



Chlamydia, Gonorrhoea & Syphilis

Prof. Hanan Habib & Dr. Khalifa Binkhamis

**Department of Pathology
College of Medicine**

Objectives

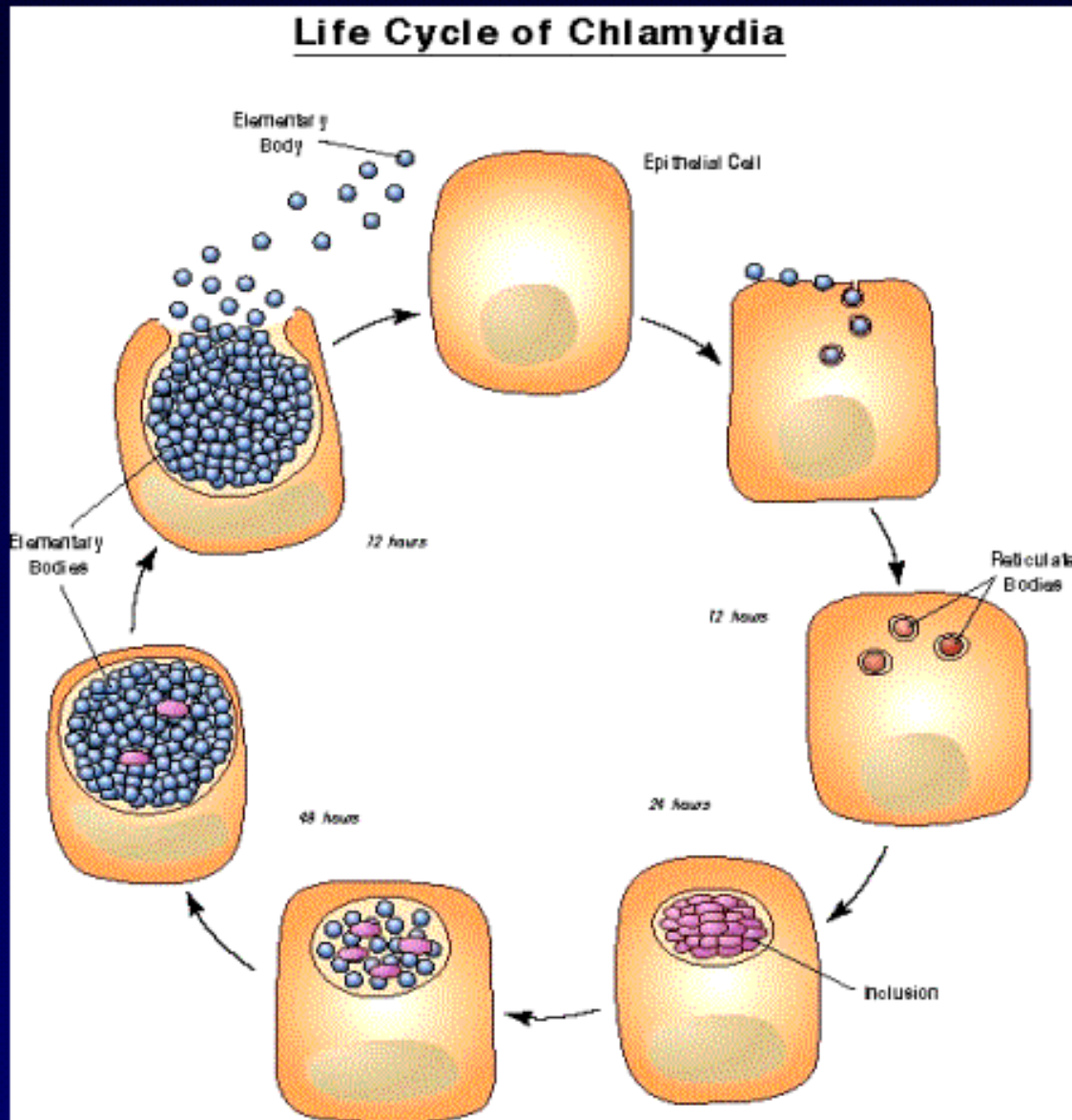
- Recall the causative agents of syphilis, gonorrhoea and Chlamydia infections.
- Describe the pathogenesis of syphilis, gonorrhoea and Chlamydia infection.
- Describe the clinical features of Chlamydial infections
- Recall the different genera, species and serotypes of the family *Chlamydia*.
- Describe the laboratory diagnosis of Chlamydia
- Describe the clinical features of gonorrhoea that affect only men, only women and those ones which affect both sexes.

