

# CDC National Infertility Prevention Project Laboratory Update

Region II  
May 13-14, 2009

Richard Steece, Ph.D., D(ABMM)  
DrRSteece@aol.com

---

---

---

---

---

---

---

---



---

---

---

---

---

---

---

---

## New CT/GC Tests

•New Nucleic Acid Amplification Tests (NAATs) for  
Chlamydia and Gonorrhea

- Abbott RealTime CT/NG
- BD ProbeTec™ *Chlamydia trachomatis* (CT) Q<sup>x</sup>  
Amplified DNA Assay
- BD ProbeTec™ *Neisseria gonorrhoeae* (GC) Q<sup>x</sup>  
Amplified DNA Assay

---

---

---

---

---

---

---

---

### Abbott RealTime CT/NG

- Technology
  - Multiplex, PCR technology with homogenous real-time fluorescence detection
- Target Regions
  - C. trachomatis*: Cyptic plasmid
  - N. gonorrhoeae*: Opa gene
- Specimen Types
  - Male: urine and urethral swab
  - Female: urine, vaginal (clinician or self collected)



---

---

---

---

---

---

---

---

### Abbott RealTime CT/NG

- Collection Device
  - Abbott multi-collection specimen collection kit
  - 14 days, 2-30° C
- Internal Control
- Sensitivity
  - Limit of detection 320 copies of CT target DNA
- Specificity
  - No cross reactivity to 111 organisms that are related to CT and NG and those found in the urogenital tract. No cross reactivity to non-pathogenic *Neisseria* strains



---

---

---

---

---

---

---

---

### BD ProbeTec™ Qx Amplified DNA Assay

- Technology
  - BD Viper Automated System with XTR Technology, FOX Extraction, Strand Displacement Amplification
- Target Regions
  - C. trachomatis*: Cyptic plasmid
  - N. gonorrhoeae*: Opa gene
- Specimen Types
  - Male: urine and urethral swab
  - Female: urine, vaginal (self collected), endocervical



---

---

---

---

---

---

---

---

## BD ProbeTec™ Qx Amplified DNA Assay

- Collection Device
  - Specific specimen collection kit
  - 14 - 30 Days, 2-30° C
- Internal Control
- Sensitivity
  - Limit of detection 15 to 30 elementary bodies (EB)
- Specificity
  - No cross reactivity to 141 organisms for CT. Two *N. cinerea* and two *N. lactamica* strains were shown to cross-react in the GC assay ( $\geq 1 \times 10^8$  cells/mL)

---

---

---

---

---

---

---

---

## Future Nucleic Acid Amplification Tests (NAATs) for Chlamydia and Gonorrhea

- HandyLab
- Cepheid
- GenProbe
- Others



---

---

---

---

---

---

---

---

## Laboratory Guidelines for the identification of *Chlamydia trachomatis*/*Neisseria gonorrhoeae*

Expert Panel Meeting  
CDC Atlanta GA  
January 13-15, 2009

---

---

---

---

---

---

---

---

Laboratory Guidelines for the identification of *Chlamydia trachomatis*/*Neisseria gonorrhoeae*

- Performance Issues
- Screening Applications
- “Confirmatory Testing” (Repeat Testing)
- Medico-legal issues

---

---

---

---

---

---

---

---

Performance Issues

- The panel recommended that the new guidelines document present sensitivity and specificity ranges by test class (NAATs, Culture, EIA, Probe, POCTs)
  - Should use published literature to prepare these tables.
- New generations of tests impact sensitivity and specificity of older tests. Older package inserts may be obsolete.
  - Ranges in the guidelines should represent current knowledge, not information stated in the product insert.
  - The newer NAATs product inserts most likely underestimate the true performance of these tests.

---

---

---

---

---

---

---

---

Performance Issues

- NAAT are the most sensitive/specific tests available for CT /GC and should be recommended as test of choice because:
  - of their superior performance.
  - the variety of sample types that can be tested.
- **All** test types have false positive and false negative results.
- Clinicians are responsible for making patient management decisions.

---

---

---

---

---

---

---

---

## Performance Issues

- No appreciable differences in NAAT test performance among those with and w/o symptoms.
  - Equal performance is seen regardless of test purpose (screening and diagnosis)
- There is also a need to maintain national reference culture capability for both CT & GC

---

---

---

---

---

---

---

---

## Performance Issues

- Urine is the preferred specimen type for testing males using NAATs
- Urine has been used in many published studies and performs well
- Many of the recommended specimen types are not yet FDA cleared for every assay
  - These will require individual laboratory verification.
- Vaginal swabs are equal or superior to endocervical swabs or urine for the detection of CT and GC using NAATs and are the preferred sample type
  - Vaginal swabs > Endocervical swabs > Urine

---

---

---

---

---

---

---

---

## Performance Issues

- Some NAATs have been FDA cleared with liquid cytology medium.
- Results of NAAT testing using rectal and pharyngeal specimens are clearly superior to culture for CT and GC detection.
  - Pharyngeal specimens should be tested using a NAAT assay known not to detect commensal *Neisseria spp.*
- Insufficient data to recommend use with ocular specimens

---

---

---

---

---

---

---

---

## Performance Issues

- Serology is not recommended for CT diagnosis
- **Gap in knowledge:** Post treatment, repeat testing can be performed after 3 weeks using the older tests. No new data exist to recommend changing current recommendations.

---

---

---

---

---

---

---

---

## Performance Issues

- Serological tests are not recommended for rectal LGV diagnosis. They may be more helpful in diagnosing the more classical inguinal presentation.
- All currently FDA cleared NAATs will detect the LGV biovar but will not differentiate it from the trachoma biovar.
- Home brews are available to differentiate LGV biovar from others.

---

---

---

---

---

---

---

---

## Screening Applications

- We are recommending many sample types for which FDA clearance is not yet available for all NAATs
- For any specimen-test combination that is not yet FDA cleared, test verification is required by each laboratory.
  - Reference CLIA: checklists are being developed in conjunction with CDC

---

---

---

---

---

---

---

---

## Screening applications

### Economic considerations

- For screening, pooling  $\leq 5$  specimens has been shown to reduce cost without sacrificing performance.
- Gaps in knowledge: other parameters that affect the cost effectiveness of screening programs; cost of false positive vs. cost of missed infection
- NAAT tests allow for non-invasive testing in clinics where no pelvic exam is required.

---

---

---

---

---

---

---

---

## Repeat Testing

- Definitions (confirmatory, supplemental, and repeat testing) and language
- **Not** recommended for CT NAAT
  - No evidence of improved test performance when repeat testing is performed

---

---

---

---

---

---

---

---

## Repeat Testing

- Recommended **ONLY** for GC NAAT for assays that detect commensal *Neisseria spp* in low PPV populations
- Repeat testing for these positives should be performed using a test that does not detect commensal *Neisseria spp*
- Will require individual lab analysis of assay performance in their population

---

---

---

---

---

---

---

---

## Medico-legal issues

- Because NAATs are significantly more sensitive and nearly equal in specificity to culture, they are recommended for medico-legal purposes
- There are numerous studies in adult rape/abuse cases that show NAATs perform superior to culture.

---

---

---

---

---

---

---

---

## Medico-legal issues

- Committee will review the study currently in press on pediatric populations
- We have dialogued with FDA about off label use in pediatric populations and will continue to firm up recommendations
- **Additional discussion with the treatment guidelines group**



---

---

---

---

---

---

---

---

## QUESTIONS?

---

---

---

---

---

---

---

---