# Chlamydia, Gonorrhea & Syphilis

*Prof. Hanan Habib & Dr.Khalifa Binkhamis*

**Department of Pathology**

**College of Medicine**

# Objectives

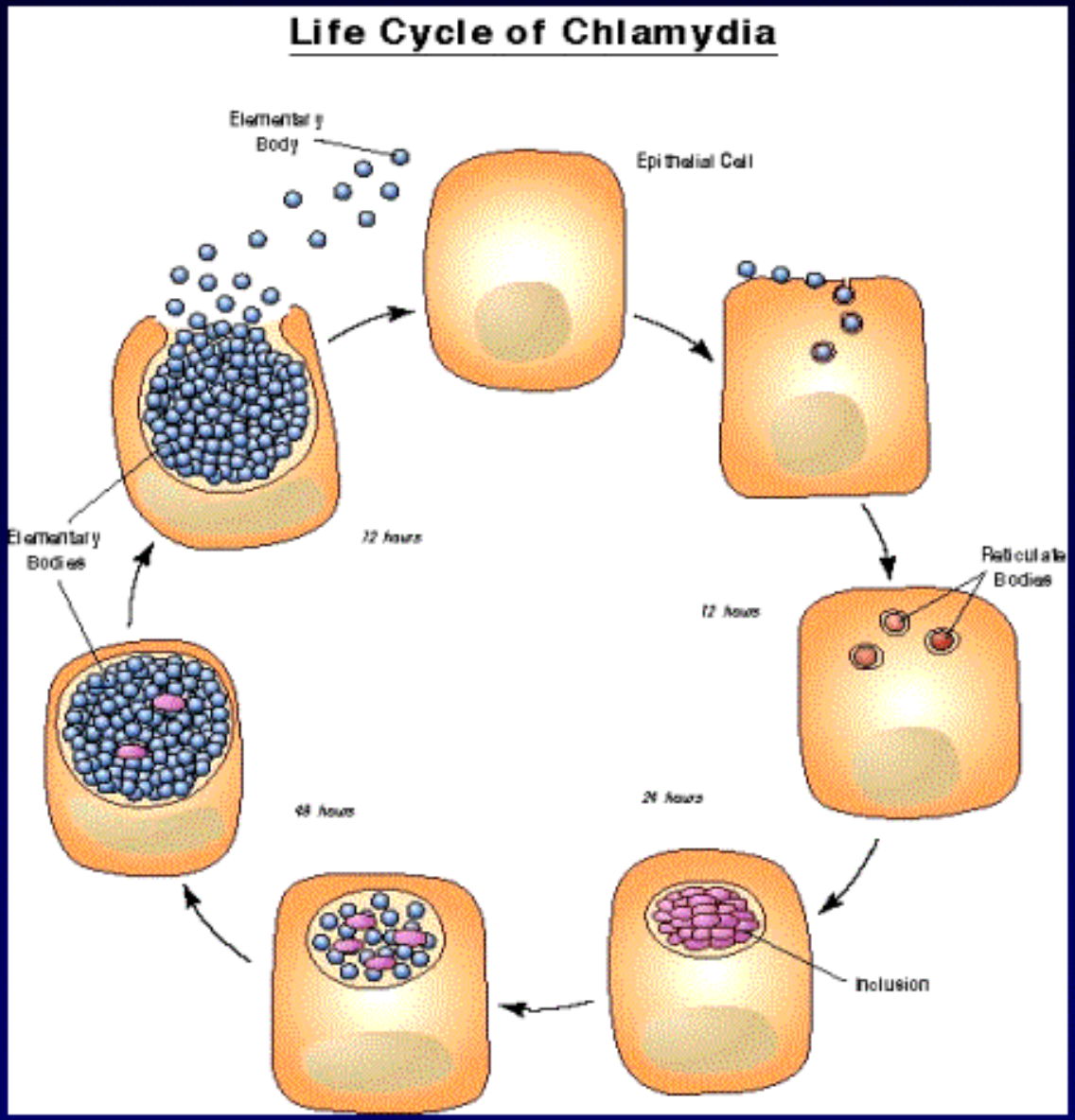
- Recall the causative agents of syphilis, gonorrhea and Chlamydia infections.
- Describe the pathogenesis of syphilis, gonorrhea and Chlamydia infection.
- Describe the clinical features of Chlamydial infections
- Recall the different genera, species and serotypes of the family *Chlamydophila*.
- Describe the laboratory diagnosis of Chlamydia
- 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 clinical feature of the primary, secondary tertiary syphilis and complications.
- Recall the different diagnostic methods for the different stages of syphilis.
- Recall the treatment regimens of syphilis, gonorrhea 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

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 pro-inflammatory cytokines, lead 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.

