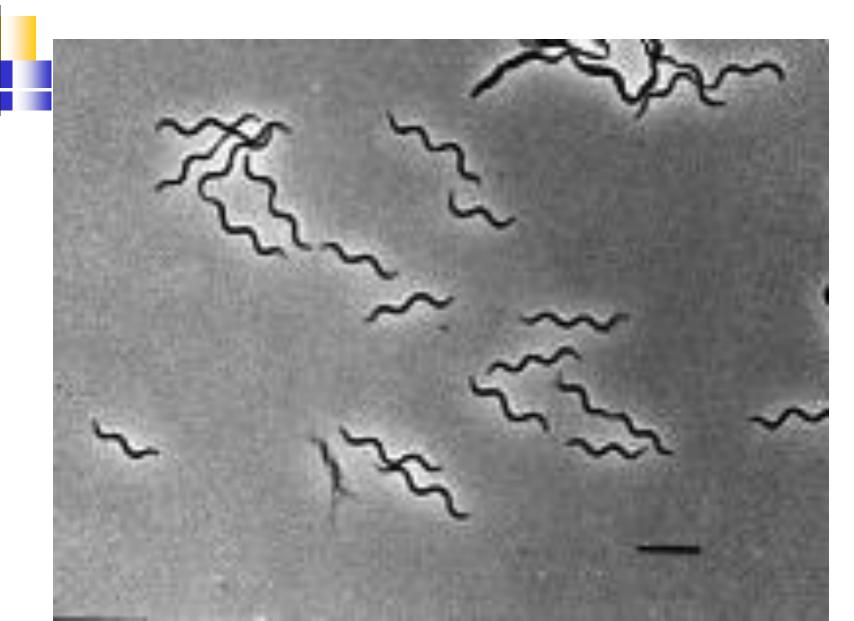
Syphilis and other Treponematoses

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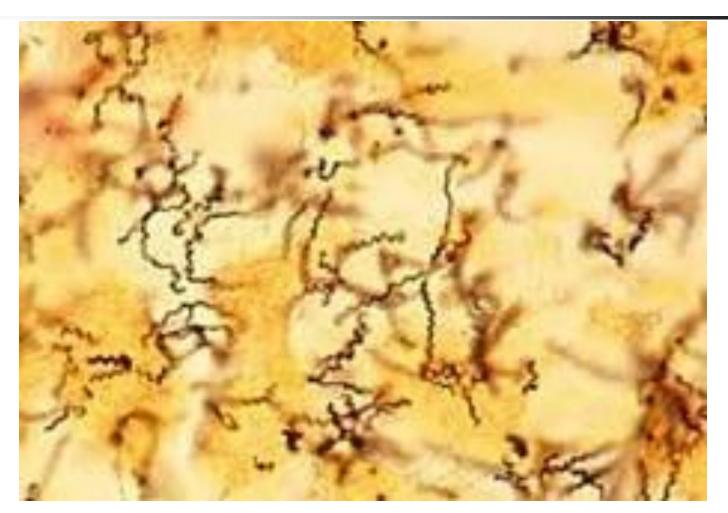
Spirochetes

- Treponema, Borrelia, Leptospira
- thin-walled, flexible, spiral or helicallyshaped rods
- motile (axial filaments)
- facultative anaerobe
- multiplied by transverse fission

Darkfield Microscopy (DF)



Silver Stain



Treponema

- with numerous tight, rigid coils, or helically shaped rods
- infect only human
- not cultivated on artifical media
- T. pallidum subspecies pallidum syphilis
- T. pallidum subspecies pertenue yaws, fambresia
- T. pallidum subspecies endemicum bejel syphilis
- d. T. pallidum subspecies carateum pinta

Syphilis

- Great pox, Italian disease, French disease
- MOT: sexual contact, blood transfusion, congenital
- 3-90 days (ave. 3 weeks)
- Stages of syphilis: primary, secondary, latent stage and tertiary stage

Primary Stage

- development of hard chancre or hunterian chancre
- appears 10 days up to several mos incubation period
- <u>chancre:</u> clean, smooth based, edge is raised and firm and painless
- Direct exams: dark field microscopy, Levaditis silver impregnation, Fontana tribondeau (gold)
- Serological tests: During this stage RPR is more sensitive than VDRL, FTA-ABS become more reactive than MHA-TP

