Advances in STI Testing
Clinical Advances in Pediatrics
Children’s Mercy Health Network
November 18, 2010
Cynthia Holland-Hall, MD, MPH
Associate Professor of Clinical Pediatrics
The Ohio State University College of Medicine
Physician, Section of Adolescent Health
Nationwide Children’s Hospital
Columbus, Ohio

Disclosures
I have no actual or potential conflict of interest in relation to this program.

Learning Objectives
At the end of this activity, the participant will be able to...
• ...screen adolescents for STIs appropriately, according to published guidelines.
• ...offer less invasive techniques for screening, without sacrificing sensitivity.
• ...consider the use of Point-of-Care vaginitis testing in appropriate settings.

Youth Risk Behavior Surveillance
• Administered biannually by CDC in all 50 states
• 9-12 grade students in public and private schools
• Anonymous, self-administered questionnaire
• 16,400 surveys analyzed in 2009
• State and national data available online
  - www.cdc.gov/yrbs
• Highest risk youth not represented

YRBS 2009: Sexual behaviors
• 46% of high school students have had sex
  – 32% of 9th graders
  – 62% of 12th graders
• 14% have had more than four sexual partners
  – 21% of 12th graders
• 40% state they DID NOT use a condom the last time they had sex
• All relatively stable throughout the past decade


CDC, 2009
Prevalence of STIs

14–19 year-old U.S. females (n=838)

<table>
<thead>
<tr>
<th></th>
<th>Overall</th>
<th>Sexually Experienced</th>
</tr>
</thead>
<tbody>
<tr>
<td>HPV (HR/6/11)</td>
<td>18.3%</td>
<td>29.5%</td>
</tr>
<tr>
<td>Chlamydia</td>
<td>3.9%</td>
<td>7.1%</td>
</tr>
<tr>
<td>Trichomonas</td>
<td>2.5%</td>
<td>3.6%</td>
</tr>
<tr>
<td>HSV-2</td>
<td>1.9%</td>
<td>3.4%</td>
</tr>
<tr>
<td>Gonorrhea</td>
<td>1.3%</td>
<td>2.5%</td>
</tr>
<tr>
<td>“Any STI”</td>
<td>24.1%</td>
<td>37.7%</td>
</tr>
</tbody>
</table>

Forhan SE, Pediatrics, 2009

“Any STI” prevalence by number of lifetime sexual partners

<table>
<thead>
<tr>
<th># of lifetime partners</th>
<th>n</th>
<th>Prevalence “any STI”</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>125</td>
<td>19.7%</td>
</tr>
<tr>
<td>2</td>
<td>62</td>
<td>38.1%</td>
</tr>
<tr>
<td>≥3</td>
<td>159</td>
<td>53.5%</td>
</tr>
</tbody>
</table>

Forhan, Pediatrics, 2009

Screening Guidelines: STI

• CDC/USPSTF: All sexually active females under 25 years of age should be screened annually for *Chlamydia trachomatis* infection.
• High risk women should be screened for gonorrhea as well
• Most Adolescent Medicine docs screen for gonorrhea, Chlamydia, and Trichomonas at least annually (more frequently for high-risk?)

Is my patient “high risk”?

• Two biggest risk factors for STI:
  – Prior STI
  – Young age
• Also consider:
  – New partners since last tested
  – Multiple partners
  – Erratic and/or improper condom use

HIV Screening

• CDC now recommends universal screening of patients >13 years old
  – Targeted screening (only) no longer recommended
  – “Opt out” testing
  – Written informed consent no longer recommended
  – Pre- and post-test counseling no longer mandatory
  – Consult state/local policy re: the above
**Syphilis Screening**
Determine on case-by-case basis
- Geography
- Sexual practices
- Demographics
- Drug use, partners’ drug use

**HPV and Cervical Dysplasia**
- Recent revision of guidelines by ACOG
- Begin screening healthy women at 21 yoa
  - Pap smear
  - No role for HPV testing in adolescents at this time
  - Regardless of sexual activity
  - Immunocompromised adolescents should be screened if sexually active

**What about the boys?**
- No widely-accepted guidelines for screening heterosexual adolescent males
  - Hard to demonstrate cost effectiveness of routine screening
  - Sequelae of missed infection less serious (and less expensive)

