Chlamydia, Syphilis & Gonorrhea

Reproductive Block

Prof. Hanan Habib

Department of Pathology & Laboratory Medicine

College of Medicine ,KSU

Objectives

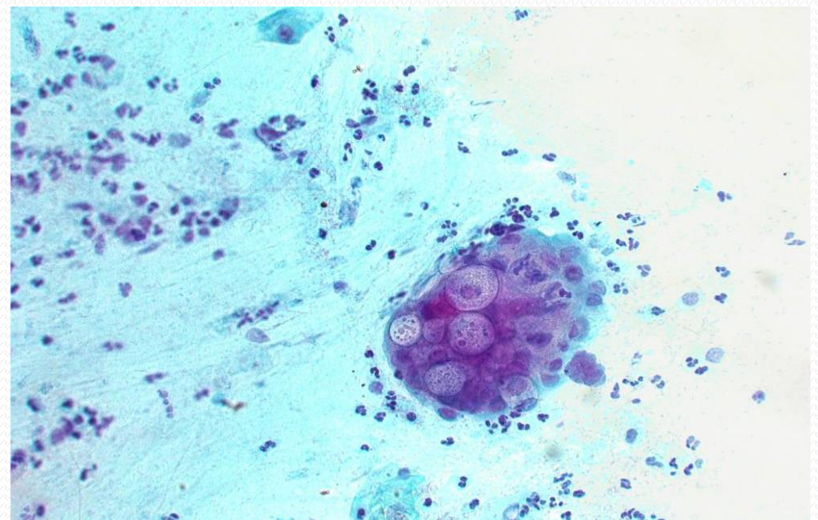
- Know the causative agents of syphilis, gonorrhea and Chlamydia infections.
- Realize that these three infections are acquired through sexual intercourse.
- Know the pathogenesis of syphilis, gonorrhea and Chlamydia infection.
- Describe the clinical feature of the primary, secondary tertiary syphilis and complications.
- Recall the different diagnostic methods for the different stages of syphilis.
- Describe the clinical features of gonorrhea that affect only men, only women and those ones which affect both sexes.

