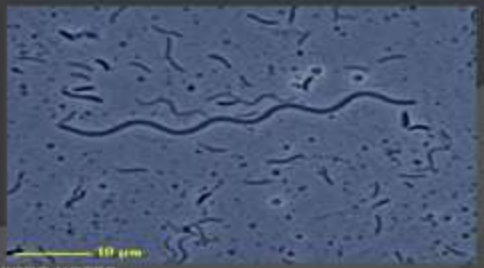
SPIROCHAETES:TREPONEMA

SPIROCHAETES

- Spirochaetes are gram negative bacteria.
- Spirochetes - are elongated motile, flexible bacteria twisted spirally along the long axis are termed spirochetes.
- Characteristically, there are varying number of fine fibrils between cell wall and cyto-plasmic membrane of bacterial cell.
- The spiral shape and serpentine motility of cell depends on integrity of these filament.



- Spirocheates do not posses flagella but are motile.
- There are three types of motility :

a) Flexion and extension

b) Corkscew like rotatory movement

c) Translatory

- Spirochetes contain – endoflegalla which are polar flagella wound along the helical protoplasmic cylinder and situated between the outer membrane and cell wall
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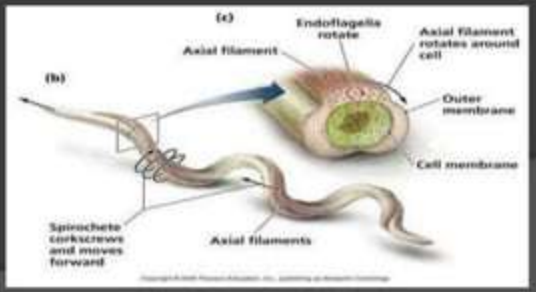


TAXONOMY

- The order spirochaetales has two families
- The family **Spirochaetaceae** -which consist of free living large spiral organisms
- The family **Treponemataceae** has three main genera: causing disease in man namely

i. Treponema
ii. Leptospira and
iii. Borrelia

TRPONEMA

- Triponema are very fine, spiral, splender with pointed or rounded ends .

Domain	Bacteria
Phylum	Spirochaetes
Order	Spirochaetales
Family	Spirochaetaceae
Genus	***Treponema***

- The genus Treponema has two spp that cause human disease
  - Treponema pallidum with 3 subspp
  a) Treponema Pallidum cause Syphilis
  b) Treponema endemicum cause Endemic syphilis (Bejel)
  c) Treponema pertenue cause Yaws
  - Treponema carateum cause Pinta

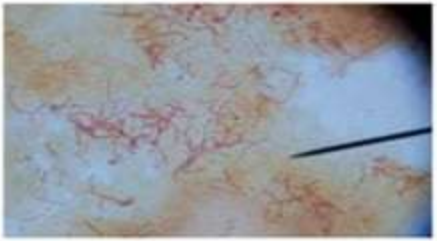
treponema

Morphology

- Slender spirals measuring 0.2 μm in width and 5-15 μm in length
- They have tight spirals i.e are regularly spaced at a distance of 1 μm
- Have pointed and tapering ends,
- Three to four endoflagella, actively motile, show rotatory corkscrew like movement
- The spiral are thin require immunofluoresence or dark field illumination, Stained by silver impregnation
- Microaerophilic surviving at 1-4% Oxygen
- In proper suspending fluid and presence of reducing agents survive for 3-6 days at 25 o C or in blood at 4 o C for 24 hrs
- They stain with difficulty except with Giemsa's stain or silver impregnation.

Dark field microscope

TREPONEMA PALLIDUM: MORPHOLOGY



epidemology

- Syphilis was first discovered in Europe near the end of the fifteenth century. The virulent strain of *T. pallidum* was first isolated 1912 from a neurosyphilitic patient by Hideyo Noguchi, a Japanese bacteriologist. Although for the past decades treatment has been available, syphilis remains a health problem throughout the world.
- (1) The WHO (world health organization) "estimates that 12 million new cases of syphilis occur each year."
- (2) This is a major problem in developing countries where prenatal testing and antibiotics are not available. In such cases syphilis can be passed from mother to unborn child. In a recent study, congenital syphilis was reported as the cause of 50% of all stillbirths in Tanzania.
- (3) Another major complication of syphilis is its ability to increase the likelihood of transmission of HIV.

