State of Clinical Diagnostics for STIs

Charlotte A. Gaydos, MS, MPH, DrPH
Professor, Division of Infectious Diseases
Johns Hopkins University
Baltimore, Maryland

IEEE Conference
November 9-10 2015
Disclosures

• I have received funding for research grants and/or have been a lecturer for Becton Dickinson, Gen-Probe Hologic, Abbott Molecular, Siemens Health Care Diagnostics, Cepheid, and Quidel
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.
(Total 19,738,800/Year)

Objective

1. To discuss current and new POC tests in the pipeline
2. To mention impact of POC testing-advantages and barriers
New Sample Types for STIs

- Traditional for culture: Cervix; Urethral
- Newer since NAATs: Urine
- Newest: Self-collected vaginal swabs
  - Self-collected penile-meatal swabs

FDA cleared

not FDA cleared
### TABLE 7. Clinical sensitivities and specificities of three assays\(^a\) for *C. trachomatis*

<table>
<thead>
<tr>
<th>Specimen type</th>
<th>Sym</th>
<th>Asym</th>
</tr>
</thead>
<tbody>
<tr>
<td>Clinician collected</td>
<td>92.5%</td>
<td>87.2%</td>
</tr>
<tr>
<td>Self-collected</td>
<td>94.7%</td>
<td>84.8%</td>
</tr>
</tbody>
</table>

No statistical difference

---

Performance of the Abbott RealTime CT/NG for Detection of *Chlamydia trachomatis* and *Neisseria gonorrhoeae*

Gaydos et al. JCM, 48:3236–3243, 2010
Female Questionnaire Results: Preference for Sample Type (N=1165)

- Pelvic: 20.7%
- Urine: 7.6%
- Vaginal or Urine: 11.5%
- Other Combo: 11.4%
- Self Vaginal: 48.8%
Conclusions: The sensitivity and specificity of vaginal self-collected swabs compared to swabs collected by clinicians supports the use of vaginal swab as the recommended specimen of choice in home-based screening for chlamydia and gonorrhea.
What About the Men?

We hypothesized self-collected penile-meatal swabs would perform as well as urethral swabs for detection of CT, NG, trichomonas (TV) and mycoplasma (MG) and that they would be acceptable to males

Dize et al. STI 2013
## Penile Swabs Vs. Urethral Swabs

**Chlamydia trachomatis** (N = 203)

<table>
<thead>
<tr>
<th></th>
<th>Urethral Positive</th>
<th>Urethral Negative</th>
</tr>
</thead>
<tbody>
<tr>
<td>Penile Positive Positive</td>
<td>30</td>
<td>2</td>
</tr>
<tr>
<td>Penile Positive Negative</td>
<td>1</td>
<td>170</td>
</tr>
</tbody>
</table>

- Sensitivity: 96.8%
- Specificity: 98.8%
- PPV: 93.8%
- NPV: 99.4%

Male Questionnaire Results
Home collection (N = 501) Chai et al. 2010

Penile Swab

- Collection Easy to Very Easy: 89.8%
- Instructions Easy to Very Easy: 94.0%
- Use Internet-based SAS again: 91.4%

Urine

- Penile Swab: 89.8%
- Urine: 95.3%
- No swab: 8; No urine: 2
The Future: Point-of-Care Tests for STIs

*Chlamydia trachomatis (CT)*

*Neisseria gonorrhoeae (NG)*

*Trichomonas vaginalis (TV)*

*Syphilis*

*HIV*

*Herpes Simples Virus (HSV)*

Gaydos, C.  Rapid Tests for STDs Current Infect Dis Reports 2006;8:115-124

Huppert et al. Point of Care tests for STIs: What’s the Point? Point of Care Journal, 2009

New POC tests for STIs

- Chlamydia
- Gonorrhea
- Trichomonas
- Syphilis
- HSV
- HIV
Use of POC in Clinical Settings

- Immediate treatment before patient leaves the clinic; no loss to follow-up
- Impact on disease epidemic?
  - Decrease interval of disease spread
- Impact on behavior?
  - Counseling on risk reduction
- **ASSURED** Criteria
  - When is a test good enough?
POCT – Build Your Own Test

• First Priority of Needs Assessment Survey
  – Chlamydia (62%); HIV – Early Seroconversion (14%)
  – Syphilis (8%)