Objectives

- Describe the different laboratory tests for the diagnosis of gonorrhoea
- Describe the clinical features of the primary, secondary and tertiary syphilis and complications.
- Recall the different diagnostic methods for the different stages of syphilis.
- Recall the treatment regimens of syphilis, gonorrhoea and *Chlamydia* infections.
- Recall 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.



Source: California STD/HIV Prevention Training Center

Chlamydia species

Chlamydia serotype

- *C. trachomatis*

A,B,C

D - K

L₁, L₂, L₃

- *C. psittaci*
- *C. pneumoniae*

Disease

- Trachoma
 - Inclusion conjunctivitis,
genital infection
- Lymphogranuloma venerum
(LGV)

Psittacosis

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 pro-inflammatory cytokines, lead to tissue infiltration by inflammatory cells, progress to necrosis, fibrosis then scarring.

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

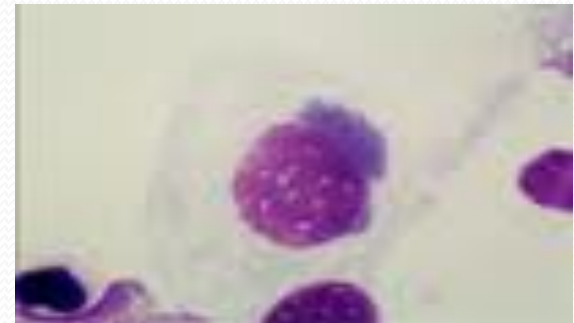
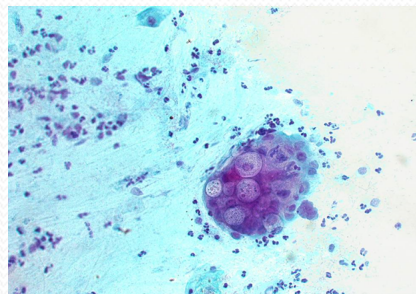
- **Polymerase chain reaction (PCR) :**

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.
- **Azithromycin or 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.

Gonorrhoea: 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.gonorrhoeae*.
- **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.

Conjunctivitis in neonates born to infected mothers

Pelvic Inflammatory Disease (PID)

- PID occurs in 10-20% of cases, include 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 blood stream.
- Clinically : Fever, migratory arthralgia and arthritis. Purulent arthritis involving large joints. Petechial and maculopapular rash.
- Metastatic infections such as Endocarditis , Meningitis & Perihepatitis may develop.

Epidemiology of Gonorrhoea

- 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.

