Syphilis and other Treponematoses

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Spirochetes

- Treponema, Borrelia, Leptospira
- thin-walled, flexible, spiral or helically-shaped rods
- motile (axial filaments)
- facultative anaerobe
- multiplied by transverse fission
Darkfield Microscopy (DF)
Treponema

- with numerous tight, rigid coils, or helically shaped rods
- infect only human
- not cultivated on artificial media
  a. T. pallidum subspecies pallidum – syphilis
  b. T. pallidum subspecies pertenue – yaws, fambresia
  c. 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
- **Chancre**: 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
2\textsuperscript{nd} stage: lesions
Spreading lesions
hand lesions
Wart like lesions
Lesions on the feet
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]
Neurosyphilis

Syphilitic meningencephalitis with perivascular infiltration

Gumma with beginning erosion of skull

Section of thoracic spinal cord in tubes dorsalis

General paresis: astrocytosis in cortex in reaction to loss of nerve cells. Small inset shows spirochetes in brain.
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.
Symptoms

- 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.
<table>
<thead>
<tr>
<th>Extent of lesion</th>
<th>Structures damaged</th>
<th>Causes</th>
</tr>
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<tbody>
<tr>
<td></td>
<td></td>
<td>- Posterior funiculus</td>
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<tr>
<td></td>
<td></td>
<td>- Posterior horn</td>
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<td></td>
<td></td>
<td>- Tabes dorsalis</td>
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</table>
Types of Serological Tests

**Antigen Detection**

I. Microscopic
   - Dark-field
   - DFA-TP
   - DFA-TP (histopath)

II. Isolation and Propagation
   - Rabbit infectivity testing

III. Nucleic acid amplification Technique

**Antibody Detection**

I. Non-Treponemal

II. Treponemal
Rabbit infectivity testing
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

Non 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
FTA-ABS

- 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
### Other Treponemal Tests

<table>
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<th>MHA-TP</th>
<th>TPCF</th>
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<td>Based upon agglutination by specific antibodies in serum w/ lyophilized, formalinized, tanned sheep’s rbc sensitized w/ T. pallidum antigen</td>
<td>Antigen used is an extract from non virulent treponemes (a reiter strain)</td>
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<td>Non reactive in the late stage of syphilis</td>
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MHA-TP
TPHA

- 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
  b. Secondary and latent: nearly all R (>1:8)
  c. 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 3\(^{rd}\) and 4\(^{th}\) mos; at least 8 fold decline on 6\(^{th}\) and 8\(^{th}\) 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

Lesion

Yes

DF or DFA

Treat

Positive

Titer

TT

Non TT

R

NR

BFP

Treat

Negative

No
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

1. **Primary lesion** – Mother Yaws or Framboise, initial lesion which develops 3-4 weeks after exposure
2. **Secondary lesion** – Daughter yaws; develops 6-12 weeks after initial lesion
3. **Tertiary lesion** – granulomatous lesion 
   crab yaws: infection of the feet which causes a crippling form of disease
Yaws

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