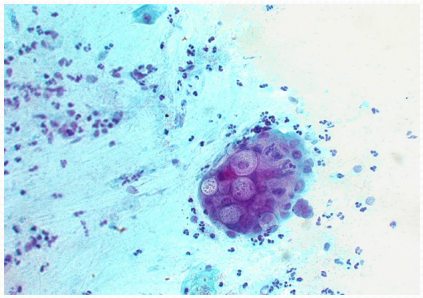
# Diagnosis of *Chlamydia* genital infections

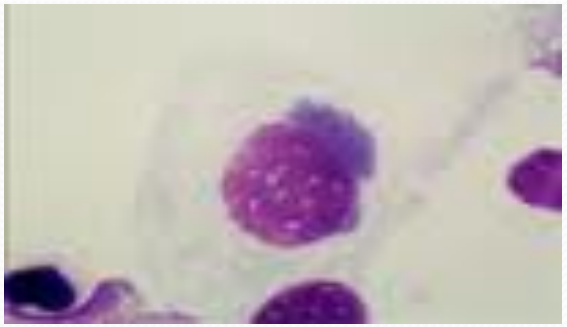
- **Polymerase chain reaction (PCR) :**

**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.
- 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.

# 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.

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 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 and 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.

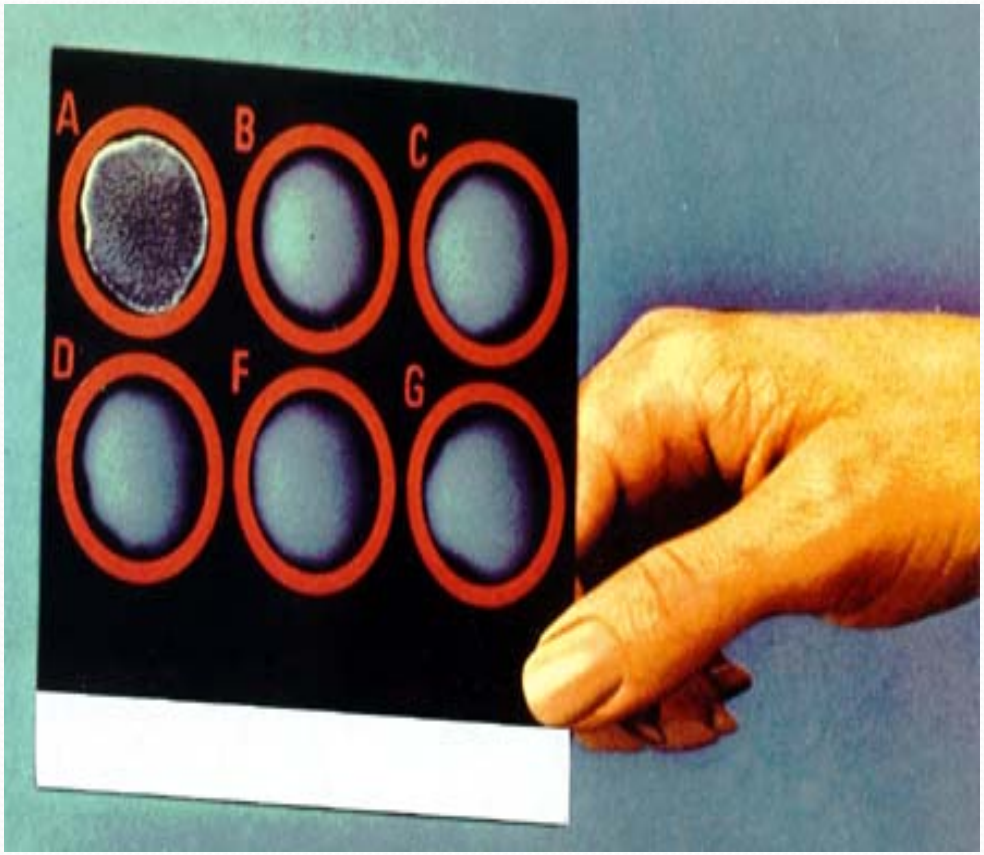
# *Neisseria gonorrheae*

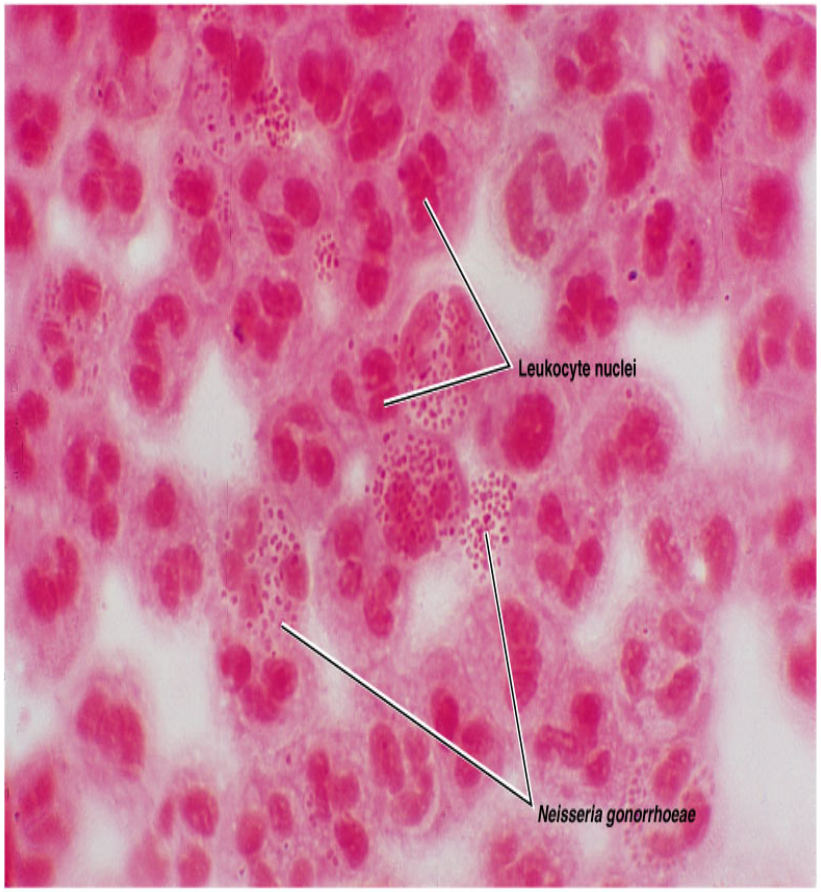
- A Gram negative diplococci grows on chocolate agar and on selective enriched media and $CO_2$ required. Not a normal flora.
- **Pathogenesis**: mainly a localized infection of epithelium ,leads to intense inflammation.
- Posses pili and outer membrane proteins that mediate attachment to non-ciliated epithelium.

# Diagnosis of Gonorrhea

- Transport media required unless transfer to the lab. is immediate.
- Direct smear for Gram stain of 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 Gonorrhea

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

Lesions are infectious.