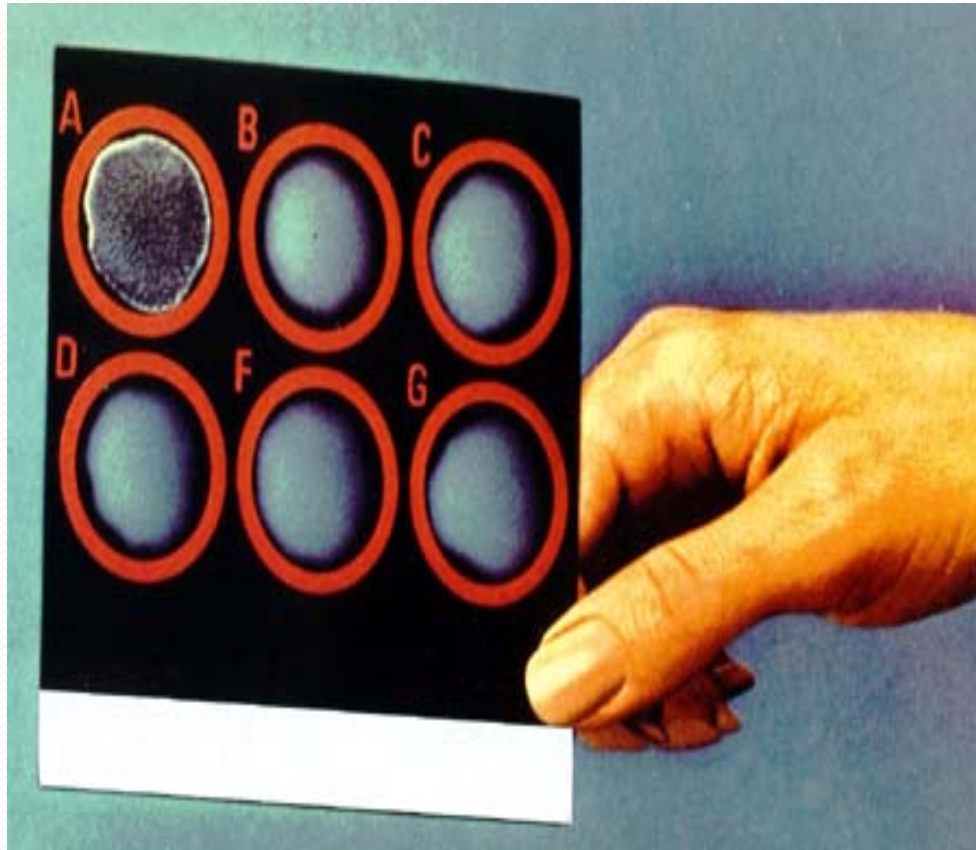
Neisseria gonorrhoeae

- 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.

Diagnosis of Gonorrhoea

- Transport media required unless transfer to the lab. is immediate.
- Direct smear for Gram stain of urethral specimens to see **Gram negative diplococci within a neutrophil (intracellular)** .
- Culture on **Thayer-Martin** or other selective medium.
- Confirmation : fermentation of **glucose** only (*does not ferment maltose or sucrose*) or **Co-agglutination test**.

Nucleic acid amplification tests (e.g **PCR**) is an option for diagnosing genital infections.



Treatment of Gonorrhoea

- Guided by local resistance pattern and susceptibility testing. Partner should be treated as well.
- **Ceftriaxone IM** (or oral **Cefixime**) recommended.
 - Combination with Azithromycin recommended
- **Alternatives:**
 - **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 immunofluorescence (IF), **dark field 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 , **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 is infectious
- 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 lesions resolve after few days to many weeks but disease continues in 1/3 of patients. Disease enters into a latent state.

Lesions are infectious.

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

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

• Tertiary syphilis

Occurs 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.