**But the girls must get it from someone, so…**
- Reasonable practice to offer screening for Chlamydia and gonorrhea
  - Urine testing with NAAT
  - Urethral swab for other tests
- RPR if risk factors present
- CDC recommends HIV testing

**Males who have sex with males (MSM)**
- Test based on sexual practices, not stated sexual orientation
- Explicit guidelines exist for males who have sex with other males (MSM)
  - Available from CDC
  - Most not empirically derived

**Screening Guidelines for MSM**
- HIV, syphilis screening annually
- Gonorrhea and Chlamydia screening
  - Annually
  - Sites for screening based in individual practices (urethral, pharyngeal, rectal)
- More often in highest risk men
STI Testing: What Tests to Use

Nucleic Acid Amplification Tests (NAAT)
- Amplify DNA over 1 million-fold
- Dramatic improvement in sensitivity for diagnosing Chlamydial infections
- Good sensitivity for gonococcal infections as well
- High sensitivity allows for testing of specimens other than urethral or endocervical swabs

Nucleic Acid Amplification Tests
- APTIMA (GenProbe)*
  - Transcription-mediated amplification (TMA)
- COBAS Amplicor (Roche)
  - Polymerase chain reaction (PCR)
- BD ProbeTec ET (Becton, Dickinson)*
  - Strand displacement amplification (SDA)
- All offer combination testing for both gonorrhea and chlamydia on a single sample
- * APTIMA and BD ProbeTec ET approved for vaginal specimens

Urine Testing
- All NAAT approved for urine testing for Chlamydia in both genders
- TMA, SDA approved for urine testing for gonorrhea in both genders
- PCR approved for urine testing for gonorrhea in males only

First-Catch Urine
- At least one hour since last void
- NOT a clean-catch specimen
- First 5-10 ml of urine stream (max!) collected in sterile specimen cup
- Remainder of void into toilet
- May be left at room temperature for 24 hours

Systematic Review of Urine Testing
Cook (Ann Intern Med 2005;142:914)
- Reviewed 29 well-done studies
- Compared urine testing using NAAT to endocervical and/or urethral testing using NAAT
- NOT a head-to-head comparison of different NAAT
- In each study, sensitivity of urine was approximately the same as sensitivity of endocervical or urethral specimen
Sensitivities of Urine NAAT

<table>
<thead>
<tr>
<th>Sensitivities</th>
<th>PCR</th>
<th>TMA</th>
<th>SDA</th>
</tr>
</thead>
<tbody>
<tr>
<td>CT/female</td>
<td>83.3%</td>
<td>92.5%</td>
<td>79.9%</td>
</tr>
<tr>
<td>CT/male</td>
<td>84.0%</td>
<td>87.7%</td>
<td>93.1%</td>
</tr>
<tr>
<td>GC/female</td>
<td>55.6%</td>
<td>91.3%</td>
<td>84.9%</td>
</tr>
<tr>
<td>GC/male</td>
<td>90.4%</td>
<td>Insufficient Data</td>
<td></td>
</tr>
</tbody>
</table>

Urine NAAT: The Good, the Bad, and the Ugly

- **GOOD**: Urine is just about as sensitive as endocervical or urethral testing.
- **BAD**: In either case, false-negatives do occur.
- **UGLY**: Cannot use PCR to diagnose gonorrhea in women using urine.

Summary: Urine testing

- Appropriate means of screening asymptomatic males and females for gonorrhea and Chlamydia
- Appropriate for symptomatic males as well
- Symptomatic females should have more thorough evaluation

Vaginal Swabs

- Equivalent sensitivity to endocervical swabs in most studies
- Presumably includes both urethral and cervical secretions
- Most studies show superior sensitivity to FCU
- Equivalence between physician-collected and patient-collected specimens
- Minimal difference between dry specimens and those in buffer (more studies needed)

