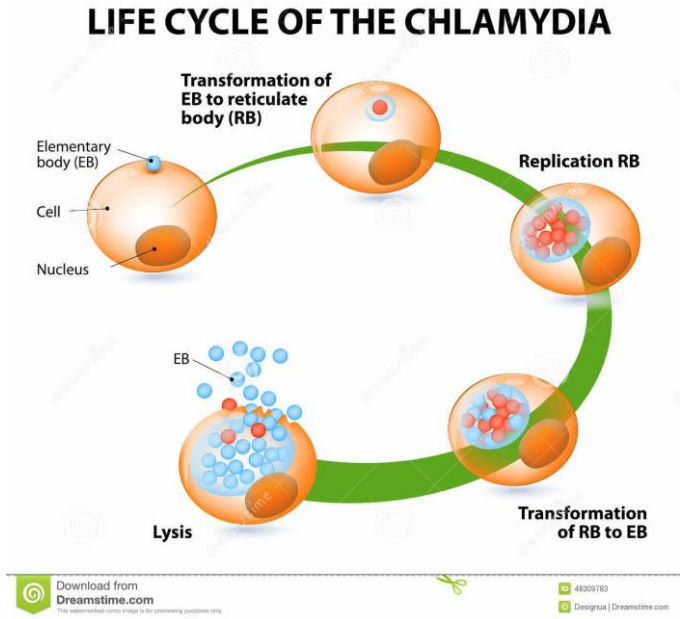
Chlamydia

- Spreads by genital secretions , anal or oral sex.
- Wide spread, 5-20 % among STD clinic in USA.
- Human are the sole reservoir .
- An obligate intracellular bacteria with elements of bacteria but no rigid cell wall.
- Fail to grow on artificial media
- Uses host cell metabolism for growth and replication.
- **Chlamydia trachomatis** is a common cause of sexually transmitted disease (STD).
- 1/3 of male sexual contacts of women with Chlamydia trachomatis cervicitis. He will develop urethritis after 2-6 w incubation period.

Chlamydia species		
C. Trachomatis	A,B & C	Trachoma
	D-K	Inclusion conjunctivits & genital infection
	L1, L2 & L3	Lymphogranulma venerum (LGV)
C. Psittaci	Psittacosis (associated with some kinds of birds e.g. parrots & pigeons etc.)	
C. Pneumoniae	Respiratory infection	

Chlamydia

- **Pathogenesis of chlamydia:**
  - ✓ Chlamydia have tropism (affinity) for epithelial cells of
    - Endocervix and upper genital tract (Fallopian tubes & ovaries) of women.
    - Epididymis in men.
    - Urethra, rectum and conjunctiva of both sexes.
  - ✓ LGV can enter through skin or mucosal breaks
  - ✓ Release of proinflammatory cytokines, leads to tissue infiltration by inflammatory cells, progress to necrosis, fibrosis then scaring.



- EB: elementary bodies
- ER: reticulate bodies

Clinical Features

- **In men:** urethritis (non gonococcal urethritis ,NGU), epididymitis & proctitis (inflammation of the anus).
- **In women:** cervicitis, salpingitis, urethral syndrome, endometritis & proctitis.
- **Symptoms and Signs:**
  - ✓ Urethritis present as dysuria (painful urination) and thin urethral discharge in 50 % of men.
  - ✓ Uterine cervix infection may produce vaginal discharge but is asymptomatic in 50-70% of women.
- Salpingitis and pelvic inflammatory disease can cause sterility and ectopic pregnancy.
- Infants born to mothers excreting C.trachomatis during labor
  - ✓ 50% show evidence of infection during the first year of life.
  - ✓ Most develop inclusion conjunctivitis,
  - ✓ 5-10% develop infant pneumonia syndrome.
- **Lymphogranuloma venerum (LGV):**
  - ✓ LGV caused by C.trachomatis strains L1,L2,L3
  - ✓ LGV is Common in S. America and Africa.
  - ✓ LGV presents as papule and inguinal lymphadenopathy.
  - ✓ Chronic infection leads to abscesses, strictures and fistulas.

Diagnosis of Chlamydia genital infection

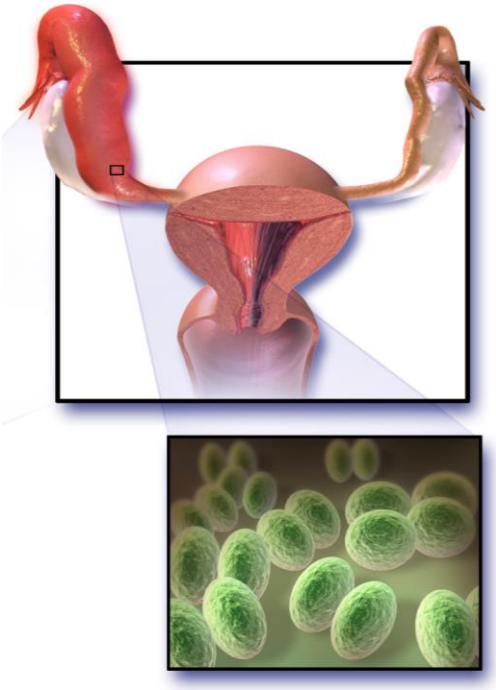
- Diagnosis of Chlamydia genital infection:
  - ✓ Polymerase chain reaction (PCR) is the most sensitive method of diagnosis. Performed on vaginal, cervical, urethral swabs or urine.
  - ✓ Isolation on tissue culture (McCoy cell line) but rarely done.