Chancre at the labia



Penile chancre



Penile chancre



Chancre at the shaft



Oral Chancre



Secondary Stage

- maculopapular rash on the skin
- involvements of the palms and sole
- white mucous patches on the mucous membrane (condylomata lata)
- loss of hair and thinning of eyebrow
- there may also be involvement of the CNS, eyes, bones and liver

2nd stage



2nd stage: lesions







hand lesions



Wart like lesions



Lesions





Lesions causing alopecia



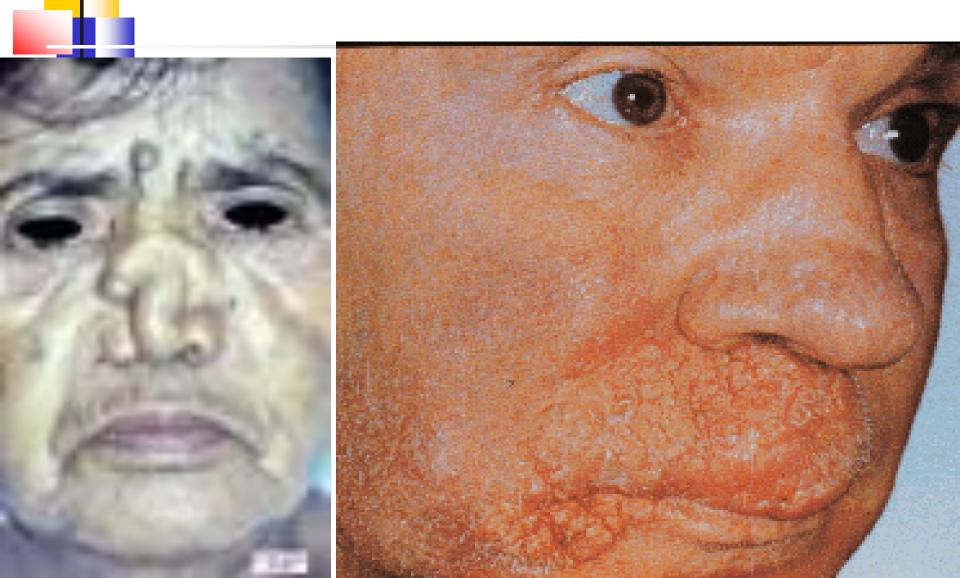
Latent Stage

- diseases becomes subclinical
- shows no sign and the disease is recognized only through serological tests

Tertiary Stage

- takes place when the latent stage is not treated
- involvement of the deep organ known (cardiac syphilis, neurosyphilis) known as gummas
- other internal organs involved are bone and skin

Tertiary stage: gumma



Jerisch-Herxheimer reaction

- reaction most commonly observed in the early stages of syphilis when treated after 2-12 hrs w/ either heavy metals or penicillin
- commonly observed reactions are headache, malaise and a temperature above 38'C