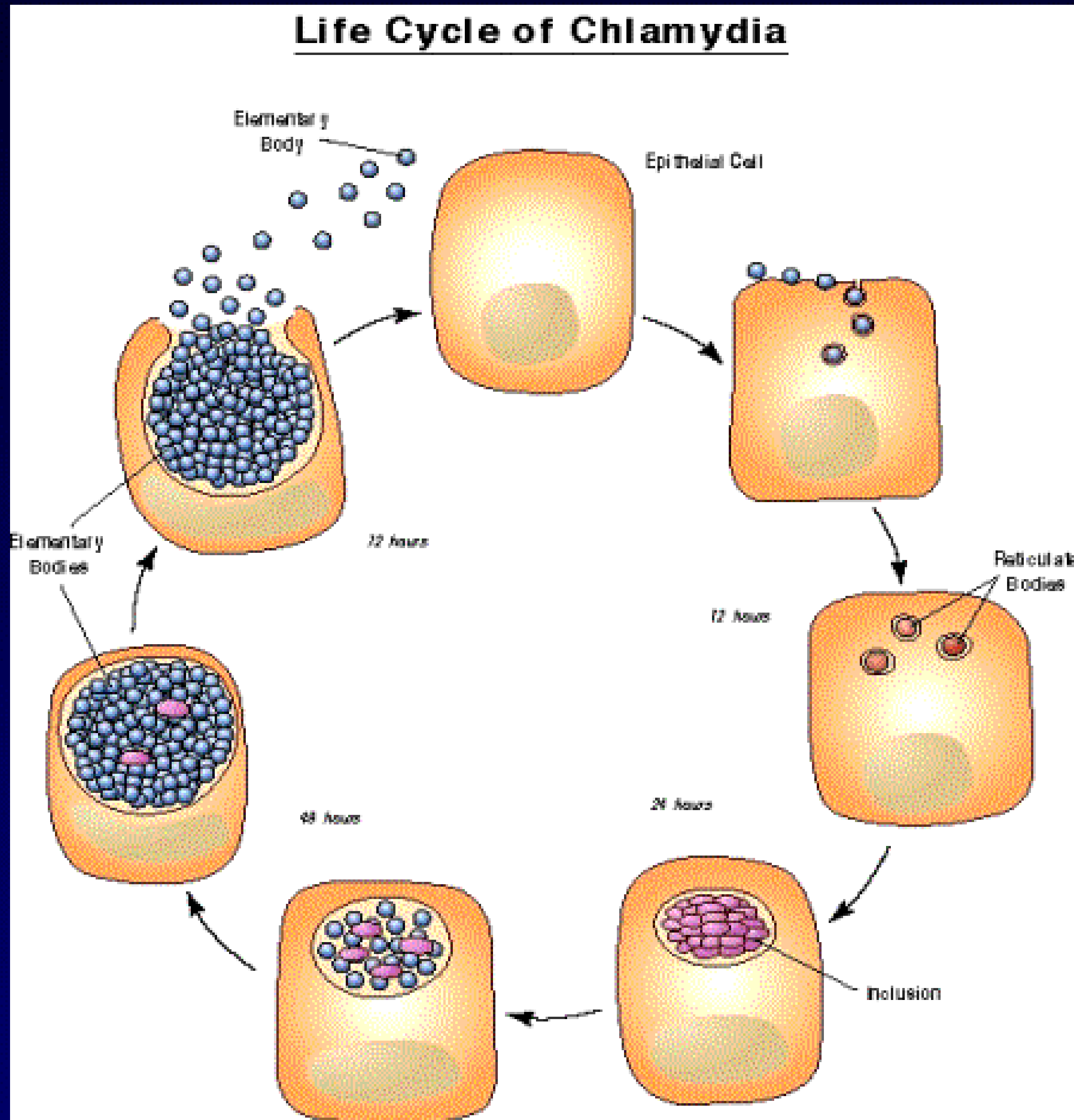
Objectives

- Describe the different laboratory tests for the diagnosis of gonorrhea
- Describe the morphology and the distinct life cycle of the *Chlamydia*.
- Know the different genera, species and serotypes of the family *Chlamydophila*.
- Recognize that *Chlamydia* cause different diseases that affect the eye (causing trachoma) and the respiratory system (mainly cause a typical pneumonia).
- Know the different urogenital clinical syndromes caused by *Chlamydia trachomatis* that affect men, women and both sex.
- Realize that these urogenital syndromes are difficult to differentiate clinically from the similar ones caused by *N.gonorrheae.*
- Know the treatment of syphilis, gonorrhea and *Chlamydia* infections.
- Realize that there are no effective vaccines against all these three diseases.

Chlamydia

- 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.
- Image of inclusion bodies:





Source: California STD/HIV Prevention Training Center

CDC
STD Prevention

Chlamydia species

Chlamydia serotype	Disease
• *C. trachomatis*	
A,B,C	• Trachoma
D - K	• Inclusion conjunctivitis, genital infection
L1, L2, L3	Lymphogranuloma venerum (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 weeks incubation period.

Pathogenesis of Chlamydia

- *Chlamydia* have tropism for epithelial cells of endocervix and upper genital tract of women, 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.

Genital infections caused by *C.trachomatis*

- **In men**: urethritis (non gonococcal urethritis (NGU)) , epididymitis & proctitis.
- **In women**: cervicitis, salpingitis, urethral syndrome, endometritis & proctitis.
- Urethritis presents 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.

Salpingitis and pelvic inflammatory disease can cause sterility and ectopic pregnancy.

- 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 is common in South America and Africa.

Papule and inguinal lymphadenopathy.

Chronic infection leads to abscesses, strictures and fistulas.