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

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

# • 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. 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.

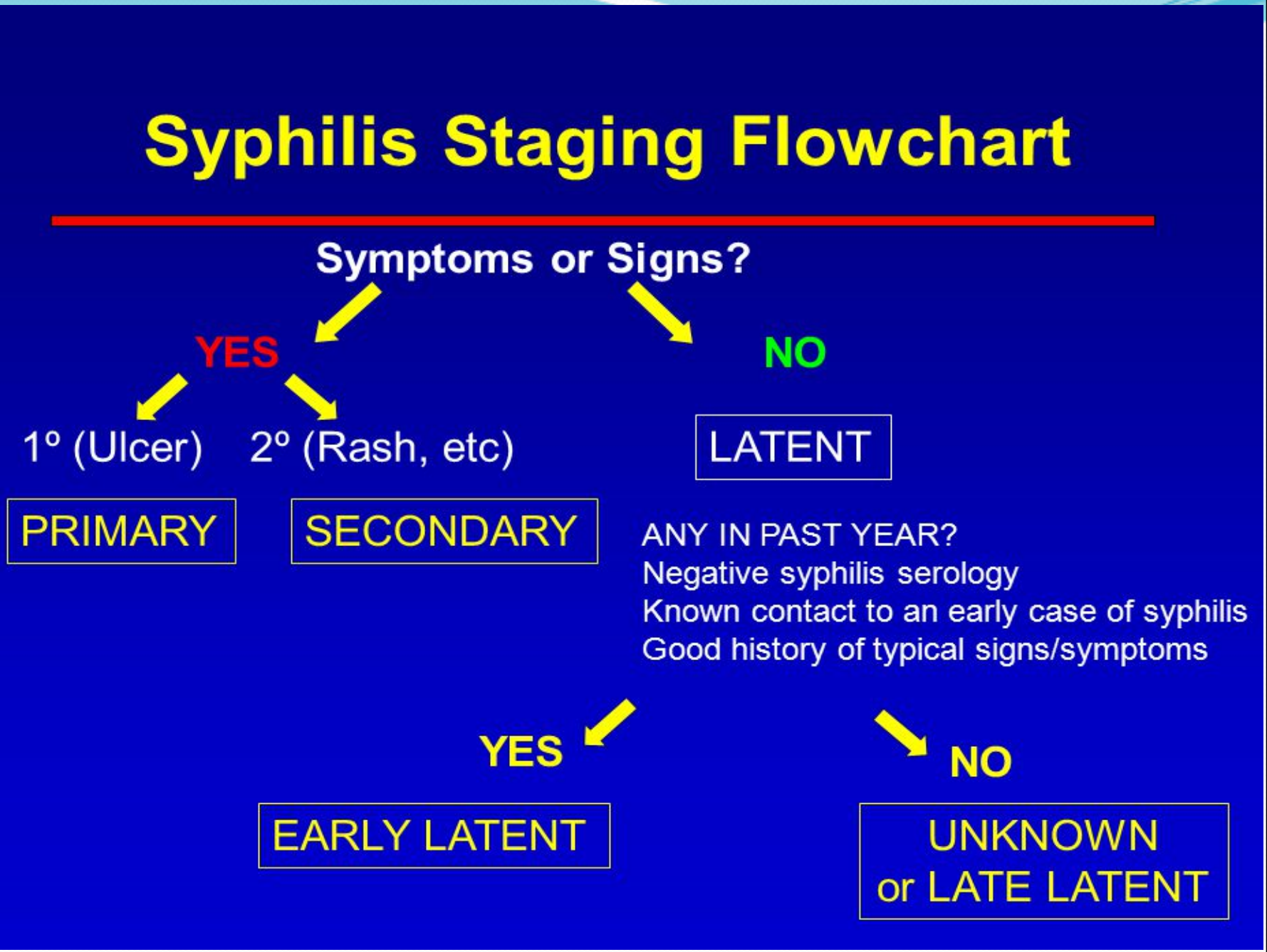
# Cardiovascular Syphilis

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