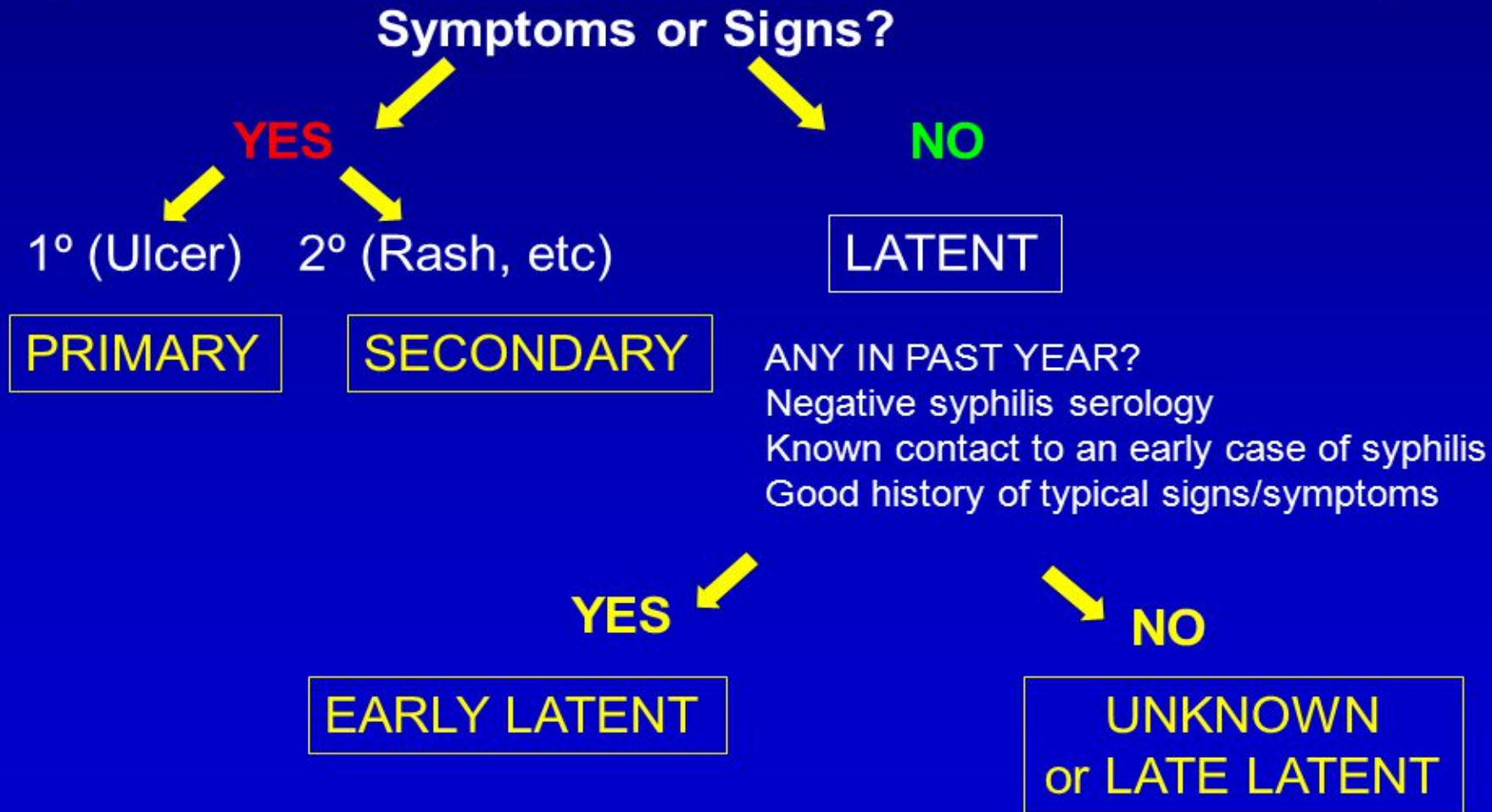
Cardiovascular Syphilis

- Due to **arteritis**, leads to aneurysm of aorta and aortic valve ring.

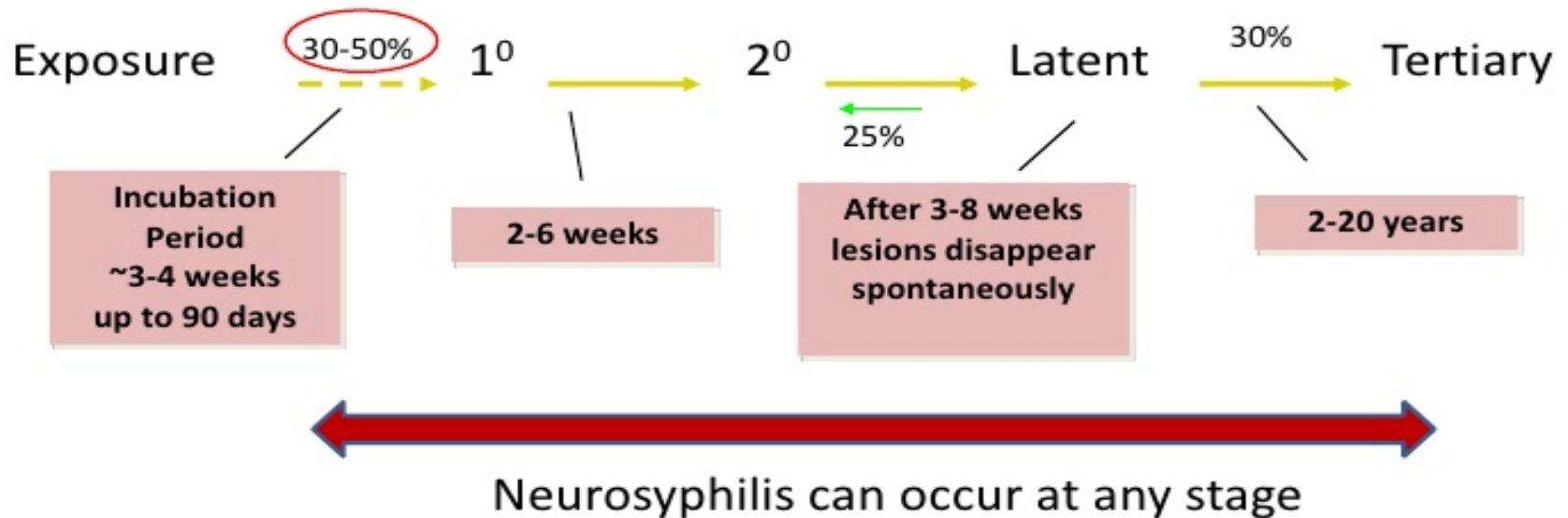
Localized granulomatous reaction called **gumma** on skin, bones, joints or other organs leads to local destruction .