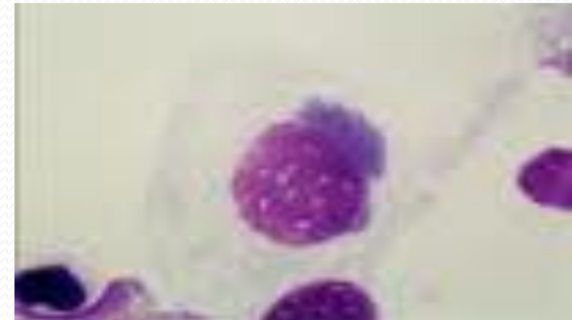
Diagnosis of *Chlamydia* genital infections

- **Polymerase chain reaction (PCR) :**

the most sensitive methods of diagnosis. Performed on vaginal ,cervical , urethral swabs, or urine .

- **Isolation on tissue culture (McCoy cell line) : *C.trachomatis* inclusions can be seen by iodine or Giemsa stained smear.**

Rarely done



Treatment & Prevention

- 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: Clinical Aspects

- A STD disease acquired by direct genital contact. It is localized to mucosal surfaces with infrequent spread to blood or deep tissues. Caused by *N.gonorrheae.*
- **Clinical manifestations: 2-5 days IP .**

Men: acute urethritis and acute profuse **purulent** urethral discharge.

Women: **mucopurulent** cervicitis, urethritis with discharge.

In both sexes: urethritis & proctitis.

Symptoms are similar to *Chlamydia* infection.

Pharyngitis may occur.

Pelvic inflammatory disease (PID) in women.

Pelvic Inflammatory Disease (PID)

- PID occurs in 10-20% of cases, include fever, lower abdominal pain, adnexal tenderness, leucocytosis with or without signs of local infection.
- Salpingitis and pelvic peritonitis cause scarring and infertility.
- Disseminated Gonoccocal Infection (DGI) due to spread to the bloodstream.

Disseminated Gonococcal Infection (DGI)

- Due to spread of the bacteria to the blood stream.
- Clinically : Fever, migratory arthralgia and arthritis. Purulent arthritis involving large joints. Petechial , maculopapular rash.
- Metastatic infections such as Endocarditis , Meningitis & Perihepatitis may develop.

Epidemiology of Gonorrhea

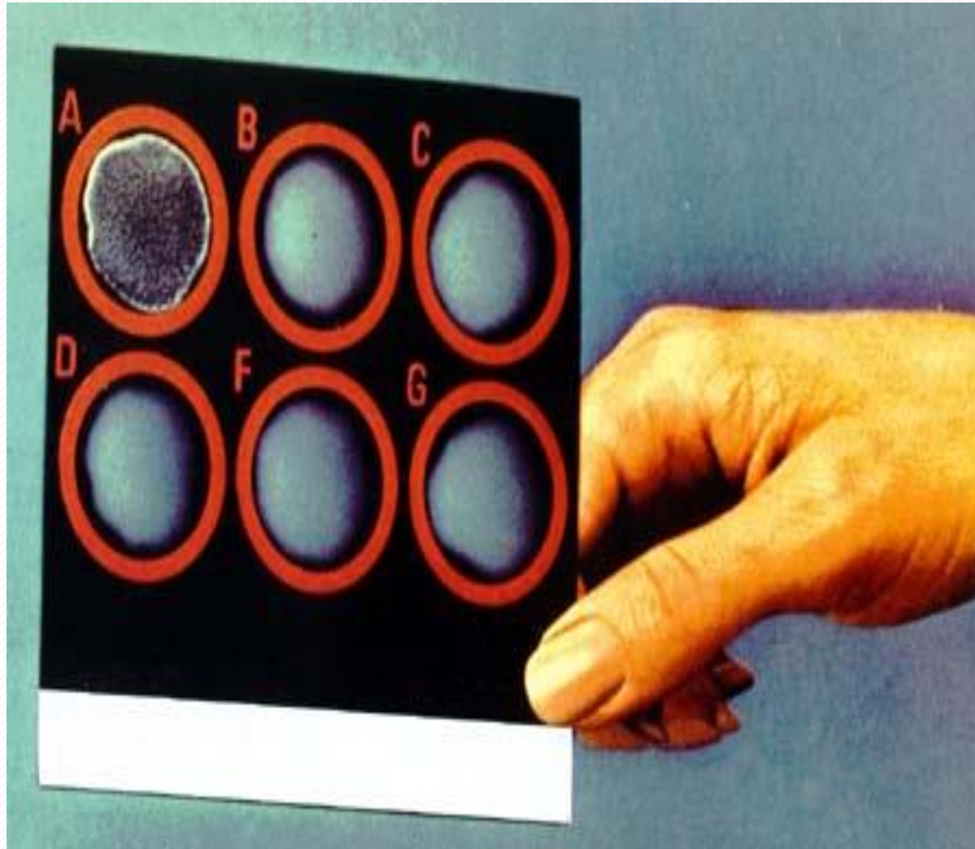
- Rates among adolescents are high, about 10% increase per year in USA .
- Inability to detect asymptomatic cases such as women and patient fail to seek medical care hampers control .
- Major reservoir for continued spread are asymptomatic cases.
- Non-sexual transmission is rare.

