The Medical Value of Laboratory Testing for STI Management

Edward W. Hook III M.D.
Departments of Medicine, Microbiology and Epidemiology
University of Alabama at Birmingham

Edward W. Hook, III, M.D.

Disclosures
Grant/Research Support: NIH, CDC, WHO, Roche Molecular, Becton Dickinson, Gen-Probe, Cepheid, Melinta
Consultant: Astra Zeneca, Melinta
Speakers Bureau: None

Contributors To Sustained STD Morbidity
- Biological Factors
  - Host
  - Pathogen
- Behavioral Factors
  - Acquisition
  - Transmission
- Social Factors
  - Stigma
  - Cross Cutting Societal Problems

Principles of STI Management
- Prevent acquisition
- Prevent transmission
- Prevent complications

Estimated Global Prevalence of Sexually Transmitted Infections
(Total 2,993,200,000)

Background: U.S. Estimates
- Estimated Prevalence of Sexually Transmitted Infections in the U.S.
(Total 110,197,000)
- Estimated New Sexually Transmitted Infections in the U.S. Each Year
(Total 19,738,800)

Satterwhite CL et al. Sexually Transmitted Diseases 2013;40:187-93
Syphilis—Reported Cases by Stage of Infection, United States, 1941–2012


Fig 29. SR, Pg 32

Gonorrhea — Rates of Reported Cases by Year, United States, 1941–2013

Gonorrhea — Rates of Reported Cases by Sex, United States, 1993–2013

Chlamydia — Rates of Reported Cases by Sex, United States, 1993–2013

NOTE: As of January 2000, all 50 states and the District of Columbia have regulations that require the reporting of chlamydia cases.

Principles of STD Management

Prevent acquisition

Prevent transmission

Prevent complications
THE NEXT GREAT PLAGUE TO GO
Thomas Parran’s Formula For Syphilis Control – 1936

1. Case Finding – Serologic Screening Programs
2. Prompt Therapy
3. Contact Identification, Testing, and Therapy
4. Mandatory Serological Evaluations – Premarital and Early Pregnancy
5. Public Education = Symptoms, Complications, Treatment

Etiologic vs. Syndromic
STD Diagnosis

<table>
<thead>
<tr>
<th>Etiologic</th>
<th>Syndrome</th>
</tr>
</thead>
<tbody>
<tr>
<td>Demonstration of presence of potential pathogen</td>
<td>Based on constellation of historical findings and signs</td>
</tr>
<tr>
<td>Not all persons with STDs defined etiologically are symptomatic</td>
<td>Often due to multiple pathogens</td>
</tr>
<tr>
<td>Not all persons with STD syndromes have demonstrable etiologic agents</td>
<td></td>
</tr>
</tbody>
</table>

Etiology of Genital Ulcers In 516 STD Clinic Patients

515 patients recruited from STD Clinics in 10 U.S. Cities With High Syphilis Rates

<table>
<thead>
<tr>
<th>PCR Result</th>
<th>Number (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>HSV</td>
<td>320 (62%)</td>
</tr>
<tr>
<td>Syphilis</td>
<td>51 (10%)</td>
</tr>
<tr>
<td>HSV and Syphilis</td>
<td>13 (3%)</td>
</tr>
<tr>
<td>Chancroid</td>
<td>16 (3%)</td>
</tr>
<tr>
<td>PCR Negative</td>
<td>116 (22%)</td>
</tr>
</tbody>
</table>

Mertz K et al JID 1998: 178: 1795-9

STI SCREENING

Goal: Detection of unsuspected, often asymptomatic infections to prevent transmission and sequelae.

Therefore, even with imperfect tests, screening is important. However, it is also important for health care providers to know the limitations of the tests they use.

Etiologic Tests

- Microscopy
- Culture
- NAATS
- Serological Tests
Major STIs

**Curable**
- Trichomonas vaginalis
- Chlamydia trachomatis
- Neisseria gonorrhoeae
- Treponema pallidum

**Incurable**
- Human papilloma virus
- Herpes simplex virus
- Human immunodeficiency virus
- Hepatitis B virus

STI Screening Goals

<table>
<thead>
<tr>
<th>Curable STIs</th>
<th>Incurable STIs</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Bacteria &amp; Protozoans</strong></td>
<td><strong>Viruses</strong></td>
</tr>
<tr>
<td>Timely Treatment for Cure</td>
<td>Slow/Delay Progression</td>
</tr>
<tr>
<td>Prevention of Complications</td>
<td>Reduce Transmission</td>
</tr>
<tr>
<td>Partner Notification</td>
<td>Partner Notification</td>
</tr>
</tbody>
</table>

Changing Paradigms For Urogenital Specimen Collection

**Pre-NAAT's:**
- Specimen Quality Critical
  - Endocervical Or Urethral Swabs
  - Swab Order Impacts Test Results
  - Culture > Non-Amplified Nucleic Acid Detection > Antigen Detection

**NAAT's:**
- More Forgiving Specimen Collection
  - Vaginal Swab > Endocervical Swab > initial Void Urine

Etiologic Tests-Direct Detection

**NAATs**

**Pros:**
- Most sensitive for detection of pathogens
- Highly specific, little need for confirmation
- Potential for pathogen subtyping (HPV, HCV)
- Test results in hours (laboratory time)
- Potential to test for multiple pathogens from a single specimen (Multiplex capability)

**Cons:**
- Potential for detection of dead organisms
- Difficulties in determining antimicrobial susceptibility

Etiologic Tests-Detection of Host Response

**Serological Testing**

**Pros:**
- Useful for prevalence estimates
- Useful for detection of chronic, difficult to directly detect infections (syphilis, HIV, HSV)
- Change in titers may reflect response to therapy

**Cons:**
- Potential for false positives without confirmatory testing
- Time required for host response to infection to develop
- Cure may be difficult to demonstrate (may remain positive long after successful treatment)

The Medical Value of Laboratory Testing for STI Management

**A Look to the Future: Room For Improvement**

- Faster time to test results
- Newer, Simpler Platforms and Test Formats
- Newer Technologies
  - Whole genome sequencing
  - Geneweave technology
- Expanded Multiplex Assays
The Medical Value of Laboratory Testing for STI Management

SUMMARY

- STIs remain common
- Detection and management of unrecognized STIs (screening) is a crucial element for effective control
- Screening using direct demonstration of the pathogen or serological testing for host response to infection must be prioritized depending on the pathogen

Genital Herpes Is Usually Unrecognized

<table>
<thead>
<tr>
<th>Source</th>
<th>Year</th>
<th>Percentage</th>
<th>Women (%)</th>
<th>Men (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Self-reported genital herpes, sexually active Americans 18-59</td>
<td>2015</td>
<td>2.1%</td>
<td>2.9%</td>
<td>1.2%</td>
</tr>
<tr>
<td>Serologic evidence of HSV-2 infection, Americans 16-74</td>
<td>1978</td>
<td>16.4%</td>
<td>19.4%</td>
<td>13.2%</td>
</tr>
<tr>
<td></td>
<td>1990</td>
<td>21.7%</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Laumann EO, et al. The Social Organization of Sexuality p.382-389