- **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.

Syphilis Staging Flowchart



Syphilis Natural History



Courtesy: Susan Philip, SF DPH & UCSF

Laboratory Diagnosis of Syphilis

- **Direct microscopic examination** of a smear of a smear from primary or secondary lesions using dark field microscopy **rarely used**. Has many limitations. *If positive it confirms the diagnosis.*
- **Serologic tests** commonly used:
 - **Specific treponemal tests**: used initially for diagnosis and for confirmation.
 - **Non specific treponemal tests** : used for screening and follow up of therapy.

Syphilis Serology

Nontreponemal tests: Non specific ,directed against lipoidal antigens released as a consequence of cell damage .becomes positive 6 weeks after infection:

❖ Rapid Plasma Reagin (**RPR**)

❖ Venereal Disease Research Laboratory (**VDRL**).

Become positive during the primary stage (*possible exception HIV*) ,antibody peak in secondary syphilis. Negative following effective therapy .

Used for screening and staging the disease & follow up therapy.

Syphilis Serology

- **Treponemal tests :**

Specific to treponemal antigens . Detect IgG and IgM directed against treponema membrane lipoproteins.

Becomes positive after 3 weeks after infection. **Used for confirmation of RPR & VDRL.** Remain positive even after effective therapy .Commonly used tests are:

- ❖ **FTA-ABS** (Fluorescent treponemal antibody-absorption)
- ❖ **TP -PA**(T. palladium particle agglutination)
- ❖ **EIA** (Enzyme Immunoassay)