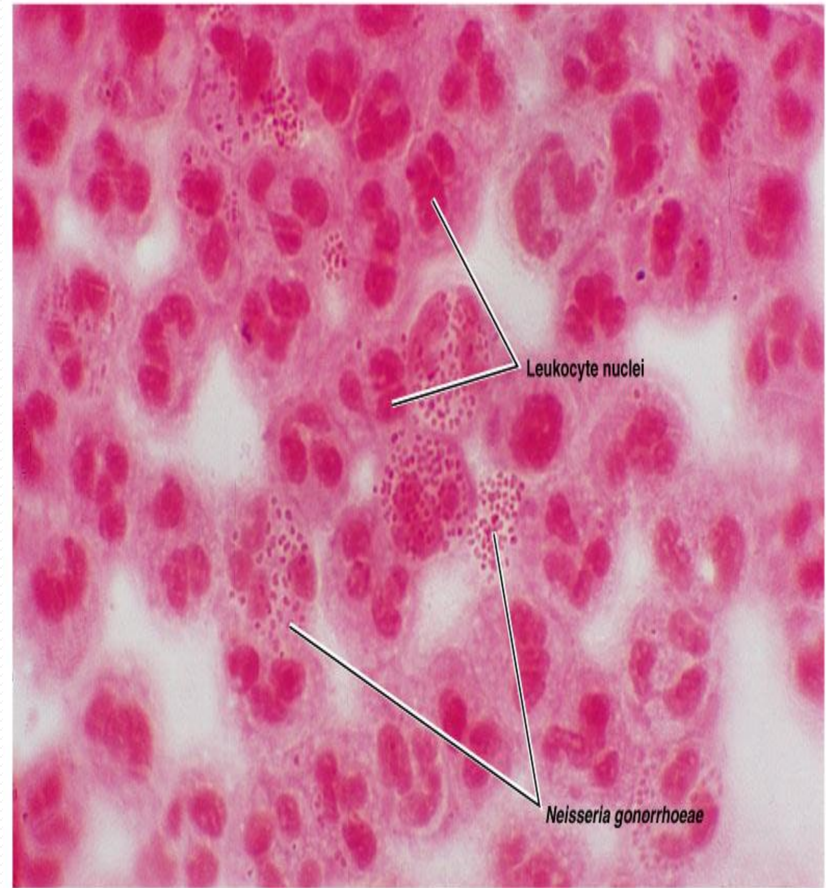
Neisseria gonorrheae

- A Gram negative diplococci grows on chocolate agar and on selective enriched media and CO_2 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.

Diagnosis of Gonorrhea

- Transport media required unless transfer to the lab. is immediate.
- Direct smear for Gram stain of urethra and cervical specimens to see **Gram negative diplococci within a neutrophil (intracellular)** , 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.**





Copyright © 2004 Pearson Education, Inc., publishing as Benjamin Cummings.

