Bacterial diseases:
Syphilis

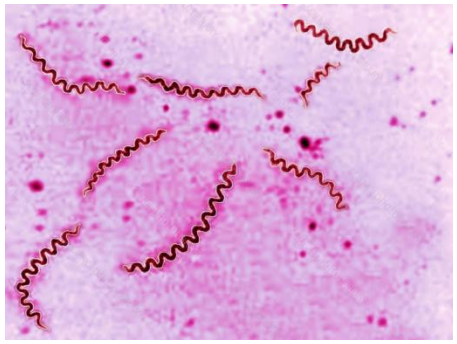
Microbiology III

HISTORY

- The exact origin of syphilis is disputed, one of the two primary hypothesis proposes that syphilis was carried from the American's to Europe by the returning crewmen from Christoper Columbus voyage to America.
- The causative organism , ***Treponema pallidum*** was first identified by Fritz schaudinn and Erich Hoffmann in 1905.
- The first effective treatment was developed in 1910 by Paul enrich, which was followed by trials of penicillin and confirmation of its effectiveness in 1943.

Morphology of *Treponema pallidum*

- It is a thin, corkscrew-shaped, microaerophilic bacterium, with tappering ends & **cannot be cultured** in vitro.
- Its body is about 10 µ long and 0.1 to 0.2 µ wide, made up of 10 sharp, rigid, regular spirals.
- It is motile and exhibits all three types of locomotion.
- The organism appears rosy red when stained with giemsa stain.
- Under a light microscope it can be seen by negative staining with Indian ink.



CULTURE

- *Treponema pallidum* has not been cultured on artificial media or in tissue culture.
- A pathogenic strain of *Treponema pallidum* known as **Nichol's strain** has been maintained in the **rabbit testis** for a very long time and is used as a control in many **diagnostic** and research experiments.
- A saprophytic strain of *Treponema* known as " **Reiter strain**" grows well in **thioglycollate medium** containing serum.

Resistance:

- Inactivated by drying or by heating at 41-42˚c for 1 hr
- It is killed in 1-3 days at refrigerator temperature.
- It can be stored for a long time at -70˚c in 10% glycerol or in liquid nitrogen.
- **Antigen structure:**
- Three types of antigens are seen in Treponema
- A lipid hapten known as **Cardiolipin** present on *T. pallidum.*

EPIDEMIOLOGY:

- It affects between 700,000 - 1.6 million pregnancies a year
- Resulting in spontaneous abortions, stillbirths & congenital syphilis.
- During 2010 it caused about 113,000 deaths down from 202,000 in 1990.
- Rates are proportionally higher among i.v drug users, those who are infected with HIV, and men who have sex with other men.

CLASSIFICATION

Syphilis is majorly classified in to two types namely:

- Veneral syphilis.
- Non-veneral syphilis.

VENERAL SYPHILIS:

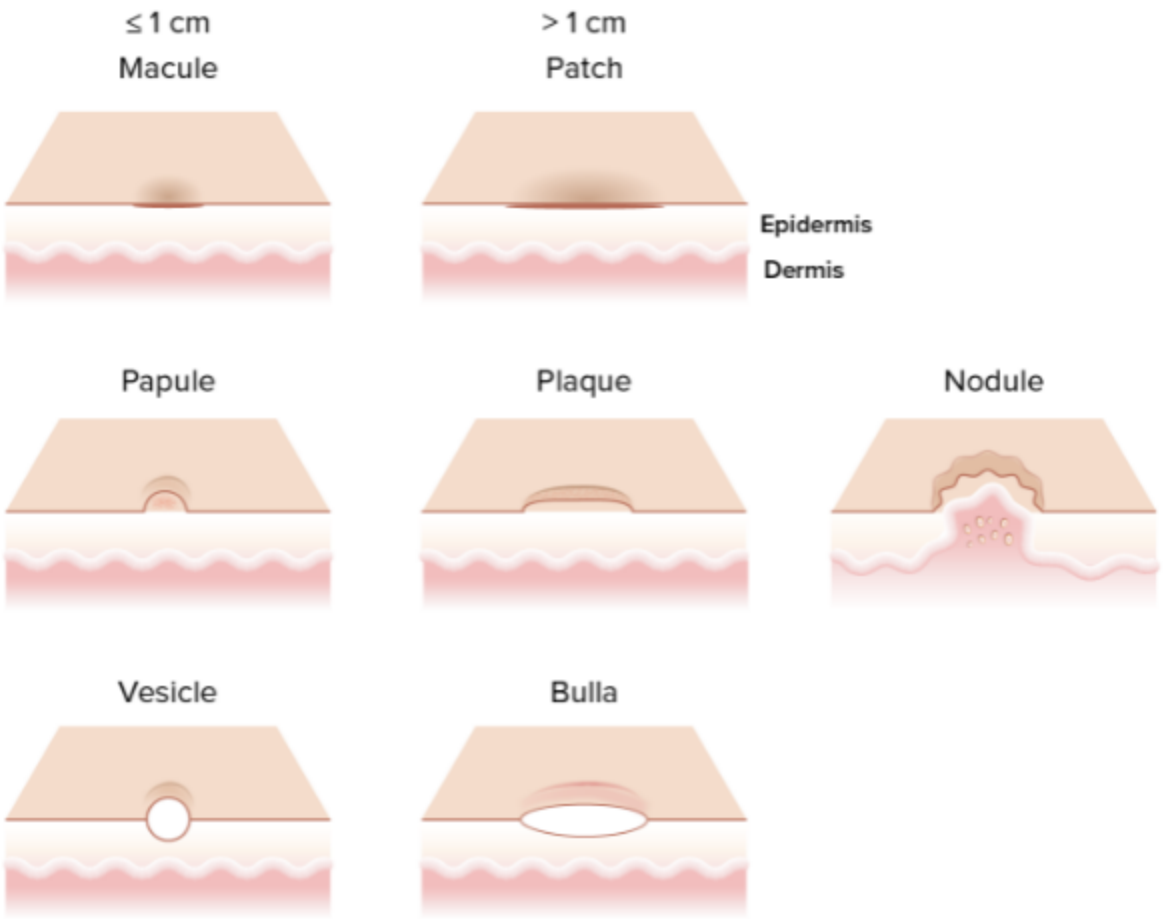
The disease falls in to 3 stages namely:

- Primary stage.
- Secondary stage.
- Tertiary stage.

PRIMARY SYPHILIS:

- Primary lesion or "chancre" develops at the site of inoculation (genital areas).
- **Chancre:**
  - Progresses from macule to papule & then to ulcer.
  - **[Macule** is a flat, distinct, discolored area of skin <1 cm. It doesn't involve any change in the thickness or texture of the skin.
  - **Papule** is a solid or cystic raised spot on the skin that is less than 1 cm. It is a type of skin lesion].
  - Typically painless, indurated, and has a clean base.
  - Highly infectious.
  - Heals spontaneously within 1 to 6 weeks.
- Regional lymphadenopathy: classically rubbery, painless, bilateral.
- Serologic tests may not be positive during early primary syphilis

Macule and Papule



SECONDARY SYPHILIS:

- Secondary lesions occur 3 to 6 weeks after the primary chancre appears; may persist for weeks to months
- Mucocutaneous lesions are most common
- Clinical Symptoms:
  - Rash (75%-100%)
  - Lymphadenopathy (50%-86%) – abnormal lymph size
  - Mucous patches (6%-30%)
  - Alopecia (5%) - hair loss
- Serologic tests are usually highest in titer during this stage