Self-Obtained Vaginal Swabs

<table>
<thead>
<tr>
<th>Author</th>
<th>N</th>
<th>Test</th>
<th>Sensitivity</th>
<th>Specificity</th>
</tr>
</thead>
<tbody>
<tr>
<td>Polaneczky 1998</td>
<td>101</td>
<td>CI/PCR</td>
<td>100%</td>
<td>95%</td>
</tr>
<tr>
<td>Carder 1999</td>
<td>104</td>
<td>CI/PCR</td>
<td>89-93%</td>
<td></td>
</tr>
<tr>
<td>Domeika 2000</td>
<td>94</td>
<td>CI/PCR</td>
<td>89%</td>
<td></td>
</tr>
<tr>
<td>Gaydos 2002</td>
<td>793</td>
<td>CI/NG PCR</td>
<td>89-96%</td>
<td>98-99%</td>
</tr>
<tr>
<td>Knox 2002</td>
<td>318</td>
<td>CI/NG PCR</td>
<td>85% / 72%</td>
<td>97% / 100%</td>
</tr>
<tr>
<td>Garrow 2003</td>
<td>349</td>
<td>CI/NG</td>
<td>89% / 96%</td>
<td></td>
</tr>
<tr>
<td>Schachter 2005</td>
<td>1464</td>
<td>CI/NG TMA</td>
<td>98% / 98%</td>
<td>97% / 99%</td>
</tr>
<tr>
<td>Fang 2008</td>
<td>342</td>
<td>CI/NG SDA</td>
<td>97% / 100%</td>
<td>95-99%</td>
</tr>
</tbody>
</table>

Vaginal Swabs: Advantages

- Superior sensitivity
- Quality of urine specimen may deteriorate in transport
- Less processing required in lab, compared to urine
- Encourages inspection of the external genitalia
- May be most cost-effective in PID prevention for high risk populations (Blake 2008)
Will Adolescents Like It?

- Multiple studies demonstrate high acceptability of all self-testing methods
- Most studies demonstrate preference for self-testing over pelvic examination
- Slight preference for FCU over SOVS

Vaginal Swabs: Potential Barriers

- Special test kits required
- Buffer solution
- Appropriate NAAT platform required in lab
- Novelty of specimen type

Rapid Diagnostic Tests

(aka Point-of-Care Tests)

Appropriate use of POC tests

- Easily performed by clinic personnel
- Modest amount of training required
- Generate results within 30-60 minutes or less
- For use while patient waits
  - High risk populations
  - Difficult to locate for follow up
  - Unlikely to return to clinic reliably

Trichomonas vaginalis

- Prevalent STI
- Limited sensitivity of widely used diagnostic tests
  - Microscopy: 36-75%
  - Culture: variable; up to 95%
- Range of clinical manifestations
  - Asymptomatic
  - Vaginal discharge
  - Severe vulvovaginitis
  - Adverse pregnancy outcomes

OSOM Trichomonas Rapid Test

- Genzyme Diagnostics
- Uses color immunochrommatographic technology (i.e., dipstick)
- Performed on vaginal swab or saline solution from preparation of vaginal swab
- CLIA waived
- Less than 15 minutes to complete
OSOM Trichomonas Rapid Test

- Huppert (2005, 2007) compared to composite reference standard
  - High prevalence setting
  - Sensitivity 83-90%
  - Specificity 99-100%
- Campbell (2008) compared to composite reference standard
  - Low prevalence setting
  - Sensitivity 95%
  - Specificity 100%

Bacterial Vaginosis

- Overgrowth of *Gardnerella vaginalis* and/or other anaerobes in the vagina
- Most common cause of vaginal discharge among sexually active women
- Commonly diagnosed by microscopy, vaginal pH, and/or amine release test ("whiff test")
- Clinical manifestations
  - Asymptomatic infection
  - Malodorous vaginal discharge, irritation
  - Pregnancy complications

OSOM BV Blue Test

- Genzyme Diagnostics
- Measures activity of sialidase in vaginal fluid
- CLIA waived; Results read after 10 minutes
- Sensitivity 88-92% compared to Nugent (Gram stain) or Amsel (wet mount) criteria (Myziuk 2003; Bradshaw 2005)
- Specificity 91-98%
- Better performance than single tests that do not require a microscope (vaginal pH, "whiff test")

Use of Rapid Tests

- Valuable for the diagnosis of Trichomoniasis and Bacterial vaginosis
- Particularly useful if microscopy is not available
  - Pediatric ED/urgent care
  - Pediatric offices
  - School-based health centers
- Existing rapid tests for gonococcal or Chlamydial infections have unacceptably low sensitivity
Summary

- Test your sexually active patients!
  - Chlamydia and gonorrhea at least annually
  - HIV
  - Consider trichomonas, RPR
- Use the best test you can!
  - Vaginal NAAT
  - Urine NAAT
- Consider rapid diagnostic tests in some settings

Online Resources

- AAP Red Book
- CDC 2006 STD Treatment Guidelines: http://www.cdc.gov/std/treatment/