Culture and growth characterisitcs

- T pallidum has never been cultured continuously in artificial culture media
- T. pallidum is usually cultured in the testes of rabbits,
- Non pathogenic /saprophytic Treponema can be cultured anaerobically invitro doubling time is 30 hrs. The saprophytic Reiter strain grows on a defined medium of 11 amino acids, vitamins, salts, minerals, and serum albumin.
- T pallidum is a microaerophilic organism; it survives best in 1–4% oxygen. In proper suspending fluids and in the presence of reducing substances, T pallidum may remain motile for 3–6 days at 25 °C.
- In whole blood or plasma stored at 4 °C, organisms remain viable for at least 24 hours, which is of potential importance in blood transfusions.

Reactions to Physical and Chemical Agents

- Drying kills the spirochete rapidly, as does elevation of the temperature to 42 °C.
- Treponemes are rapidly immobilized and killed by trivalent arsenical, mercury, and bismuth (contained in drugs of historical interest in the treatment of syphilis.
- Penicillin is treponemicidal in minute concentrations, but the rate of killing is slow, presumably because of the metabolic inactivity and slow multiplication rate of T pallidum (estimated division time is 30 hours).
- Resistance to penicillin has not been demonstrated in syphilis.

Virulence Factors

- Several gene products associated with virulent strains,
- Their roles in pathogenesis are unknown.
- The outer membrane proteins are associated with adherence to the surface of host cells,
- Virulent spirochetes produce hyaluronidase, which may facilitate perivascular infiltration.
- Virulent spirochetes are also coated with host cell fibronectin, which can protect against phagocytosis.

RESISTANCE

- Inactivated in one hour at 41-42˚c
- Inactivated when in contact with oxygen, soap, distilled water, arsenicals, mercurials, common antiseptic agents.

ANTIGENIC STRUCTURE

- Treponemal infection induces three types of antibodies:

1) The first type of antibody reacts in non specific serological test like VDRL, Kahn, Wasserman.
2) It is protein antigen present in Treponema pallidum and non pathogenic strain Reiter treponema . It is group antigen.
3) The third antigen present in Treponema pallidum and is species specific. It may be demonstrated by Treponema pallidum immobilization test.

Mode of Transmission

- Organism is very fragile, destroyed rapidly by heat, cold and drying.
- Sexual transmission most common, occurs when abraded skin or mucous membranes come in contact with open lesion.
- Can be transmitted to fetus.
- Rare transmission from needle stick and blood transfusion.

Pathology

Penetration:

- T. pallidum enters the body via skin and mucous membranes through abrasions during sexual contact
- Also transmitted transplacentally

Dissemination:

- Travels via the lymphatic system to regional lymph nodes and then throughout the body via the blood stream
- Invasion of the CNS can occur during any stage of syphilis

Treponema pallidum causes Syphilis which can be :

1) Venereal syphilis
2) Congenital syphilis
3) Non venereal syphilis

VENEREAL SYPHILIS

- Sexually transmitted disease
- Entry through minute abrasions on mucosa or skin.
- Incubation period –about a month (10 to 90 days).
- Infectivity is maximum during first 2 years of disease- primary, secondary & early latent stage.

STAGES OF VENEREAL SYPHILIS

1. Primary
2. Secondary
3. Latent
   - Early latent
   - Late latent
4. Late or tertiary

- May involve any organ, but main parts are:
- Neurosyphilis
- Cardiovascular syphilis
- Late benign (gumma)

PRIMARY SYPHILIS (The Chancre)

- Incubation period 9-90 days, usually ~21 days.
- • Develops at site of contact/inoculation.
- • Multiplies at the site of entry, a small painless primary lesion called chancre is formed.