Treatment of Gonorrhea

- 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 .
- Counseling.

Syphilis

- A chronic systemic infection , sexually transmitted , caused by a spiral organism called *Treponema pallidum* subsp.*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.

Epidemiology of 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.**
- Late disease is not infectious .

Pathogenesis

- Bacteria access through inapparent skin or mucosal breaks.
- Slow multiplication produces **endarteritis & granulomas.**
- **Ulcer heals but spirochete disseminate.**
- Latent periods may be due to surface binding of host components.
- Injury is due to delayed hypersensitivity responses to the persistence of the spirochetes.

Clinical Manifestations-Stages of Syphilis

- **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.

•Secondary Syphilis

- Develops 2-8 weeks after primary lesion healed.
- 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.

Secondary lesion resolve after few days to many weeks but disease continue in 1/3 of patients. Disease enter into a latent state.

- **Latent syphilis**: a stage where there is no clinical manifestations but infection evident by **serologic tests**. Relapse cease.

Risk of blood-borne transmission from relapsing infection or mother to fetus continue.

- **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. Demylination 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 ring.

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 ,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**: commonly used .

Nontreponemal tests: antibody to cardiolipin (*lipid complex extracted from beef heart*) , anticardiolipin antibody 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.

Used for **screening** .Titer used to **follow up therapy**.

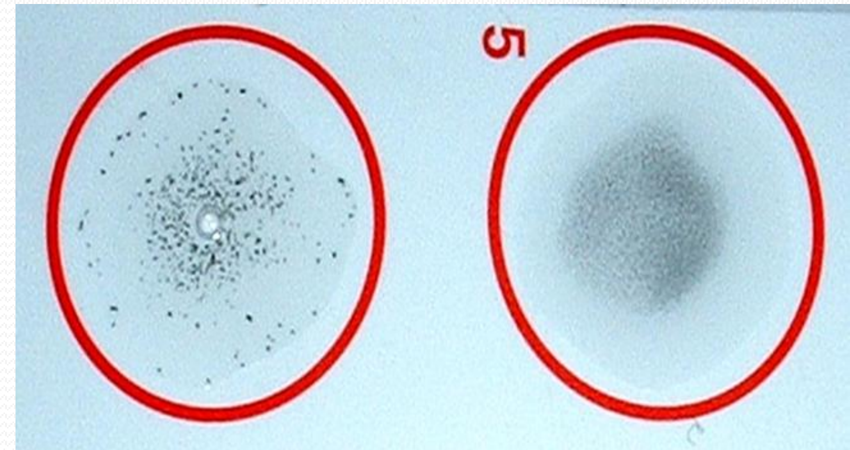
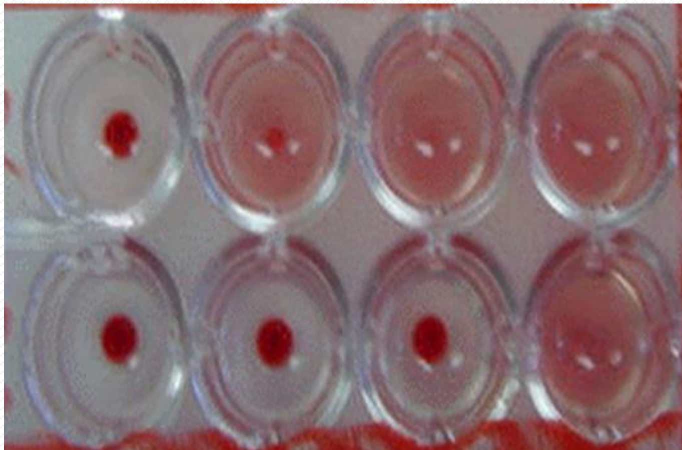
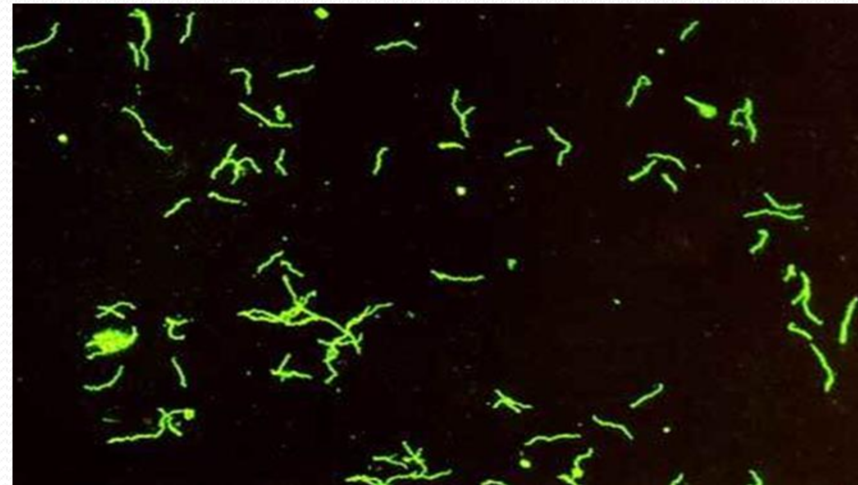
SYPHILIS SEROLOGY