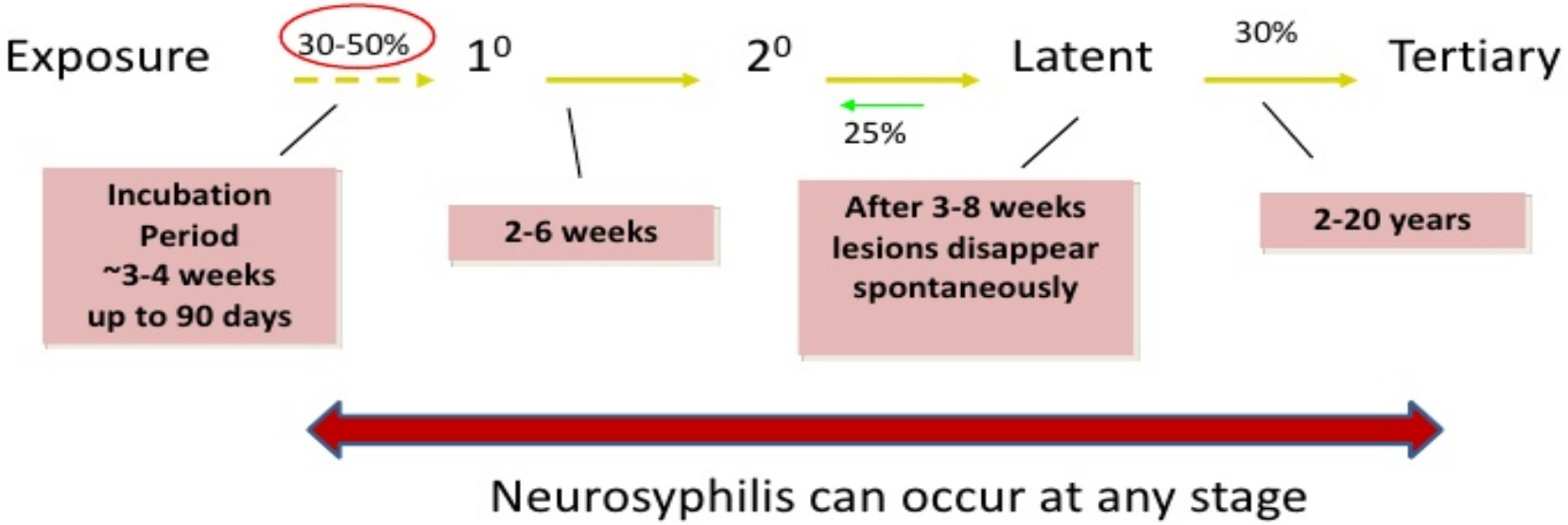
Localized granulomatous reaction called **gumma** on skin, bones, joints or other organs leads to local destruction .

- **Congenital syphilis :**develop if the mother not treated ,fetus susceptible **after 4$^{th}$ 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