- Treatment:
  - ✓ **Azithromycin** single dose for non-LGV infection.
  - ✓ **Erythromycin** for pregnant women.
  - ✓ **Doxycycline** for LGV.
- Prevention and control through early detection of asymptomatic cases , screening women under 25 years to reduce transmission to the sexual partner.

Gonorrhea

- 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 reservoir for continued spread are asymptomatic cases.
- Nonsexual transmission is rare.
- A STD disease acquired by direct genital contact.
- It is localized to mucosal surfaces with infrequent spread to blood or deep tissues.
- Caused by **Neisseria gonorrhoeae**.
- Clinical manifestations:
  - ✓ Incubation period = 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.
- Pharyngitis may occur.
- Pelvic inflammatory disease (PID) in women (next slide).

- Pelvic inflammatory disease (PID):
  - ✓ 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 to the bloodstream.



- 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.

Neisseria gonorrheae

- A Gram negative diplococci 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.
  - ✓ Posses pili and outer membrane proteins that mediate attachment to non-ciliated epithelium.
  - ✓ Invasion by IA and Opa proteins (types of proteins found on the surface of the outer membrane. Used from the bacteria to enter the epithelium cells) .
- **Diagnosis:**
  - ✓ Transport media required unless transfer to the lab. is immediate.
  - ✓ Direct smear for Gram stain of urethra and cervical specimens to see **Gram negative intracellular diplococci** , more sensitive in men .
  - ✓ Culture on Thayer-Martin or other selective medium.
  - ✓ Isolates identified by sugar fermentation of glucose only (does not ferment maltose or sucrose) or Coagglutination test.
- **Treatment:**
  - ✓ Guided by local resistance pattern and susceptibility testing. Partner should be treated as well.
  - ✓ Ceftriaxone IM (or oral Cefixime recommended).
  - ✓ Ciprofloxacin or Ofloxacin
  - ✓ Azithromycin, Doxycycline (orally for 7 days) both cover C.trachomatis infection as well .
  - ✓ Counselling.

Syphilis

- 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 but late disease is not infectious .
- A chronic systemic infection , sexually transmitted , caused by a spiral organism called Treponema pallidum
- 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.
- **Pathogenesis of syphilis:**
  - ✓ Bacteria access through in-apparent skin or mucosal breaks.
  - ✓ Slow multiplication produces endarteritis (inflammation of the inner lining of an artery) & granulomas.
  - ✓ Ulcer heals but spirochete[1] disseminates.
  - ✓ Latent periods may be due to surface binding of host components.
  - ✓ Injury is due to delayed hypersensitivity responses to the persistence of the spirochetes.

1. Spirochaete: is a phylum (شعبة) which contains treponema pallidum and other organism.

Clinical manifestation of syphilis

Primary syphilis	Secondary syphilis	Tertiary syphilis
▪ it is a painless, indurated ulcer with firm base and raised margins on external genitalia or cervix , anal or oral site appear after an Enlarged inguinal lymph nodes may persist for months.	▪ Characterized by ✓ symmetric mucocutaneous rash , ✓ 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 condylomata lata: which are painless mucosal warty erosions on genital area and perineum	▪ 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 (personality, affect , reflexes, eyes, senorium, intellect, speech) due to the effect on the brain parenchyma and posterior columns of spinal cord and dorsal roots (tabes dorsalis).
IP of about 2-6 weeks . Lesion heals spontaneously after 4-6 weeks.	Develops 2-8 weeks after primary lesion healed. Secondary lesion resolve after few days to many weeks but disease continue in 1/3 of patients. Disease enter into a latent state. (next slide)	in 1/3 of untreated cases. Manifestations may appear after 15-20 years or may be asymptomatic but serological tests positive.

Clinical manifestation of syphilis

Latent syphilis	Cardiovascular syphilis	Congenital syphilis
▪ Happens after secondary lesion resolves and before tertiary stage starts to appear. ▪ A stage where there is no clinical manifestations but infection evident by serologic tests. Relapse cease. ▪ Risk of blood-borne transmission or from relapsing infection or mother to fetus continue.	▪ Due to arteritis leads to aneurysm of aorta and aortic valve ring. ▪ Localized granulomatous reaction called gumma on skin, bones, joints or other organs leads to local destruction	▪ Develop if the mother not treated , fetus susceptible after 4th month of gestation. ▪ Fetal loss or congenital syphilis result. ▪ Rhinitis ,rash and bone changes (saddle nose, saber shine) ,anemia thrombocytopenia, and liver failure

Diagnosis of syphilis

- Dark field microscopy of smear from primary or secondary lesions. May be negative.
- Serologic tests:

Nontreponemal tests	Treponemal tests
POSITIVE during primary stage ,screening, follow up therapy	POSITIVE at all stages , confirm RPR & VDRL
(RPR & VDRL)	(FTA-ABS) & (MHA-TP)
• antibody to cardiolipin (lipid complex extracted from beef heart) called reagin . • The tests are called rapid plasma reagin (RPR) and venereal disease research laboratory (VDRL). • Become positive during the primary stage (possible exception HIV) , antibody peak in secondary syphilis. Slowly wane in later stages.	Fluorescent treponemal antibody (FTA-ABS) . Microhemagglutination test(MHA-TP) (antigen attached to erythrocytes)
Used for screening and titer used to follow up therapy.	Positive results confirm RPR and VDRL.

- IgM is used for detection of congenital syphilis

Treatment and prevention of syphilis

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