SYPHILIS SEROLOGY & IF

Reactive



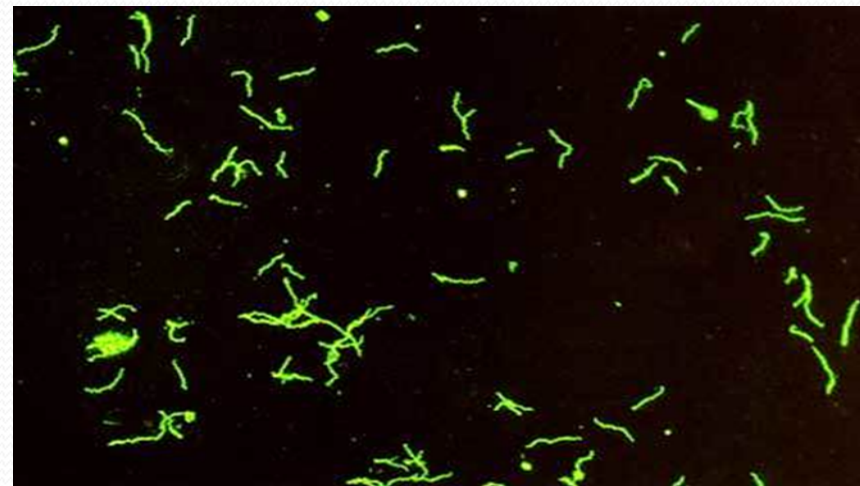
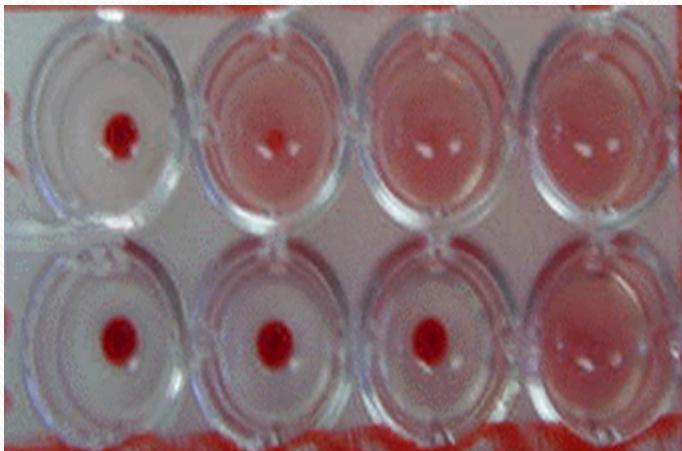
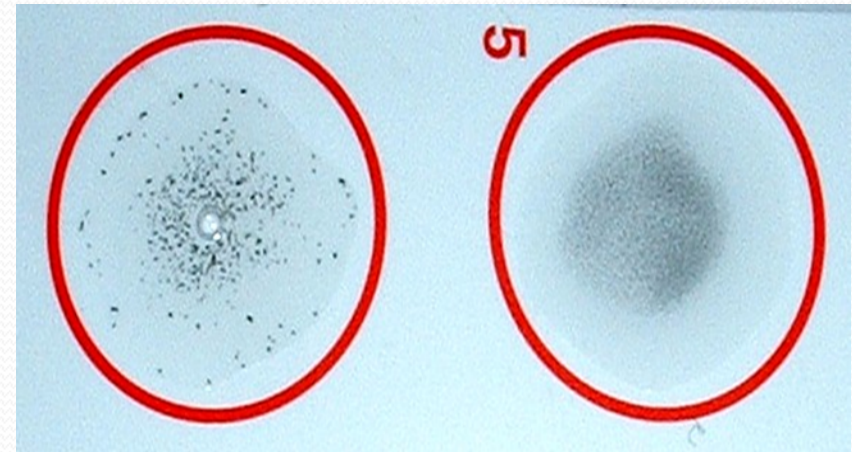
Weak Reactive