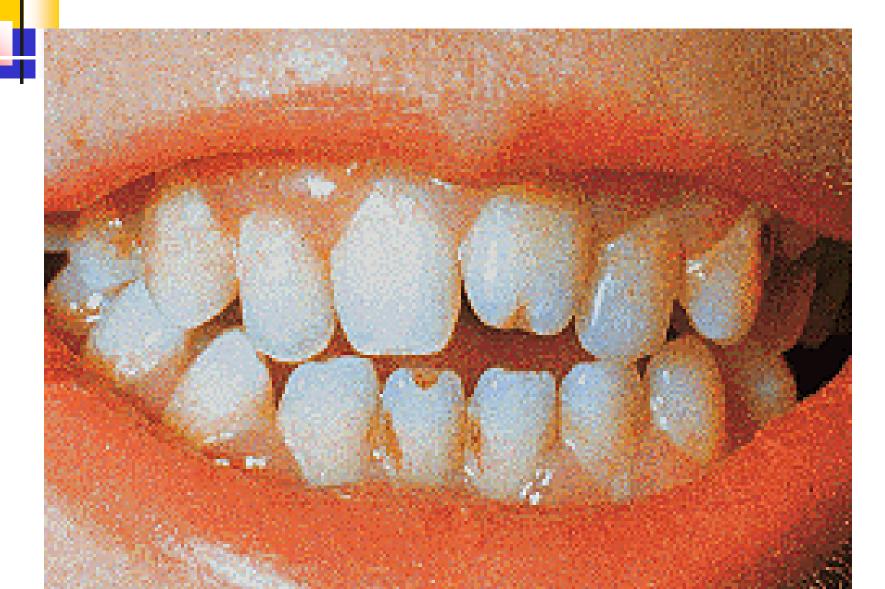
Congenital Syphilis

- transmission of the disease from syphilitic mother to the fetus through the placenta
- fetal death
- interstitial keratitis
- saddle nose
- periodontitis
- Hutchinson's teeth
- CNS anomaly

Stages of Congenital Syphilis

- 1. early
- 2. late
- 3. stigmata

Hutchinson's teeth



Interstitial Keratitis

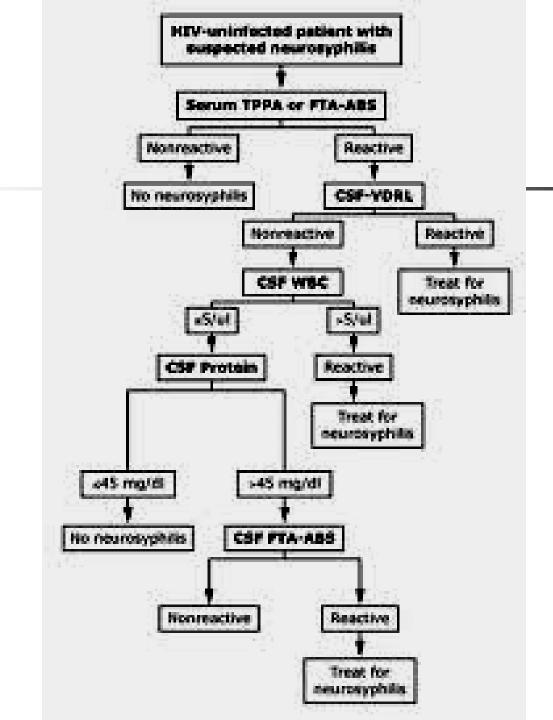


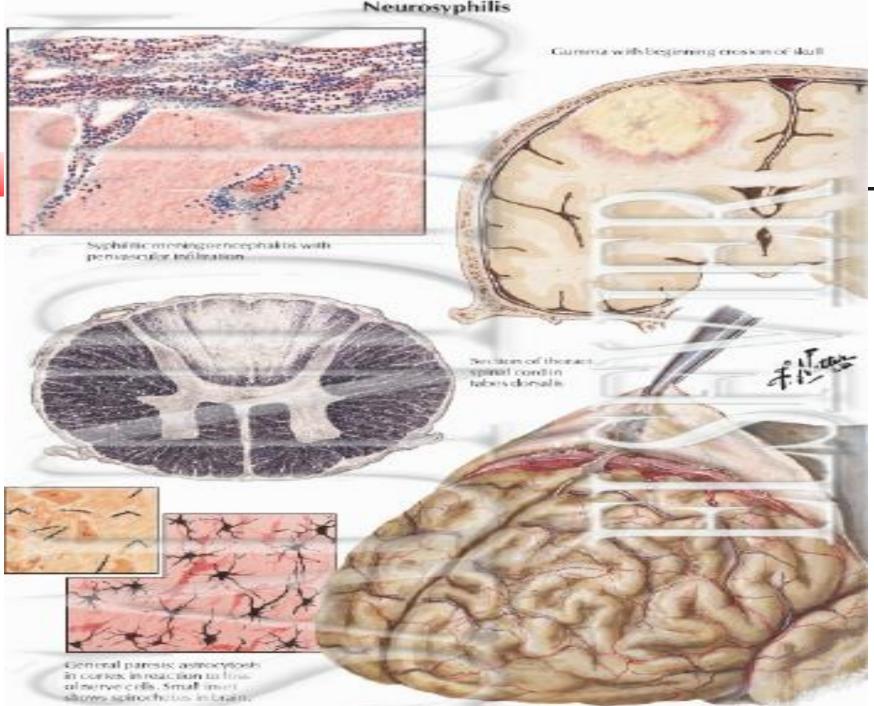
Saddle nose



Neurosyphilis

- refers to a site of infection involving the neurologic system
- There are four clinical types.
- Asymptomatic Neurosyphilis
- Meningovascular Syphilis
- Tabes Dorsalis
- General Paresis [3]