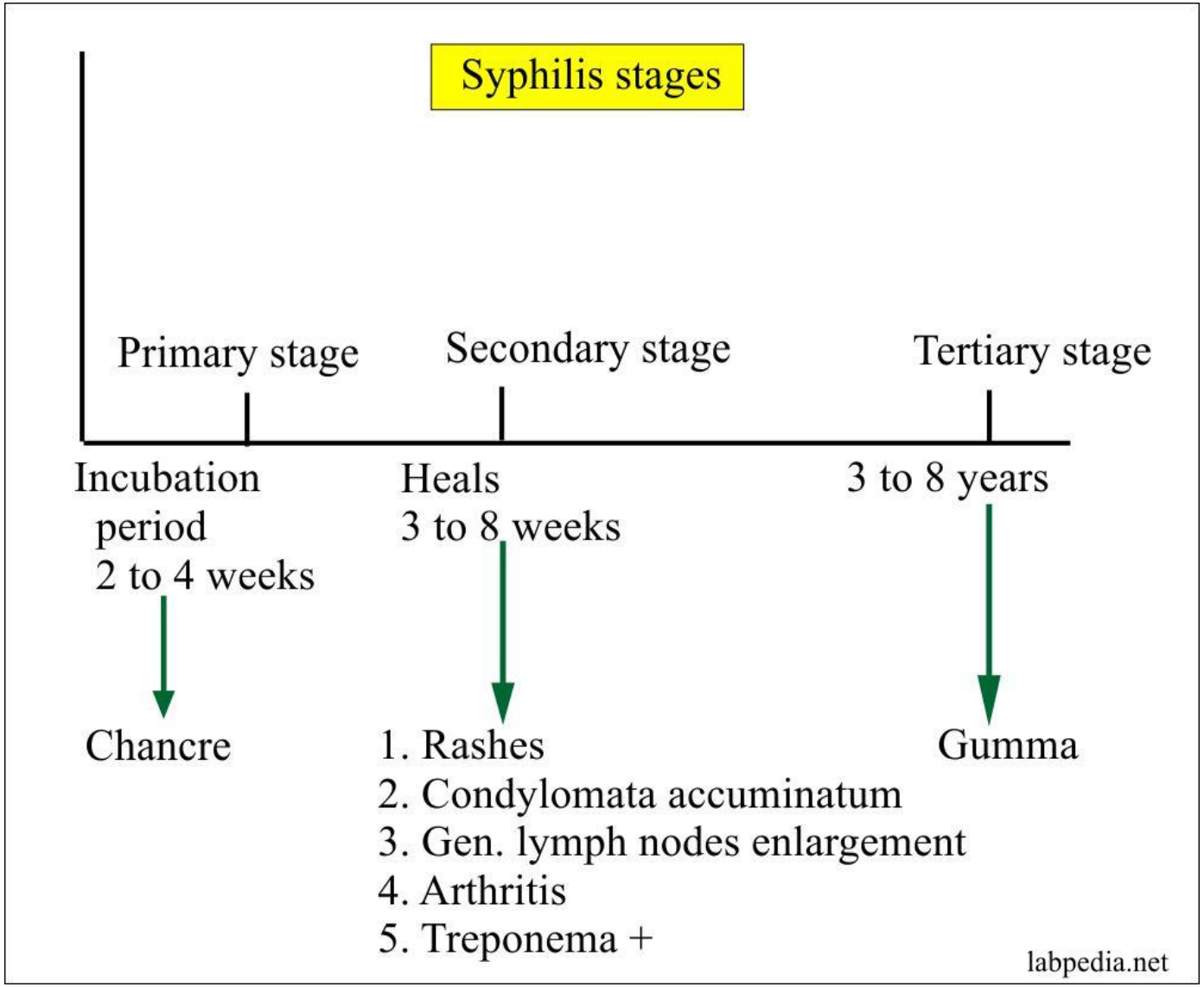
Latent Syphilis

- Host suppresses the infection enough so that no lesions are clinically apparent
- Only evidence is positive serologic test for syphilis
- May occur between primary and secondary stages, between secondary relapses, and after secondary stage
- Categories:
  - Early latent: <1 year duration
  - Late latent: ≥1 year duration

Tertiary (Late) Syphilis

- Approximately 30% of untreated patients progress to the tertiary stage within 1 to 20 years
- Rare because of the widespread and use of antibiotics

- Clinical symptoms:
  - Gummatous syphilis (15%) [**Gumma** is a mass of dead and swollen fiber-like tissue.]
  - Cardiovascular syphilis (10%)
  - Late neurosyphilis (6.5%)


Syphilis stages
Primary stage
Secondary stage
Tertiary stage
Incubation period 2 to 4 weeks
Heals 3 to 8 weeks
3 to 8 years
Chancre
1. Rashes
2. Condylomata accuminatum
3. Gen. lymph nodes enlargement
4. Arthritis
5. Treponema +
Gumma
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Congenital Syphilis

- Occurs when *T. pallidum* is transmitted from a pregnant woman with syphilis to her foetus.
- May lead to stillbirth, neonatal death, and infant disorders such as deafness, neurologic impairment, and bone deformities.
- The risk is much higher during primary and secondary syphilis.
- Early lesions (most common): Infants <2 years old; usually inflammatory.
- Late lesions: Children >2 years old; tend to be immunologic & destructive
- Congenital Syphilis - Hutchinson's Teeth , perforation of Palate