CALIFORNIA STD/HIV PREVENTION TRAINING CENTER

*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

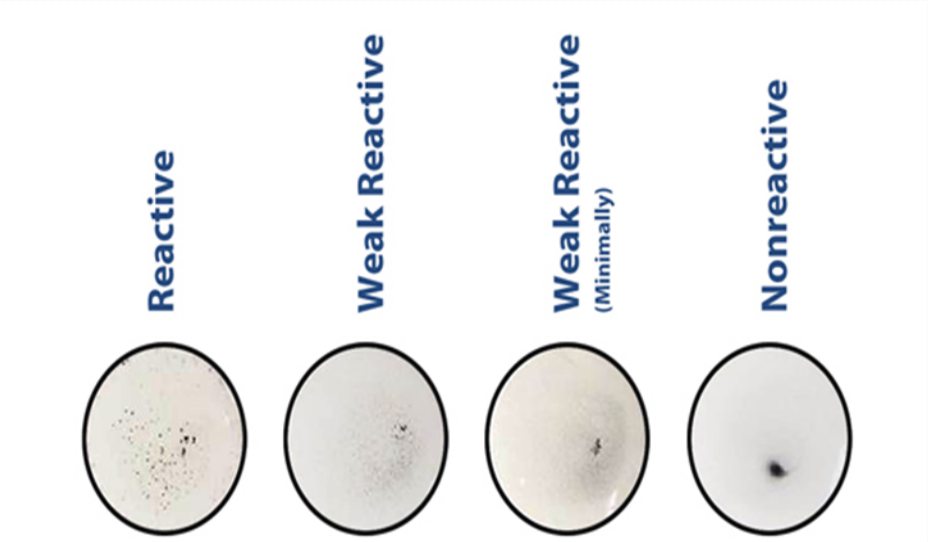
- **Treponemal tests :**

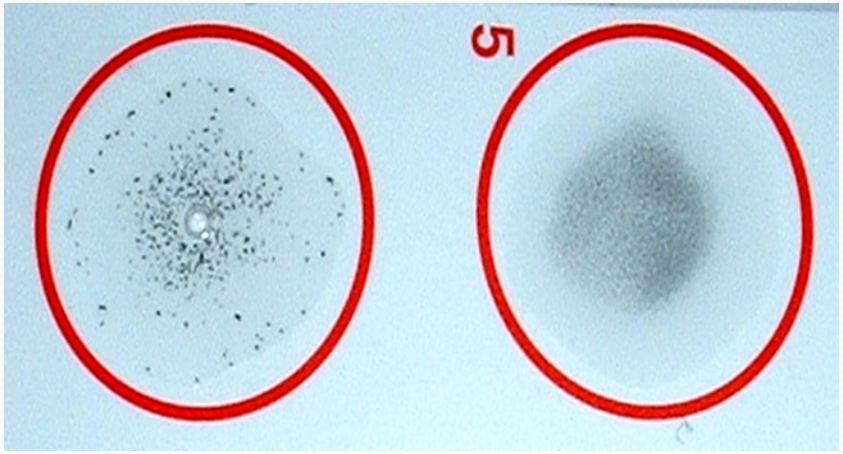
Specific to treponemal antigens . Detect IgG and IgM directed against *Treponema* membrane lipoproteins.

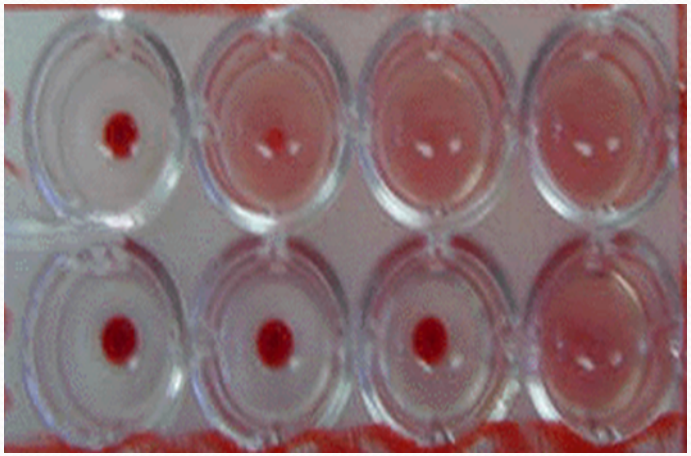
Becomes positive after 3 weeks after infection. **Used for confirmation of RPR & VDRL**. Remain positive even after effective therapy .Commonly used tests are:

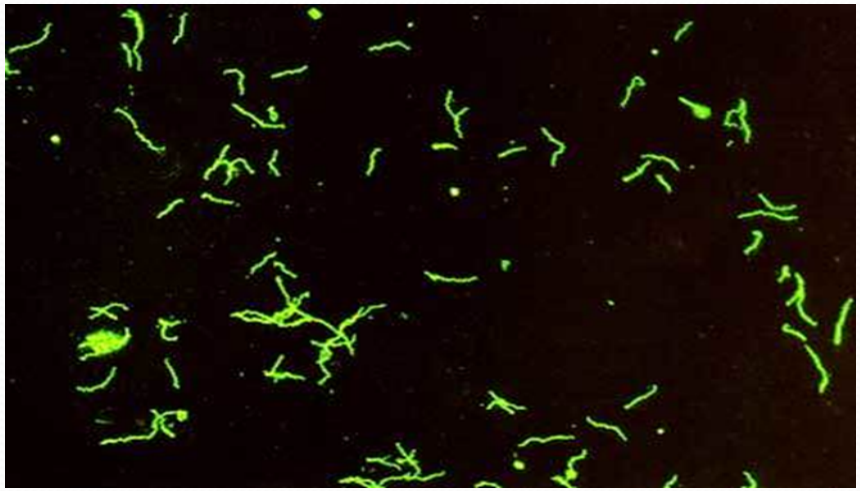
- **FTA-ABS** ( Fluorescent treponemal antibody-absorption)
- **TP -PA**( T. palladium particle agglutination)
- **EIA** ( Enzyme Immuonoassay)