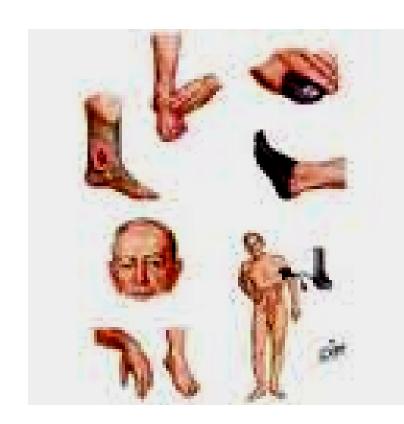




General pares is: atrophy of brain and chronic subdural hematoma.

Tabes dorsalis

- a slow degeneration of the nerve cells and nerve fibers that carry sensory information to the brain.
- Tabes dorsalis is the result of an untreated syphilis infection.





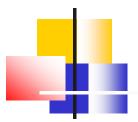


- Weakness
- Diminished reflexes
- Unsteady gait
- Progressive degeneration of the joints
- Loss of coordination

- episodes of intense pain and disturbed sensation inclusive glossodynia
- personality changes
- dementia
- deafness
- visual impairment
- impaired response to light

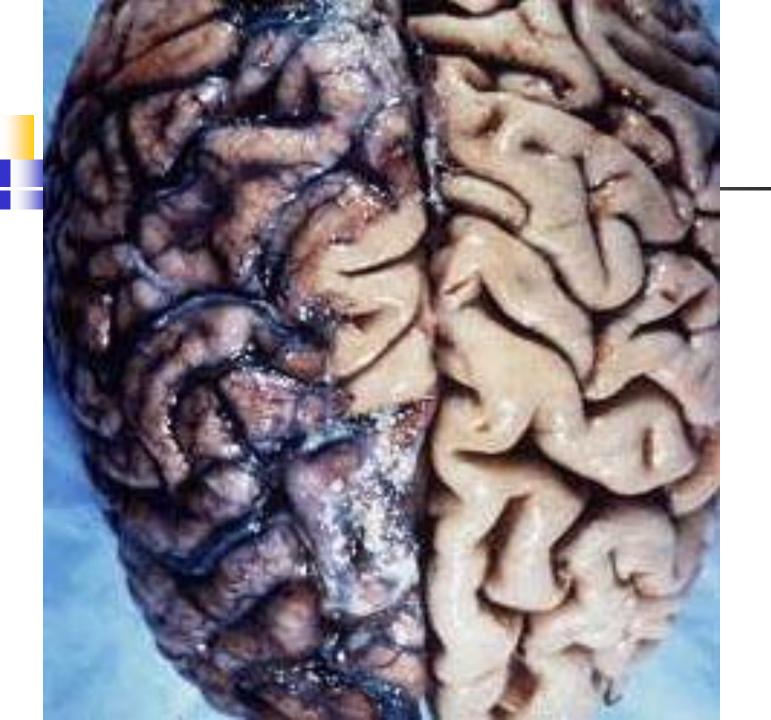






- If left untreated, tabes dorsalis can lead to
- paralysis
- dementia
- blindness

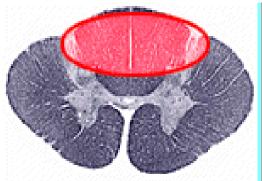
Existing nerve damage cannot be reversed.