**Weak Reactive
(Minimally)**



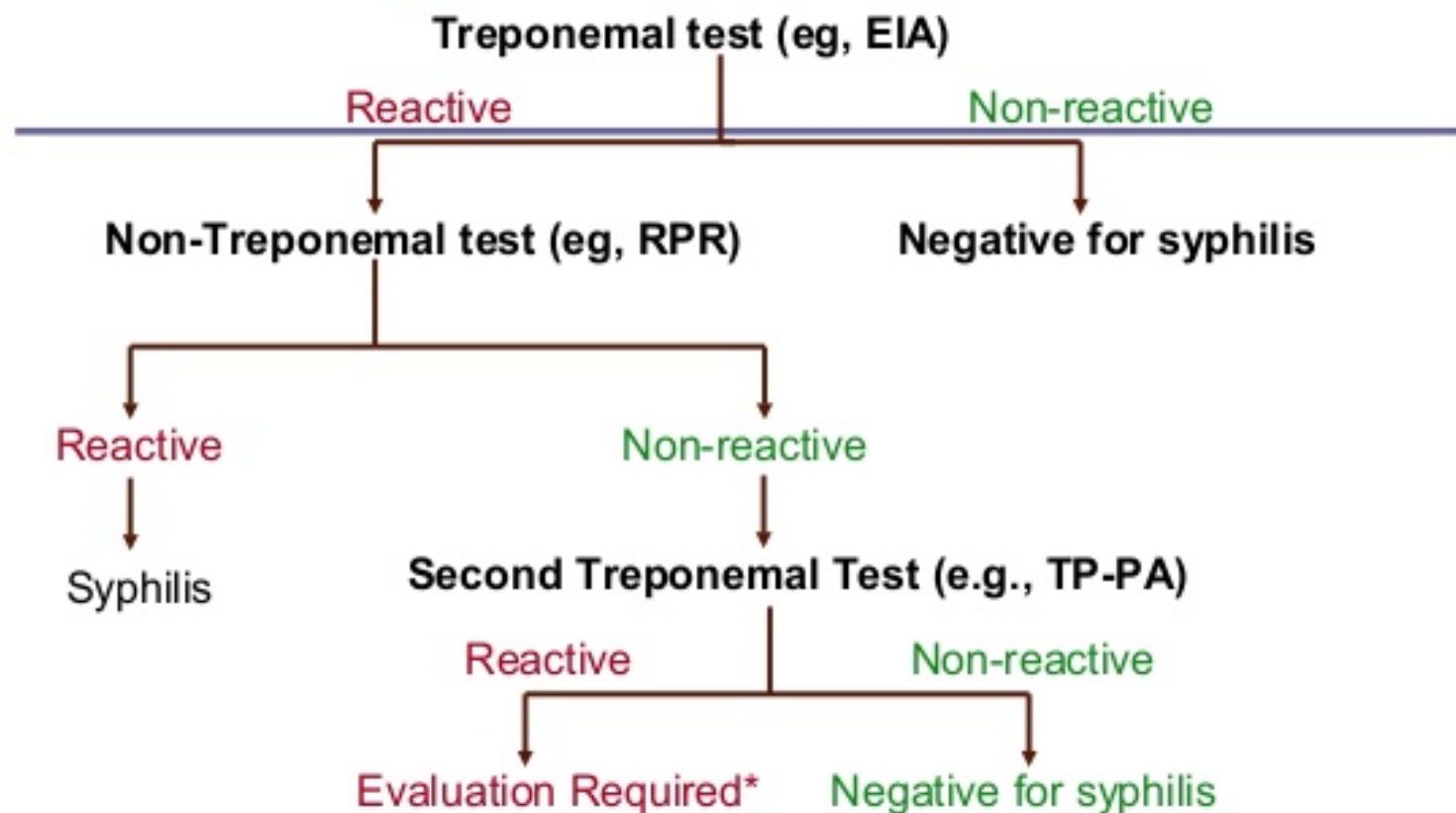
Nonreactive

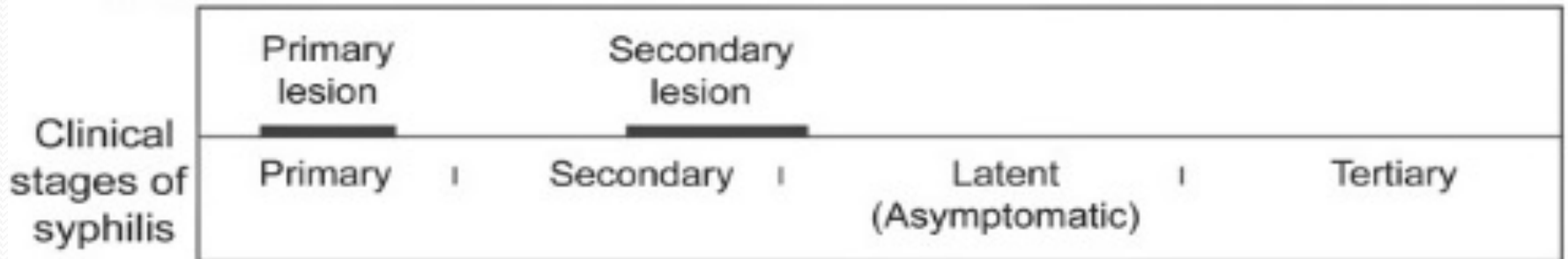
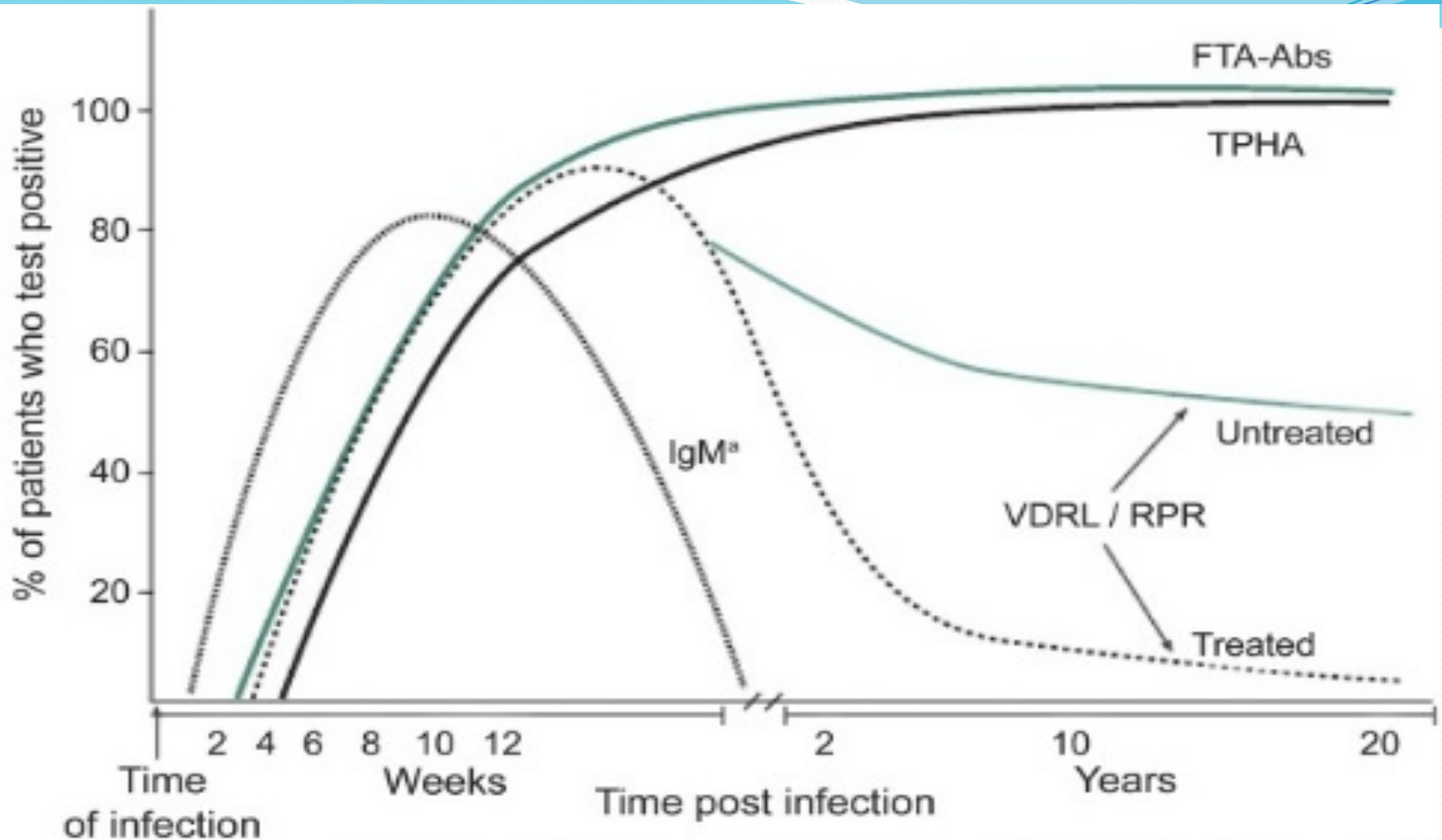


INTERPRETATION OF SEROLOGICAL TESTS FOR SYPHILIS

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

Reverse Algorithm





Summary of Syphilis Serology

Reverse Sequence Syphilis Serology

Test

- Treponemal tests
FTA-ABS , TP PA , EIA
- Non-treponemal tests (RPR
or VDRL)
- IgM antibody

Stage

- **Positive** at all stages , confirm
RPR & VDRL
- **Positive** during primary &
secondary stages .Used for
screening ,staging and follow
up effective therapy.
- Congenital syphilis

Treatment and Prevention

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

Syphilis Bacteria



Syphilis



Take Home Message

- Syphilis, Chlamydia and Gonorrhoea 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 .



Reference book

Ryan, Kenneth J. Sherris Medical Microbiology.
Latest edition.

Mc Graw –Hill education