CHANCRE

- Appears on external genitilia corona of the penis labia, vaginal wall.
- also occurs in cervix, perianal area, mouth, anal canal.
- It possesses a hard ridge covered by thick, glairy exudate rich in spirochaetes.
- Serological tests are positive in 80% individuals at this stage.

Secondary Syphilis

- Secondary syphilis at 2- 10 weeks after primary lesion – diffuse symptoms:
  - Fever
  - Headache
  - Skin pustules
- Usually disappears even without
- Skin rashes, nucleus patches in oropharynx.
- Multiplication of spirochaetes and their dissemination through blood.
- Headache, anorexia, malaise, weight loss, nausea and vomiting, sore throat and slight fever.
- Temporary alopecia may occur
- Nails become brittle and pitted

Latent syphilis

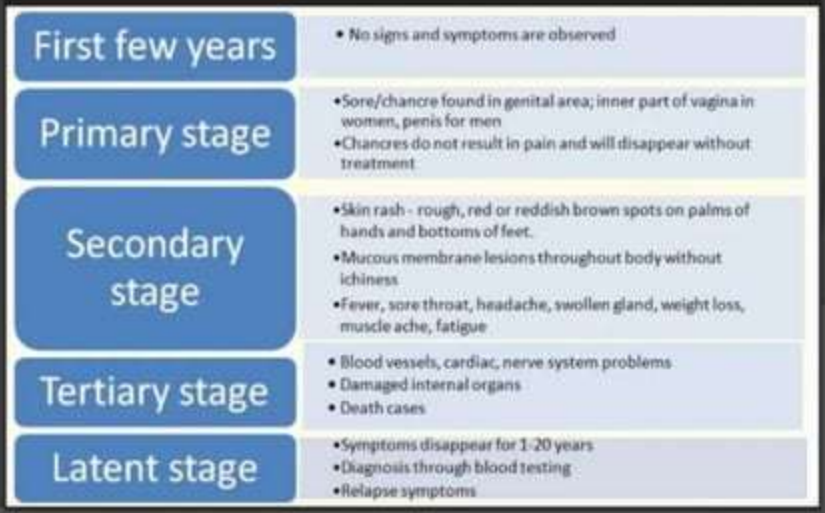
- After several weeks, secondary lesions disappear and disease becomes latent.
- Not infectious at this stage,
- Except for transmission from mother to foetus (congenital syphilis)