Structures damaged

Causes



- Posterior funiculus
- Posterior hom

Tabes dorsalis

Types of Serological Tests

Antigen Detection

- Microscopic
 - Dark-field
 - DFA-TP
 - DFA-TP (histopath)
- II. Isolation and Propagation
 - -Rabbit infectivity testing
- III. Nucleic acid amplification Technique

Antibody Detection

- Non-Treponemal
- II. Treponemal

Rabbit infectivity testing









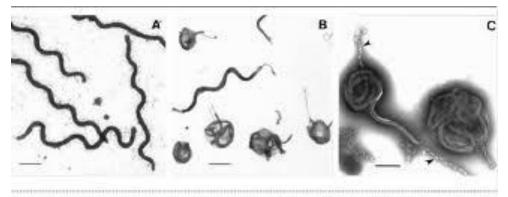


Fig. 1. Transmission electron micrographs demonstrating cyst formation of 8 burg/orferi in response to serum stansation. A, Typical vegetative spinochaetes observed in BSKII or RPMI+5. B, C, Cyst forms occurring after 48 h incubation in RPMI. Amonheads indicate membrane 'beading', Bars, 2 µm (A and 8); 1 µm (C).

Antibody Detection Tests for Syphilis

NON TREPONEMAL TEST

- cardiolipin: source of antigen
- it detects reagin
- screening test
- non confirmatory
- CF test: Wasserman, Kolmer
- Flocculation tests: VDRL, RPR

TREPONEMAL TESTS

- T. pallidum: source of antigen
- it detects Treponemal antibodies (IgG or IgM)
- confirmatory
- FTA-ABS, TPI, TPCF, MHA-TP, TPHA

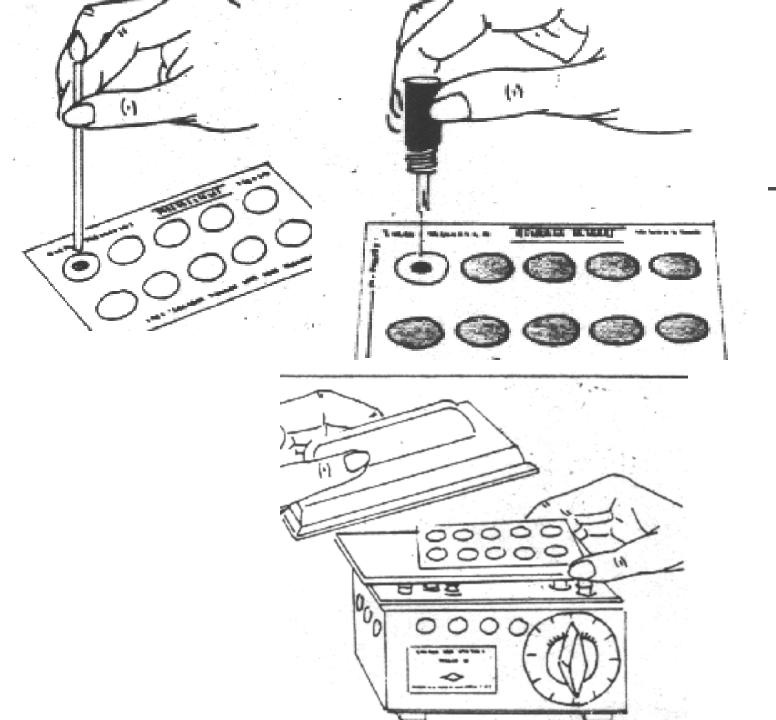
Flocculation Tests

Classical VDRL

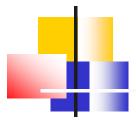
- requires inactivation of serum
- heat the serum 56'C 30 min to destroy native complement
- results are read macroscopically; 8 mins
- (+) flocculation

RPR

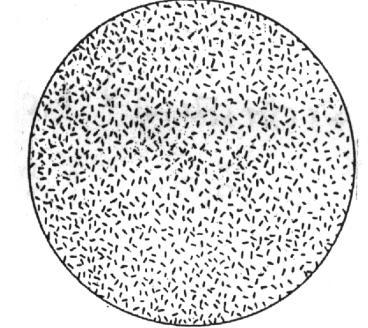
- no need for inactivation of serum
- charcoal: indicator, adsorbed w/ choline chloride
- results are read macroscopically against white background 4 mins
- (+) flocculation



