

CDC National Infertility Prevention Project
Laboratory Update
Region VIII
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Laboratory Update

- Public Health Laboratory
 - History
 - Mission
 - Core Functions
- New CT/GC Tests
- Laboratory Guidelines
- Marketing by Commercial Companies
 - Public vs. Private

Public Health Laboratory

- History
 - History of Bacteriology – Methods and Tools
 - Louis Pasteur, Robert Kock, Paul Ehrlich, Emil Behring, and others
 - Major movement in the late 1800's and the early 1900's to establish State Public Health Laboratories
 - Diphtheria
 - 1900's est. up to 200,000 case year (10-20% mortality)
 - Iditarod - 1925
 - TB
 - Food and Water

Public Health Laboratory

- **Mission:** Provide a wide range of screening, reference, diagnostic and analytical services for assessment and surveillance of infectious, communicable, genetic, chronic diseases and environmental health concerns, for the citizens of the state (city, county) and national health disease prevention programs. The Public Health Laboratory also helps to coordinate and promote quality assurance for private clinical & environmental laboratories through training, consultation, certification and quality assurance programs. In addition, the Public Health Laboratories provide scientific and managerial leadership for the development of public health policy.

Public Health Laboratory

- Core Functions (11)
 - Disease prevention, control, and surveillance
 - Integrated data management
 - Reference and specialized testing
 - Environmental health and protection
 - Food safety
 - Laboratory improvement and regulation
 - Policy development
 - Emergency response
 - Public health-related research
 - Training and education
 - Partnerships and communication

Public Health Laboratory

- Disease prevention, control, and surveillance
 - Provide accurate and precise analytical results in a timely manner for different diagnostic and analytical functions for assessment and surveillance of infectious, communicable, genetic, and chronic diseases, and environmental exposures
 - Serve as a first line of defense in rapidly recognizing and preventing the spread of communicable diseases by:
 - examining specimens for identifying disease outbreaks
 - isolating and identifying the causative agent
 - determining the source of infection
 - identifying carriers and locating sources of infection in the environment.

Public Health Laboratory

- Disease prevention, control, and surveillance (cont.)
 - Serve as a center of expertise for the detection and identification of biologic agents of significance in human disease; as such, ensure access to laboratory expertise and capabilities in the disciplines of bacteriology, virology, mycobacteriology, and etc.
 - Provide specialized tests for low-incidence, high-risk diseases (e.g., tuberculosis, rabies, botulism, and plague); detect epidemiologic shifts (influenza); and detect newly emerging pathogens (SARS), and etc.

Public Health Laboratory

- Disease prevention, control, and surveillance (cont.)
 - Provide population surveillance, or screening, for conditions of interest to the public health community, including screening for inherited neonatal metabolic disorders, environmental toxins, immune status, risk factors, chronic blood diseases, blood lead, and antibiotic resistance.
 - Perform tests to meet specific program needs of public health agencies.



New CT/GC Tests

- New Nucleic Acid Amplification Tests (NAATs) for Chlamydia and Gonorrhea
 - Abbott RealTime CT/NG
 - BD ProbeTec™ *Chlamydia trachomatis* (CT) Q^x Amplified DNA Assay
 - BD ProbeTec™ *Neisseria gonorrhoeae* (GC) Q^x 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, 2-30⁰ 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™ Q^x 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

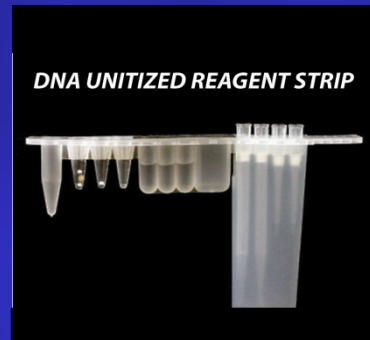


BD ProbeTec™ Q^x Amplified DNA Assay

- Collection Device
 - Specific specimen collection kit
 - 14 - 30 Days, 2-30⁰ 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

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 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 ≤ 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 needed among treatment guidelines group**



Public vs. Private

Privatization

- **ADVANTAGES**
 - Lower Costs

Privatization

- **ADVANTAGES**
 - Lower Costs?

Privatization

- **ADVANTAGES**

- Lower Costs?

- Remember the private laboratory is in business to make \$\$\$

Privatization

- **DISADVANTAGES**

- Lost Leader – Cheap the first year
- Cost of Contracting (10-20% of the value of the contract)
- Cost of Monitoring QA
- Repeat test, e.g. questionable results
- Specimens available for special studies, evaluations
- Technology changes – stuck with contract

Privatization

- **DISADVANTAGES**

- Manufacturers go out of business (Abbott)
- Need additional information, e.g. new data request from CDC
- Laboratory costs can rise for other tests
- Public Standards - Watchdog
- Public Health Team vs. \$\$\$
- Maintain Core Public Health Infrastructure

QUESTIONS?