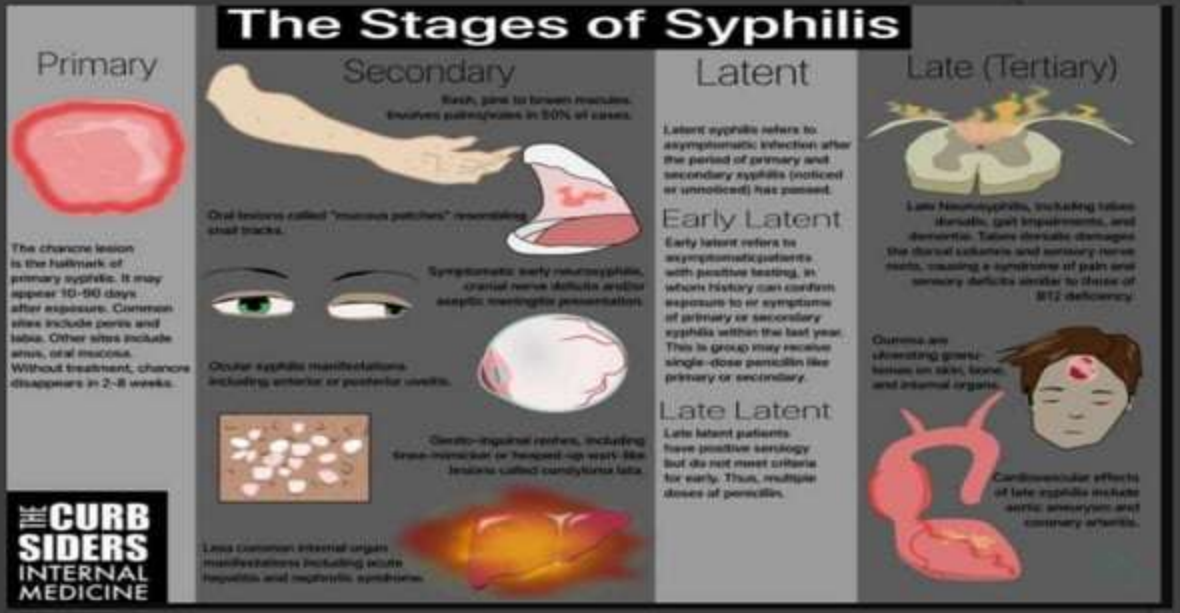
Tertiary Syphilis

- Develops after many years in persons with untreated secondary syphilis.
- Appearance of degenerative lesions called GUMMAS in skin, bone and nervous system.
- Reduction in number of spirochaetes observed.

Affects 2/3 of untreated cases

- Gummata: rubbery tumors
- Bone deformities
- Blindness
- Loss of coordination
- Paralysis
- Insanity

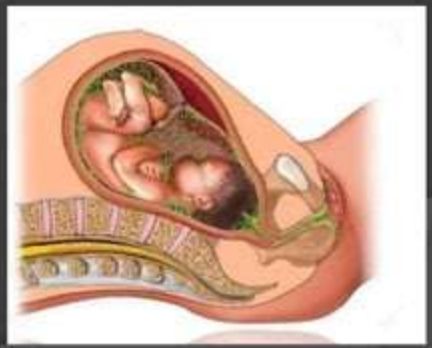



The Stages of Syphilis
Primary
The chancre lesion is the hallmark of primary syphilis. It may appear 10-90 days after exposure. Common sites include penis and labia. Other sites include anus, oral mucosa. Without treatment, chancre disappears in 2-8 weeks.
Secondary
Rash, pink to brown macules, involves palms/soles in 50% of cases.
Oral lesions called "mucous patches" resembling snail tracks.
Symptomatic early neurosyphilis, cranial nerve deficits and/or aseptic meningitis presentation.
Ocular syphilis manifestations including anterior or posterior uveitis.
Genito-inguinal rashes, including linear-nonscalar or flesped-up wart-like lesions called condylomia lata.
Less common internal organ manifestations including acute hepatitis and nephritic syndrome.
Latent
Latent syphilis refers to asymptomatic infection after the period of primary and secondary syphilis (noticed or unnoticed) has passed.
Early Latent
Early latent refers to asymptomatic patients with positive testing, in whom history can confirm exposure to or symptoms of primary or secondary syphilis within the last year. This is group may receive single-dose penicillin like primary or secondary.
Late Latent
Late latent patients have positive serology but do not meet criteria for early. Thus, multiple doses of penicillin.
Late (Tertiary)
Late Neurosyphilis, including tabes dorsalis, gait impairments, and dementia. Tabes dorsalis damages the dorsal columns and sensory nerve roots, causing a syndrome of pain and sensory deficits similar to those of B12 deficiency.
Gumma are ulcerating granulomas on skin, bone, and internal organs.
Cardiovascular effects of late syphilis include aortic aneurysm and coronary arteritis.
THE CURB SIDERS INTERNAL MEDICINE


Treponema pallidum
Pathogenesis and Clinical manifestations
Organism spreads by lymph and blood
Inoculation
Primary syphilis
Asymptomatic period up to 24 weeks
Secondary syphilis
Reversion to secondary stage
Latent syphilis
Tertiary syphilis
No symptoms: Average incubation period is 3 weeks.
Chancre: May be at site of inoculation—for example, on penis, labia, or vagina.
Rash: May be accompanied by hepatitis, meningitis, or glomerulonephritis.
No symptoms: Treponema pallidum persists in latent state. Latent period may last 3 to 30 years.
Gumma of skin: These lesions may also occur in deep organs, along with CNS degeneration and ascending aortic aneurysm.

Congenital syphilis

- Mother to Child Transmission
- After 4th month gestation.
- Infection in utero may have serious consequences for the fetus. Rarely, syphilis has been acquired by transfusion of infected fresh human blood.