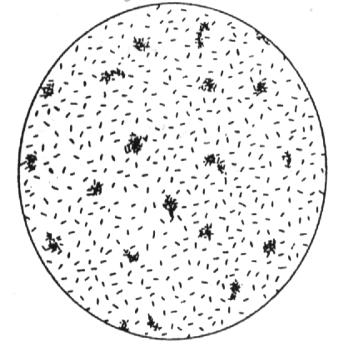
Reactive







Weakly Reactive



VDRL Latex: no need for inactivation

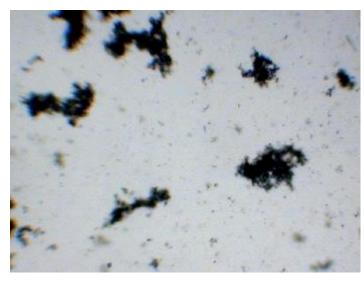


Interpret the results







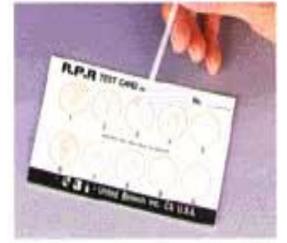


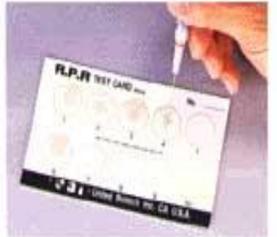
VDRL slide rotator



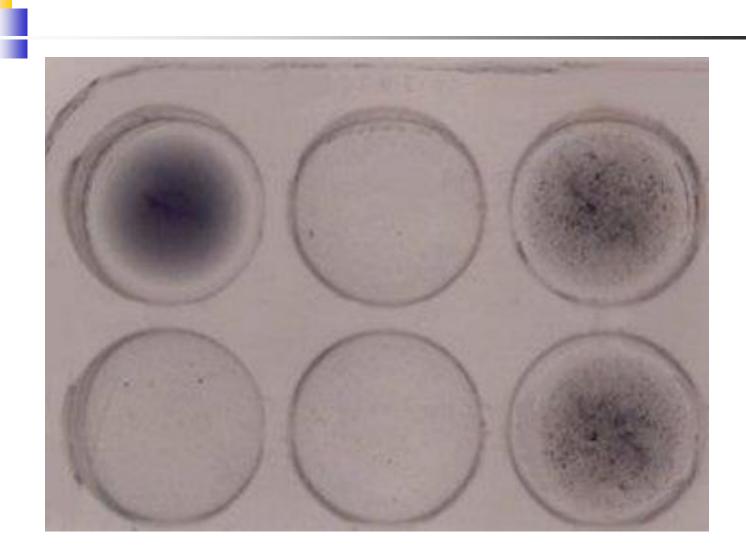
RPR Kit







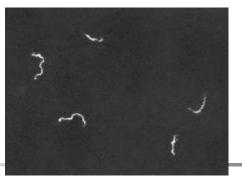




Test Limitation

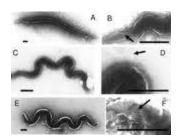
- Cannot be used for CSF
- Prozone may be encountered
- Reactive in yaws and non venereal syphilis
- Biological false positive