Signs & Symptoms

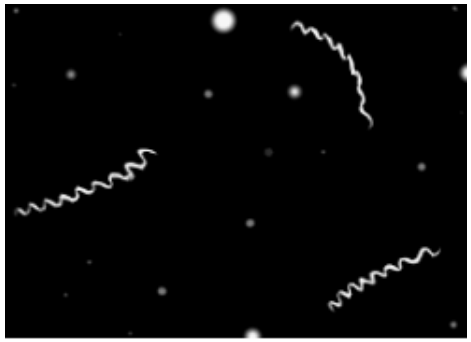
- Signs & symptoms of syphilis vary depending in which of the four stages (primary, secondary, tertiary, latent) it is present:

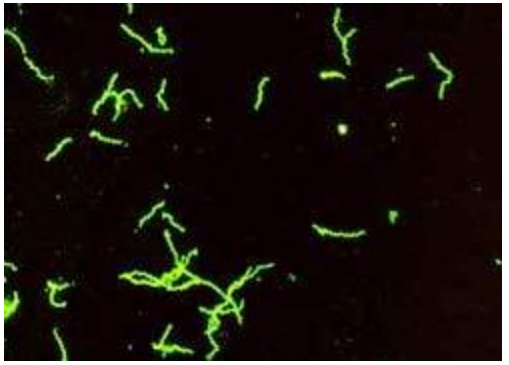
Common symptoms are:

- Fever, Malaise, Sore throat, Rashes, Headache
- Lymphadenopathy
- Mucous patches, Perforation of palate.
- Alopecia, Weight loss
- In severe conditions it causes mental retardation, shuffle walk e.t.c.

Laboratory Diagnosis

- Identification of *Treponema pallidum* in lesions
  - Darkfield microscopy
  - Direct fluorescent antibody - *T. pallidum* (DFA-TP)
- Serologic tests
  - Nontreponemal tests (qualitative and quantitative)
  - Treponemal tests (qualitative)





Darkfield Microscopy

Identification:

- *T. pallidum* morphology and motility

Advantage:

- Definitive immediate diagnosis

Disadvantages:

- Requires specialized equipment and an experienced microscopist.
- Possible confusion with other pathogenic and nonpathogenic spirochetes.
- Must be performed immediately.
- Generally not recommended on oral lesions

Syphilis Serology

Non-treponemal tests

- VDRL (Venereal Disease Research Laboratory)
- RPR (Rapid Plasma Reagin)
- TRUST (Toluidine Red Unheated Serum Test)
- USR (Unheated Serum Reagin)

Treponemal tests

- TP-PA (Treponema Pallidum Particle Agglutination)
- FTA-abs (Fluorescent Treponemal Antibody -Absorbed)
- EIA (Enzyme Immunoassay)

Non-treponemal Serologic Tests

Principle:

- Measure antibody directed against a cardiolipin - lecithin - cholesterol antigen
- Not specific for *T. pallidum*
- Titers usually correlate with disease activity and results are reported quantitatively, may be reactive in life