Syphilis Diagnosis And Treatment

- Aspects of Syphilis Diagnosis

1. Clinical history
2. Physical examination
3. Laboratory diagnosis

- Clinical History Assess:

- History of syphilis
- Known contact to an early case of syphilis
- Typical signs or symptoms of syphilis in the past 12 months
- Most recent serologic test for syphilis

- **Physical Examination**
  - Oral cavity
  - Lymph nodes
  - Skin
  - Palms and soles
  - Genitalia and perianal area
  - Neurologic examination
- **Laboratory Diagnosis**
  - Identification of Treponema pallidum in lesions
  - Darkfield microscopy
  - Direct fluorescent antibody - T. pallidum (DFA-TP)
  - Serologic tests
  - Nontreponemal tests
  - Treponemal tests

Nontreponemal Serologic Tests

- Principles
  - 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 for life
- Nontreponemal tests include VDRL, RPR Diagnosis

Treponemal Serologic Tests

- Principles
  - Measure antibody directed against T. pallidum antigens
  - Qualitative
  - Usually reactive for life
- Treponemal tests include , FTA-ABS, EIA

Provisional Diagnosis of Syphilis

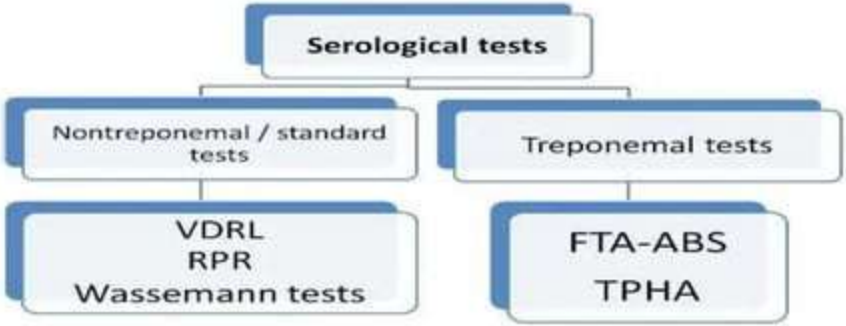
A presumptive diagnosis is possible with sequential serologic tests (e.g. VDRL, RPR), using the same testing method each timeConfirmatory tests should be performed

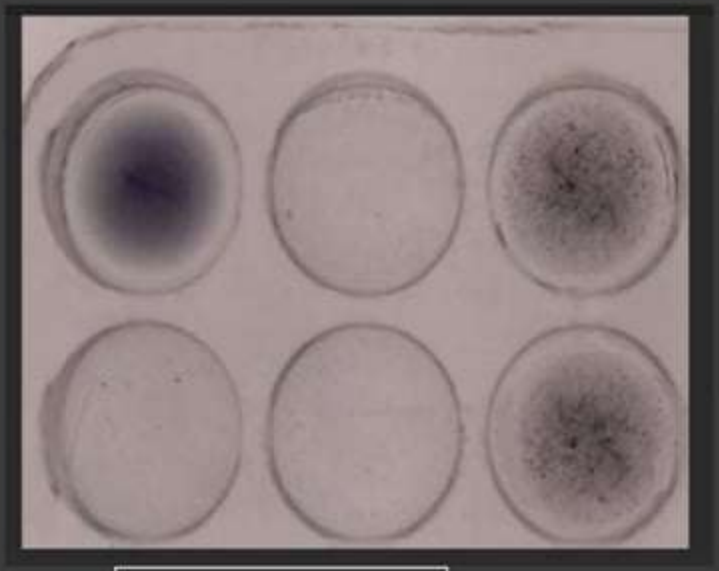
DFA-TP TEST:-

Smears of exudate are fixed with acetone.