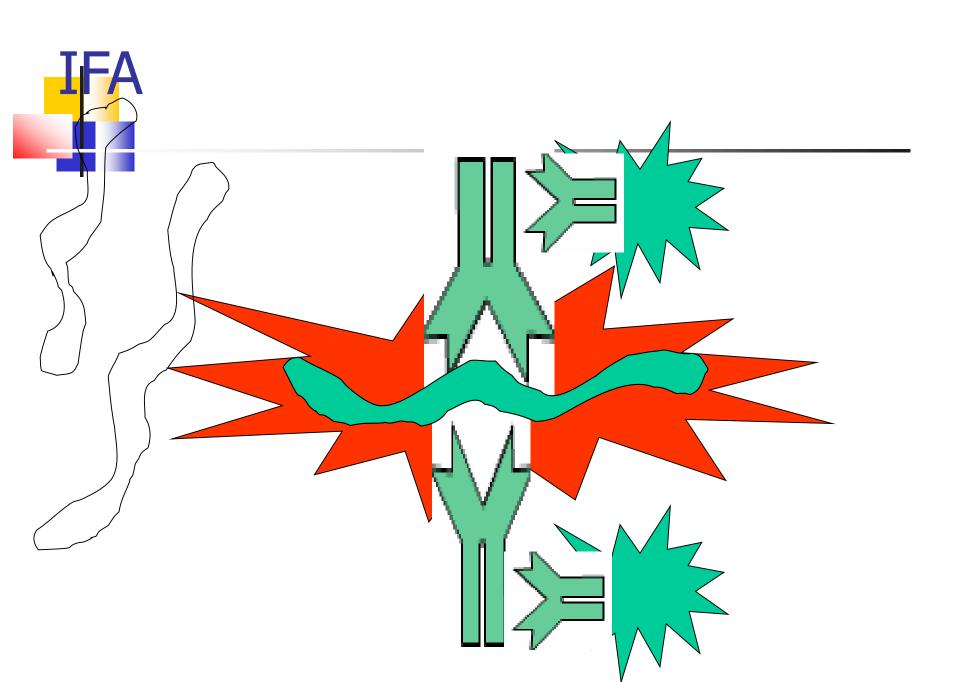




- antigen: T. pallidum (Nichol's strain)
 extracted from rabbit testicular tissue
- FTA-ABS sorbent test: prepared from cultures of Reiter's treponemes

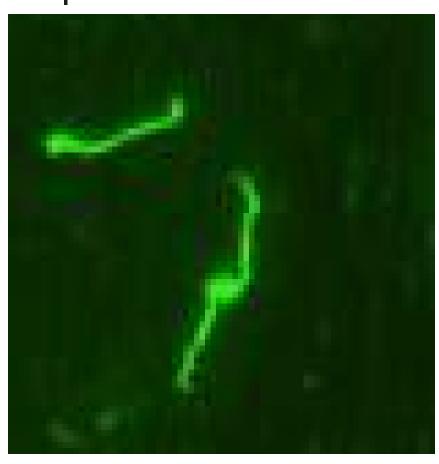


- fluorescein labeled antihuman globulin
- (+) result: fluorescent treponemes



Positive Reaction







Sources of errors

- Cross contamination
- Improper alignment of microscopes
- Used of repeatedly thawed antigen slides

Test Limitation

- Transient false +
- Systemic, discoid and drug induced LE
- Reactive in yaws and pinta
- Reactive among elderly

Treponema pallidum Immobilization

- reference test
- requires live T. pallidum extracted from testicular chancre of rabbit
- (+) results: immobilization of Treponema pallidum
- does not distinguish trepanematoses







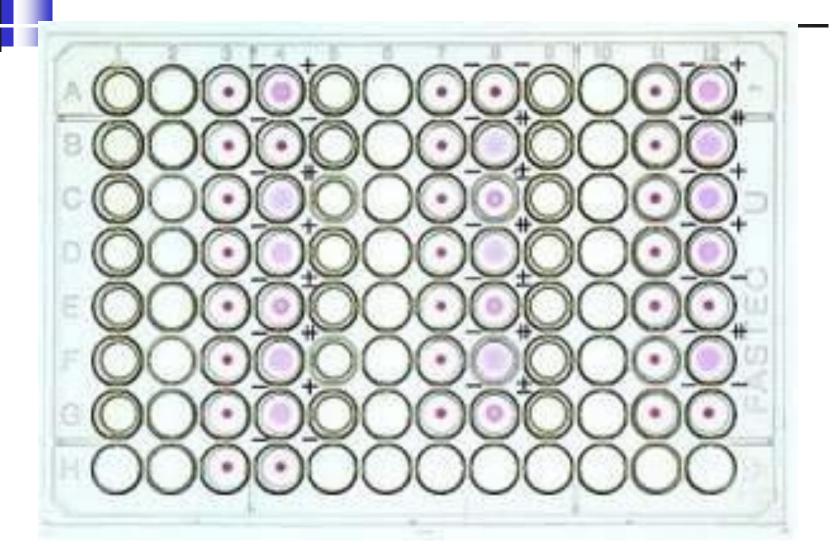
MHA-TP

 based upon agglutination by specific antibodies in serum w/ lyophilized, formalinized, tanned sheep's rbc sensitized w/ T. pallidum antigen

TPCF

- antigen used is an extract from non virulent treponemes (a reiter strain)
- non reactive in the late stage of syphilis

