Overview of Syphilis Diagnostics: Background and History
**Treponema pallidum**

- **Spirochete**
- **Mechanism of transmission**
  - Sexually transmitted
  - Person to person through direct contact with an infected ulcer
  - Can be transmitted from mother to child (congenital syphilis)
History of Syphilis
History of Syphilis

1905 - T. Pallidum first identified (Schaudinn & Hoffman)
1906 - Dark-field microscopy introduced (Landsteiner)
1910 - First serologic assay (Wasserman), First treatment (Ehrlich)
1940 - First effective treatment - penicillin

Role of the Public Health Laboratory

• Syphilis reporting is mandated by state laws

• Information about syphilis cases is reported to CDC from all states and territories

• Syphilis surveillance provides data for planning, implementation and evaluation for public health programs and interventions
Syphilis Rates—Still not gone

Reported cases by Stage of Infection, US, 1941-2013
Highest Syphilis Rates Amongst Young Men

Primary and Secondary Syphilis – Rates of Reported Cases by Age and Sex, US, 2013
Syphilis Challenges

• Efforts to eliminate syphilis are falling short
• Ease of treatment – penicillin works
• Lack of knowledge – syphilis has been eliminated?
• Dependence on serologic tests to detect syphilis
  – Indirect evidence
  – Requires normal immune response (HIV)
  – Non-specific (false positive) and false negative reactions
Diagnosis of Syphilis is Challenging

• Syphilis is the “great imitator”
• Persons present without symptoms or signs
  – Painless primary lesion can be in nonvisible locations and resolve without treatment
  – Inapparent lesions
  – Latent infections
• Culture is not a diagnostic option
• Direct detection of early infection limited
Syphilis Infection

Figure 10.1
Schematic representation of the course of untreated syphilis
Common patterns of serologic reactivity

- Direct Detection
- Serologic Detection of Treponemal Antibodies
- Serologic Detection of Non-Trep Antibodies

Graph showing the percentage of patients who test positive over time for different antibodies.

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<th>Clinical stages of syphilis</th>
<th>primary lesion</th>
<th>secondary lesion</th>
<th>latent (asymptomatic)</th>
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Direct Detection

• Ideally suited for early detection before antibodies are generated

• Available Tests (not FDA-cleared)
  – Darkfield microscopy
  – Immunostaining-DFA
  – Nucleic Acid Amplification tests

• Challenges
  – Limited availability
  – False negatives
  – Expertise CLIA requirements
Serologic Diagnosis of Syphilis

Always requires detection of two types of antibodies

- Non-Treponemal antibodies
  - Directed against lipoidal antigens
  - Most common tests: RPR and VRDL

- Treponemal antibodies
  - Directed against *T. pallidum*
  - Most common tests: FTA-ABS, TP-PA, EIA, CIA and MBIA

- POC Testing
  - FDA-cleared: Syphilis HealthCheck (Treponemal Ab only)
  - Non FDA-cleared: Chembio: Treponemal and Non-treponemal Ab
Syphilis Diagnosis

No testing algorithm can take the place of clinical judgment

– Test results must be used in conjunction with the patient’s clinical symptoms, medical and sexual history, and other clinical and/or laboratory findings to produce an overall clinical diagnosis.
References


Resources

Images

- http://phil.cdc.gov/phil/home.asp

General

- CDC Sexually Transmitted Disease Surveillance 2013
- STD Treatment Guidelines 2015
- Syphilis Fact Sheets
- Laboratory Diagnostic Testing for *Treponema pallidum*, Expert Consultation 2009
- CDC Division of STD Prevention (DSTDP)
- APHL STD Homepage