# SYPHILIS SEROLOGY& IF



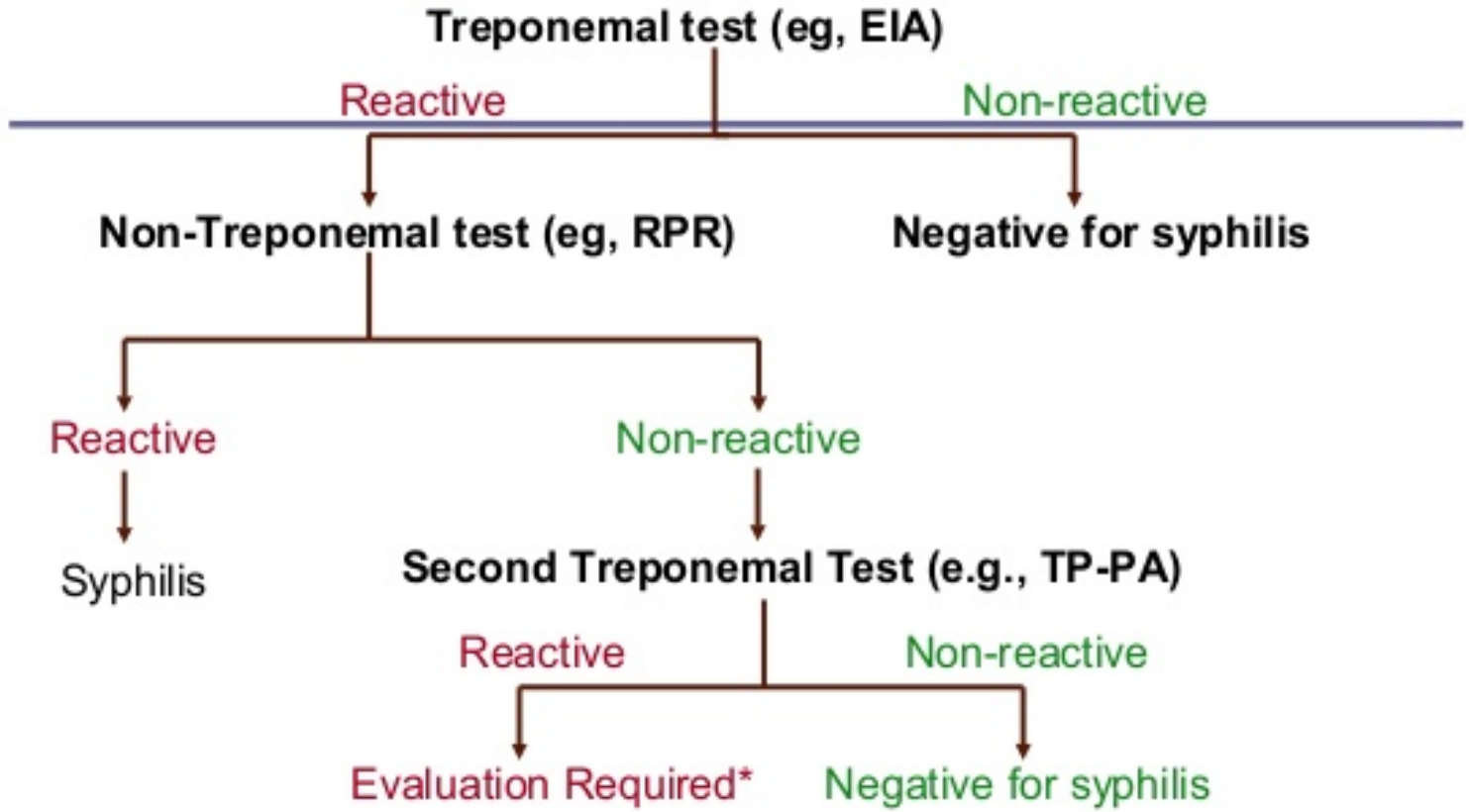



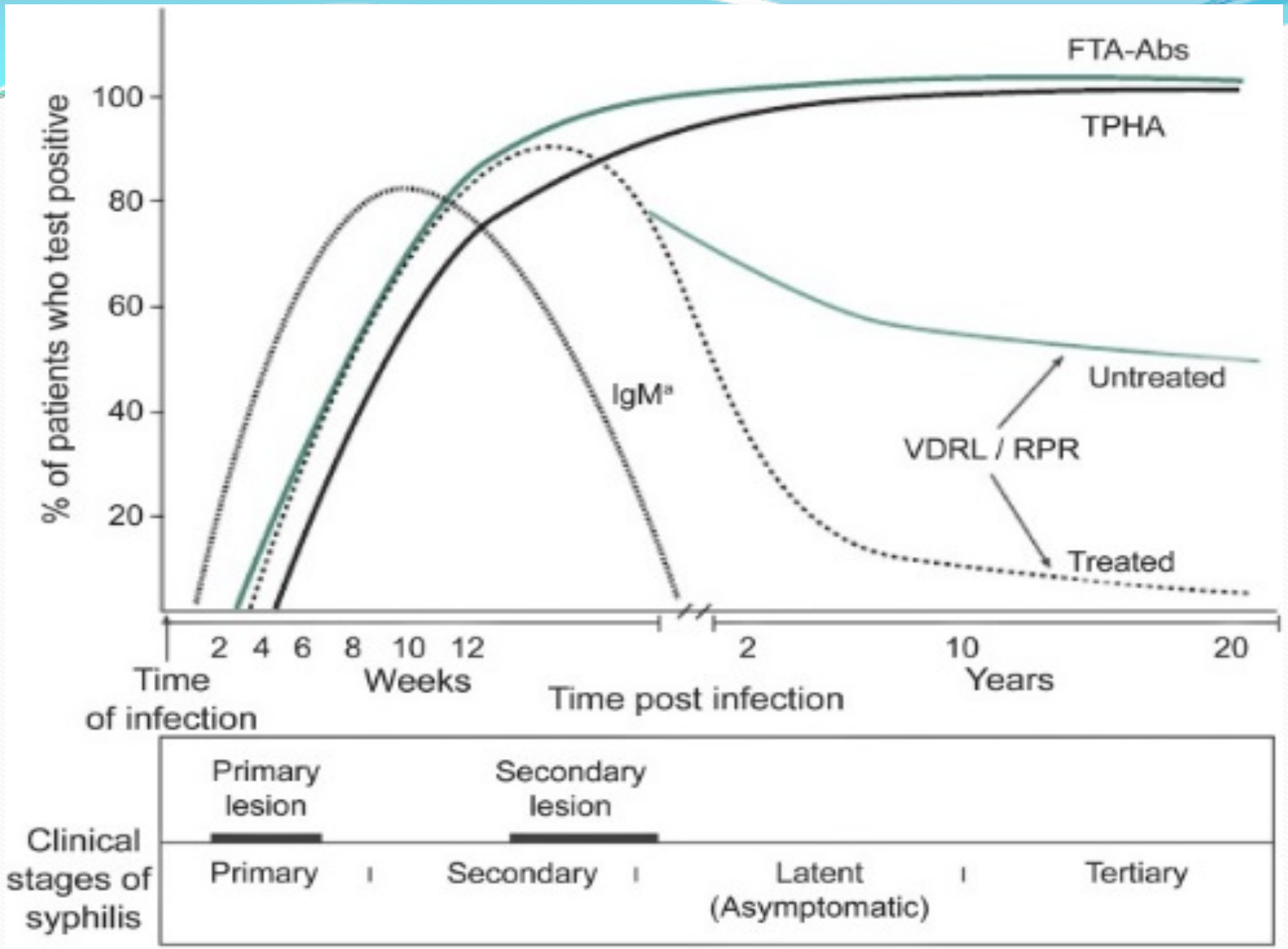


# INTERPRETATION OF SEROLOGICAL TESTS FOR SYPHILIS

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

# Reverse Algorithm




FTA-Abs
TPHA
% of patients who test positive
100
80
60
40
20
IgM*
Untreated
VDRL / RPR
Treated
2 4 6 8 10 12
2
10
20
Time of infection
Weeks
Time post infection
Years
Primary lesion
Secondary lesion
Clinical stages of syphilis
Primary
Secondary
Latent (Asymptomatic)
Tertiary

# Summary of Syphilis Serology

## Reverse Sequence Syphilis Serology

| Test | Stage |
| --- | --- |
| • Treponemal tests<br>FTA-ABS , MP PA , EIA | • Positive at all stages , confirm RPR & VDRL |
| • Non-treponemal tests ( RPR or VDRL) | • Positive during primary & secondary stages .Used for screening ,staging and follow up effective therapy. |
| • IgM antibody | • Congenital syphilis |

# 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 .

# Reference book

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

Mc Graw –Hill education