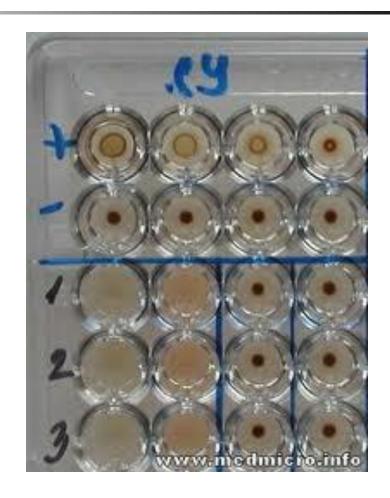
MHA-TP





- T. pallidum : ag
- Detection of antibodies directed against cellular components







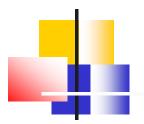
New test for syphilis

- ELISA
- Western Blot
- PCR

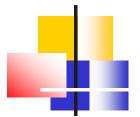


Interpretation of Results

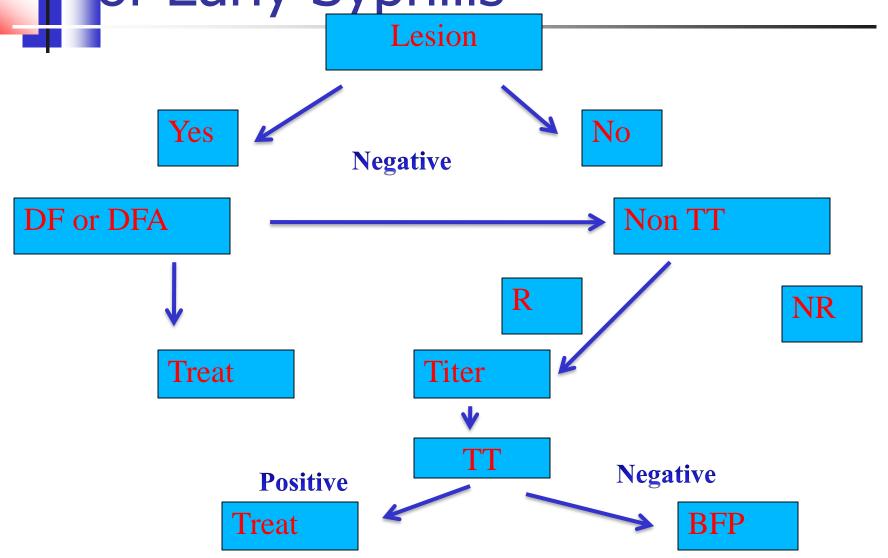
- Based on where test will be used low risk population: must be confirmed
- Must be interpreted accdg to the stage of the disease
- a. early: 30% NR repeat 1 wk, 3 mos
- Secondary and latent: nearly all R (>1:8)
- Late latent: 20% NR non treponemal, 86% R treponemal for life



- Pregnancy: confirm with treponemal test, if R treated
- When used to follow therapy:
- -performed at 3 mos interval for at least 1 year; at least 4 fold decline on 3rd and 4th mos; at least 8 fold decline on 6th and 8th mo late latent
- -gradual decline
- -low titer persists at least 50% after 2 yrs



 Indicator of re-infection- four fold increase, needs re-treatment Schematic Diagram for Lab Dx of Early Syphilis



Important Notes!

- When laboratory results contradict the physician's opinion or the patient's history, a repeat specimen should be submitted
- The dx of syphilis should be based on serologic tests as well as history, a thorough PE, and a plausible explanation for the source of infection

Treponema pertenue

- causes yaws or frambesia which is a disease
- non venereal and transmitted to man through the aid of flies
- Primary lesion Mother Yaws or Framboise, initial lesion which develops 3-4 weeks after exposure
- Secondary lesion Daughter yaws; develops 6-12 weeks after initial lesion
- Tertiary lesion granulomatous lesion crab yaws: infection of the feet which causes a crippling form of disease







Facial disfigurement associated with yaws. W. Peters, H.M. Gilles. A Colour Atlas of Tropical Medicine and Parasitology. Third Edition, 1989.

Treponema carateum

- causative agent of Carate or Pinta which is characterized by hyperpigmented lesion
- affects only the skin, initially appears as red and blue lesions but later become depigmented