Treponemal Serologic Tests

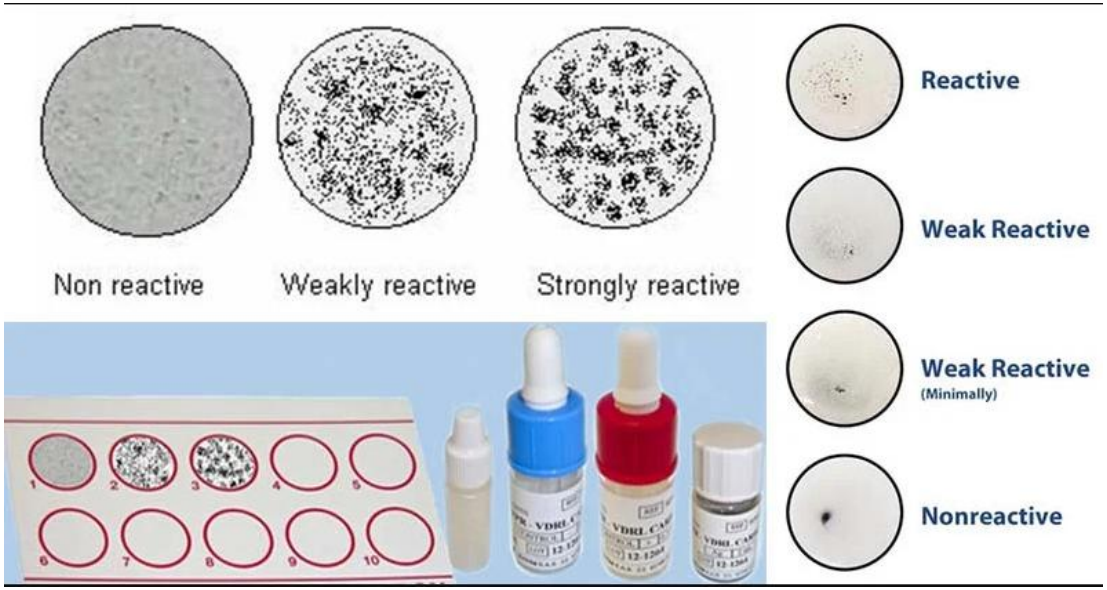
Principle:

- Measure antibody directed against *T. pallidum* antigens
- Qualitative, usually reactive in life

VDRL test: (Veneral Disease Research Laboratory)

- 0.5ml of the patient's inactivated serum is placed on a special slide with ring.
- 1 drop of **cardiolipin** antigen is added & the slide rotated for about 4 minutes.
- The reaction is observed under a low power microscope.
- Cardiolipin will form **clumps** with the **regain** antibody, if present , presence of clumps indicates a **positive** reaction.
- **Serial dilutions** of the positive serum are tested to determine the **antibody titre**.

VDRL TEST



VDRL

Cardiolipin + Serum of patient heated → (Ag+Ab) reaction

Non-trep Antigen — Antibody — Slide test

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TREPONEMA PALLIDUM AGGLUTINATINATION (TPA) TEST:

- In this test, formalin killed *T.pallidum* is used as an antigen.
- It is mixed with patients serum & incubated.
- After incubation it is examined under dark background microscope.
- **Agglutination** indicates positive test.

TREPONEMA PALLIDUM IMMOBILISATION (TPI) TEST:

- Patients serum is incubated **anaerobically** with treponemal suspension.
- Examined under dark background microscope.
- If **antibodies** are present ,treponemes are **immobilised** ,that is, they loose their motility this indicates **positive test**.
- TPI is a **highly specific test** for the diagnosis of syphilis.
- Because of its **technical complexity** it is not used as a routine diagnostic test.

Treatment for Syphilis

- Benzathine penicillin G 2.4 million units IM in a single dose

If penicillin allergic:

- Doxycycline 100 mg orally twice daily for 14 days
- Tetracycline 500 mg orally 4 times daily for 14 days.

Therapy for Tertiary Syphilis without Neurologic Involvement:

- Benzathine penicillin G 7.2 million units total
- Administered as 3 doses of 2.4 million units IM each at 1-week intervals
- **Penicillin allergic:**
  - Doxycycline 100 mg orally twice daily for 28 days
  - Tetracycline 500 mg orally 4 times daily for 28 days

Therapy for Syphilis in Pregnancy

- Treat with penicillin according to stage of infection.
- Erythromycin is no longer an acceptable alternative drug in penicillin-allergic patients.

Jarisch-Herxheimer Reaction

In some cases penicillin treatment induces ‘Jarich-Herxheimer’ reaction. This is characterised by:

- Fever, malaise, nausea/vomiting; may be associated with chills and exacerbation of secondary rash
- Occurs within 24 hours after therapy
- It is frequent but harmless in early syphilis but rare & dangerous in gummatous, cardiovascular or neurosyphilis
- This reaction is believed to be due to the liberation of toxic products from the destruction of treponemas or due to hypersensitivity.

NON-VENERAL SYPHILIS

- Causative organism *is T.endemicum.*
- The disease is called by different names in different parts of the world & is more common in children of poor hygiene.
- Clinical manifestations include **mucous patches** in the mouth & skin eruptions, may progress to **gummatous lesions** on skin, bone & nasopharynx.
- Congenital syphilis are not common.
- Laboratory diagnosis & treatment of endemic syphilis are similar to those of veneral syphilis.