• Overall, participants selected sensitivity as their top priority, followed by cost, specificity, and time

• Choices (statistically significant)
  Sensitivity: 90-99% > 80-90% > 70-80%
  Cost: $20 > $35 > $50
  Specificity: 99% > 95% > 90%
  Time: 5 > 15 > 25 minutes

Chlamydia trachomatis and Neisseria gonorrhoeae
“Near Patient” Test for Chlamydia and Gonorrhea

GeneXpert® CT/NG, Cepheid (90 minutes)

## Results CT/NG

1,722 female & 1,387 males

### Xpert CT/NG vs. Patient Infected Status

<table>
<thead>
<tr>
<th>Specimen</th>
<th>Sensitivity</th>
<th>Specificity</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>CT Cervical</strong></td>
<td>97.4%</td>
<td>99.6%</td>
</tr>
<tr>
<td><strong>CT Vaginal (Self)</strong></td>
<td>98.7%</td>
<td>99.4%</td>
</tr>
<tr>
<td><strong>CT Female Urine</strong></td>
<td>97.6%</td>
<td>99.8%</td>
</tr>
<tr>
<td><strong>NG Cervical</strong></td>
<td>100%</td>
<td>100%</td>
</tr>
<tr>
<td><strong>NG Vaginal</strong></td>
<td>100%</td>
<td>99.9%</td>
</tr>
<tr>
<td><strong>NG Female Urine</strong></td>
<td>95.6%</td>
<td>99.9%</td>
</tr>
<tr>
<td><strong>CT Male Urine</strong></td>
<td>97.5%</td>
<td>99.9%</td>
</tr>
<tr>
<td><strong>NG Male Urine</strong></td>
<td>98.9%</td>
<td>99.9%</td>
</tr>
</tbody>
</table>

Pointing to the Future for CT/NG

1. MAMEF-based DNA detection (microwave accelerated metal enhanced fluorescence)

2. Atlas Velox TM System

3. MobiLab
1. MAMEF-based DNA detection

Microwave-based lysing

Ultra-rapid and sensitive detection of biomolecules

Less than 10 minutes       $1.50/ test
$2,500 reader

Microwave-Accelerated Metal-Enhanced Fluorescence DNA detection

Melendez et al. JCM 2013;51:2913-2920
2. Atlas Genetics io™ System

The io™ Reader

• Low cost instrument
• Simple to use
• Small footprint
• No on-board reagents
• Robust. No fragile optical sensors
• Minimal calibration and servicing required
• Results provided as clear, unambiguous output. No interpretation or analysis needed

94.4% sensitivity
97.0% specificity
N=186

3. MobiLab

Droplet cartridge platform

C. Chiou and D. J. Shin et al., Biosens Bioelectron, 2013
**Trichomonas vaginalis**

- Wet Preparation - 55%–65% sensitive
- Affirm - 46.3% sensitive
- **OSOM POC** - 83.3-90% sensitive
- NAAT - 98.3-100% sensitive

OSOM Rapid TV Antigen Test

- Immunochromato-graphic detection
- TV membrane proteins
- Mouse antibodies
- Latex beads/ capillary action

Huppert et al, JCM 2005; STI 2007: Sensitivity 83-90%, Specificity 98-100%

**POSITIVE**
- A blue Test Line and a red Control Line is a positive result

**NEGATIVE**
- A red Control Line but no blue Test Line is a negative result.
AmpliVue® Trichomonas Assay

1) simple sample preparation with one-step dilution/heating
2) isothermal DNA amplification of target sequences specific to *T. vaginalis* by HDA
3) lateral-flow strip based colorimetric detection in a self-contained, disposable device

Sensitivity 100%; specificity 98.2% vs. culture/wet prep. Vs. NAAT PPA 87.2-90.1%

Syphilis

Reverse Algorithm testing recommended in by CDC the U.S.

New POC serology tests for diagnosing syphilis have proliferated; test for treponemal antibody.