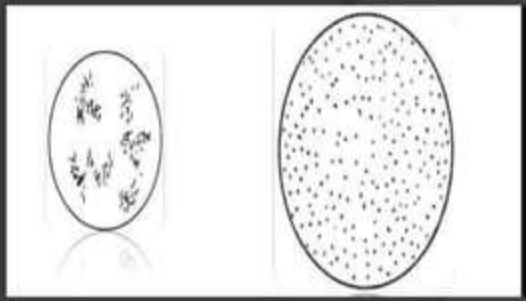
Direct fluorescent antibody for T.pallidum test is performed using fluorescent tagged anti-T.pallidum antiserum.

SERLOGICAL TESTS OF SYPHILIS (depending upon antigen)

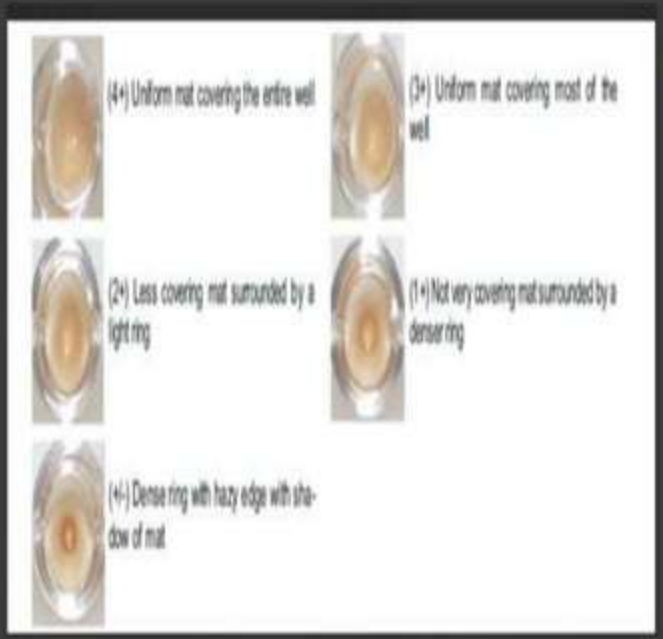




Rpr test



Vdrl test



Treponema pallidum haemagglutination (TPHA)

Adapted to micro techniques (MHA-TP)

- Tanned sheep RBCs are coated with T. pallidum antigen from Nichol's strain.
- Agglutination of the RBCs is a positive result.

PREVENTION AND CONTROL

- Screening
  - All pregnant woman at first prenatal visit
  - Individuals with other STDs
  - High risk behaviors (drugs use, prostitution, etc,); again at 28 weeks gestation pregnant
  - Exposure
- Reporting of contacts and tracing of sexual partners
- education

TREATMENT OF SYPHILIS

- Early syphilis:
  - benzathine penicillin G 2.4 million units intramuscularly once
  - procaine penicillin 600,000 units intramuscularly daily for 10 days
  - if the patient is unable to take penicillin, then give tetracycline or erythromycin 500 mg 4 times a day by mouth – or doxycycline 100 mg x2- for 15 days.
  - Ceftriaxone, 2 gm qd IM/IV for 10-14 d is a new alternative treatment and is effective specially in neurosyphilis.

- Other Disease caused by Treponema
- The non-venereal treponematoses bejel, or endemic syphilis (T. pallidum endemicum),
- yaws (T. pallidum pertenue),
- pinta (T. carateum)

Yaws (Frambesia) -*Treponema pertenue*

- Resembles syphilis
- Acquired in childhood other than sexual contact •
- Mother yaw (or framboise), a painless erythematous papule occurs a month after primary infection
- Secondary lesion resemble primary lesion occurs 1-3 months after
- Tertiary lesions involve the skin & bones, crab yaws
- DOC: Penicillin

Pinta - *Treponema carateum*

- Acquired by person-to-person contact & rarely by sexual contact
- Primary & secondary lesions are flat, erythematous & non-ulcerating; healing first becomes hyper pigmented and later depigmented scarring; occurs in hand, feet & scalp
- Tertiary lesions are uncommon
- DOC: Penicillin

Bejel - Treponema pallidum variant

- Endemic syphilis
- Acquired by direct contact during childhood
- Similar to syphilis
- DOC: Penicillin

pinta

yaws

Endemic syphilis

reference

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Thank
you!