Reactive

Weak Reactive

Weak Reactive (Minimally)

Nonreactive

Treponemal tests: treponemal antigen used.

Detects specific antibody to *T.pallidum*

- Fluorescent Treponemal Antibody (**FTA-ABS**) .
- Microhemagglutination treponema test(**MHA-TP**) (*antigen attached to erythrocytes*)

Positive results confirm RPR and VDRL.

- **IgM** used to diagnose congenital syphilis.

Summary of syphilis serology

Test

- **Nontreponemal tests**
(**RPR & VDRL**)

- Treponemal tests
(**FTA-ABS)**&**(MHA-TP**)

- IgM antibody

Stage

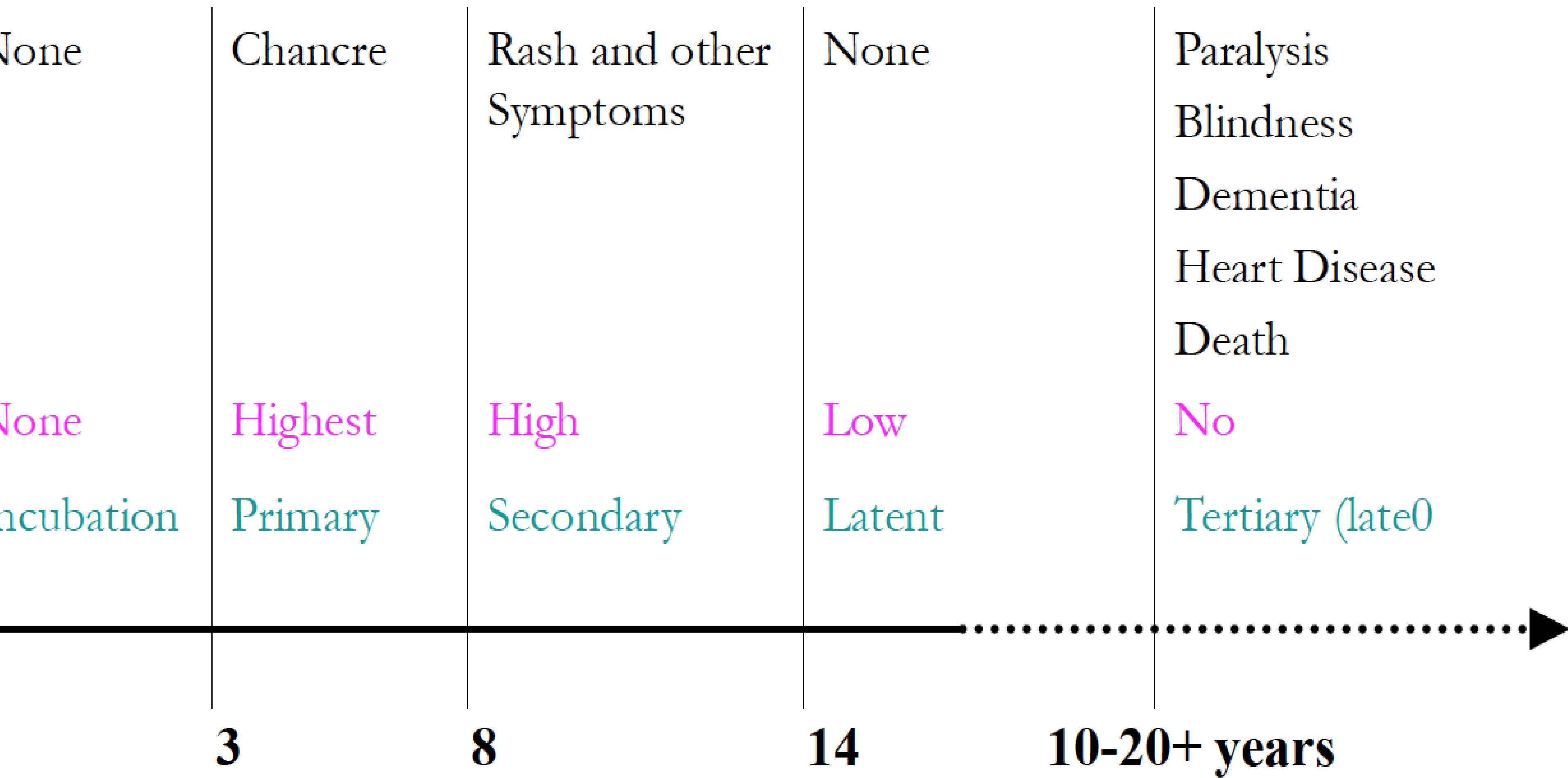
- **Positive** during primary stage ,screening, follow up therapy

- **Positive** at all stages , confirm RPR & VDRL

- Congenital syphilis

INTERPRETATION OF SEROLOGICAL TESTS FOR SYPHILIS

Non-Treponemal tests (RPR/ VDRL)	Treponemal Tests (TP-PA/ FTA-ADS)	Possible Explanation
+	+	Syphilis - recent or previous Yaws or pinta
+	—	No syphilis False positive
—	+	Consistent with previously treated or untreated Syphilis Yaws, Pinta, Bejel
—	—	No syphilis Syphilis in incubation period