Their use is important to syphilis elimination programs worldwide, especially MTCT.
Syphilis serologic screening algorithms

**Traditional**

- Quantitative RPR
  - RPR+
    - TP-PA or other trep. test
      - TP-PA+
        - Syphilis (past or present)
      - TP-PA-
        - Syphilis unlikely
  - RPR-

**Reverse sequence**

- EIA or CIA
  - EIA/CIA+
    - EIA/CIA-
      - Quantitative RPR
        - RPR+
          - Syphilis (past or present)
        - RPR-
          - TP-PA
            - TP-PA+
              - Syphilis unlikely
            - TP-PA-
              - Syphilis unlikely

CDC recommended algorithm for reverse sequence syphilis screening followed by nontreponemal test confirmation.

POC tests

Non-Treponemal

If at risk for syphilis, repeat RPR in several weeks.
POC Syphilis Health Check™

Syphilis Antibody Rapid Immunochromatographic Test

• Rapid qualitative screening for human TP antibodies in whole blood, serum or plasma
• Results in 10 minutes; 2 steps; room temperature
• 98% agreement to other treponemal tests
• Serum, plasma or whole blood or finger-stick

Negative: 1 colored band in control area
Positive: Colored bands in test area and control area
Inconclusive: No distinct color bands in either area

FDA Cleared
CLIA Waived
Chembio Diagnostic Systems has developed the first dual HIV 1/2 and Syphilis Treponemal antibodies Point-of-Care (POC) test utilizing patented Dual Path Platform (DPP®) technology.
HIV

CLIA-Waived Point-of-Care Rapid HIV Tests

OraQuick Advance

Clearview Complete

Uni-Gold Recombigen

Clearview Stat Pak

INSTI
Among 827 sexually active non-HIV-positive participants, 89% had been tested for HIV.

Most preferred by participants was home rapid testing (46%), followed by standard-of-care (23%) and rapid testing in healthcare (20%) or community settings (7%).

About 73% of participants preferred rapid over non-rapid testing, and 56% preferred testing in non-healthcare settings rather than in healthcare settings.
OraQuick Kit:

1. First open part A of the OraQuick Kit, remove the lid from the vial, and place both firmly in the blue stand.

2. Next, using the collection device, swab once around the gums, both top and bottom. Make sure the swab rubs against the base of the gums.

3. Last, insert the collection device fully into the vial so that it is sitting in the liquid in the bottom of the vial. Then set a timer for 20 minutes and read your results.

NEGATIVE RESULT:
- Control Bar
- Test Bar
Any visible pink line at the test bar (T), even a faint line means you have a positive result.

POSITIVE RESULT:
- Control Bar
- Test Bar
- Test Bar

INVALID RESULT:
- Control Bar
- Test Bar
- Test Bar
Emergency Departments: Critical Venue HIV Tests
Feasibility, Acceptability, and Accuracy
HSV

HSV-1
HSV-2
The IsoAmp® HSV Assay (Biohelix Corp)

- FDA-cleared for HSV in genital and oral lesions
- The IsoAmp HSV has a test-to-result time of <1.5 hr.
- Isothermal helicase-dependent amplification (HDA) technique; no nucleic acid extraction
- The rapid and simple characteristics of the IsoAmp HSV assay make it potentially suitable for POC testing

Lemieux et al. Expert Reviews Ltd. 437-443, 2012;
Why do POCTs?

- Improve patient satisfaction (privacy)
- Treat patients before leave clinic
- Provide counseling on risk reduction
- Decrease interval of disease spread
- Improve clinical practice efficiency
- Improve medical outcomes

Published data to substantiate these claims are rare to date
Barriers to implementation of POCTs

- Financial viability
- Money for instruments and consumables
- Obtaining CLIA certificate
- Validating the new test(s)
- Policies and procedures (training manuals)
- Operator training (recertification, proficiency)
- Getting results into the EMR (interface- $7K?)
- Space
- Work Flow Disruption
- Billing and Reimbursement
Conclusions

• POCTs in primary/STI care have great potential
• But there are barriers to successful implementation that need to be overcome which can be costly, time consuming, and require learning new skill sets
• Better POC tests are coming; the future is promising
• Can researchers point the way?
POINTING the WAY for POC Tests

Acknowledgements

• Anne Rompalo
• Mary Jett-Goheen
• Mathilda Barnes
• Justin Hardick
• Jeff Holden
• Laura Dize
• Perry Barnes
• Brianna Kyburz

cgaydos@jhmi.edu
410-614-0932