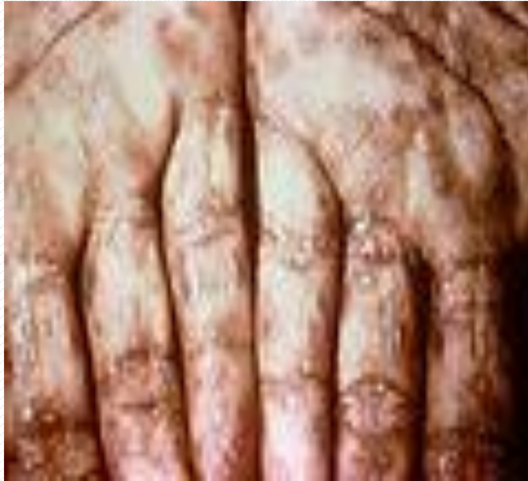


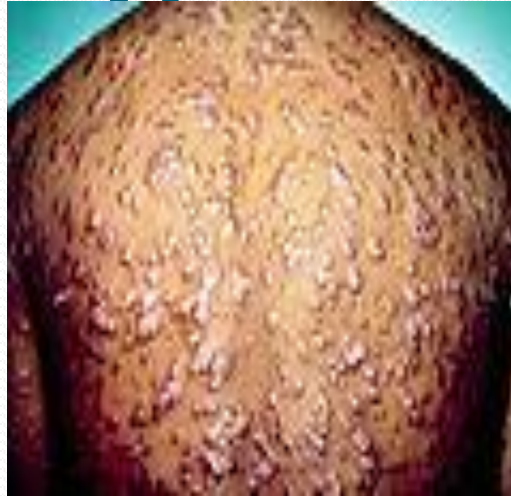
n with
pallidum

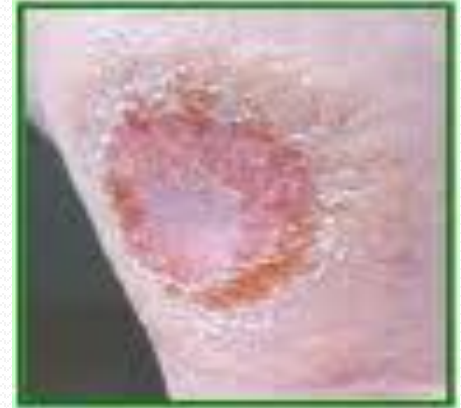
Treatment and Prevention

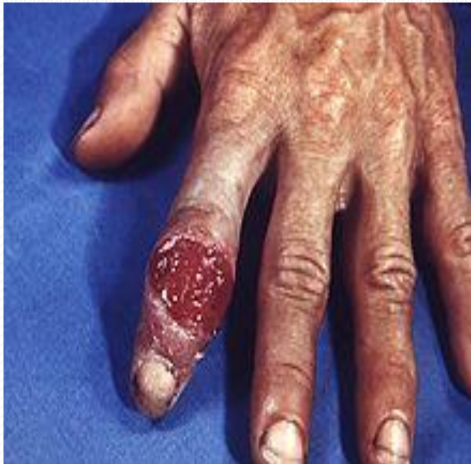
- **Treponema is sensitive to Penicillin.**
- Hypersensitive patients treated with Tetracycline, Erythromycin or Cephalosporins
- **Prevention**: counseling.

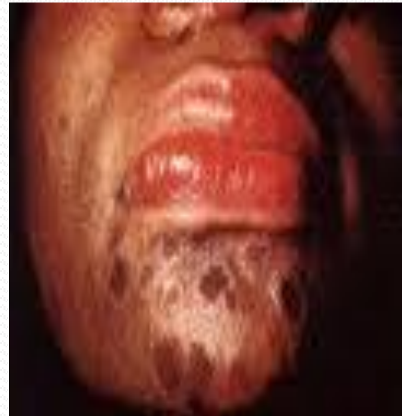
Syphilis

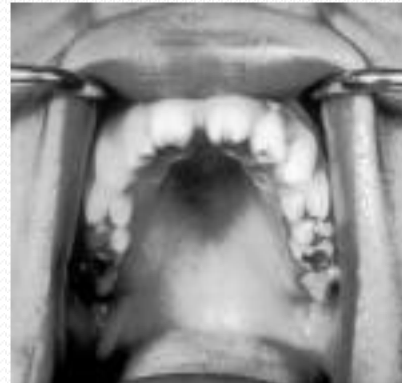


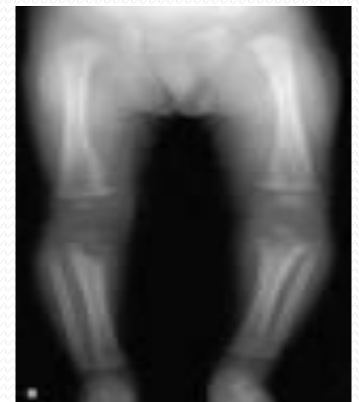












Take Home Message

- Syphilis, Chlamydia and Gonorrhea are main STDs ,caused by delicate organisms ,cannot survive outside the body.
- Infection may not be localized.
- Clinical presentation may be similar (urethral or genital discharge, ulcers).
- One or more organisms (Bacteria, virus, parasite) may be transmitted by sexual contact.
- Screening for HIV required .
- If not treated early may end in serious complications .