2011 Annual Meeting Abstracts

Bacterial ID-Molecular Methods

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Why Use A Molecular Method?

- Need Speed
  - Rapid diagnosis leads to an intervention in the patient
  - Culture takes days to weeks
- Need Sensitivity
  - Down to a very few organisms
  - Non-culturable
- Need quantification, not just a qualitative result
- Need safety
- No other way to differentiate organism

Nucleic Acid Amplification Tests

Pros	Cons
Don't need live organism	Might detect dead organisms
Low limit of detection	Too sensitive-sometimes one is not enough to be relevant.
Turn Around time	High cost-reagents, instrumentation
Safety of nucleic acid	Potential for cross-contamination

FDA Cleared or Approved Tests-Bacterial

- *C. difficile*
- *C. trachomatis*
  - NAA: considered gold standard/ standard of care
  - Up to 30% more sensitive than culture
  - Specificity approaching 100%
  - Broad range of acceptable specimen types
- *N. gonorrhoeae*
  - Standard of care is NAAT
  - Specificity improved over 1st generation tests
  - Broad range of specimen types
- Group A and Group B Strep
- MRSA/MSSA
  - PCR available for screening for carriage, screening to optimize patient management, quality measure for hospitals
- Mycobacteria species
- Vancomycin resistance
- Bio-threat agents

Gene Sequencing

- Use as a secondary approach when easy identification methods fail
- Instead of multiple biochemical test algorithms
- Less proficiency with some biochemical tests

Pros and Cons of Gene Sequencing

Pros	Cons
Relatively fast	Costly Equipment, Reagents, labor
Very specific	Need pure isolate
Same protocol all isolates Versus many biochemical assays	Database can fool you
	Taxonomy and nomenclature issues

The Future of Molecular Diagnostics

- Molecular ID of positive blood cultures
- Increasing multiplex capabilities
    - Relevant pathogens within specimen type or clinical presentation
- Gene Sequencing
    - To remain the gold standard for isolate ID
    - Use for unusual organisms
- MALDI-TOF MS to replace conventional phenotypic identification for routine pathogens

Antimicrobial Stewardship: Focus on the Role of Microbiology

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Defining Antimicrobial Stewardship

- Activity that includes the appropriate section, dosing route and duration of antimicrobial therapy
- Primary goal is to optimize clinical outcome while minimizing unintended consequences of antimicrobial use including:
    - Toxicity
    - Selection of pathogenic organisms
    - Emergence of resistance
- Secondary goal-reduce health care costs without adverse impact on quality of care
    - Delite et al. Clin Infect Dis.2007;44:159-77

Antimicrobial Stewardship Team

- ID physician
- Clinical Pharmacists with ID training
- Clinical Microbiologist

- Information system specialist
- Infection control professional
- Hospital epidemiologist (optional)

What are the Elements of Antimicrobial Stewardship

- Core Strategy 1: Prospective Audit with Intervention and Feedback
    - Concurrent review of patients receiving antimicrobials
    - Inappropriate orders initiate interaction between antimicrobial members and the prescriber

- Core Strategy 2: Formulary Restriction/Preauthorization
    - Effective method to control antibiotic use and cost

Microbiology Role In Stewardship

- Detection and identification (rapid) of organisms
- Susceptibility testing in individual patients
    - Reporting procedures (cascade reporting)
        - IF the microbe is susceptible to X don't report Y
    - Reporting procedures (Hiding susceptibilities)
        - Don't report drugs you don't want prescribers to sue (e.g. fluroquinolones for *Staphylococcus aureus* bacteremia)
    - Reporting procedures (notes on reports)
        - Helpful notes attached to culture reports
        - Link to guidelines
        - Help with interpreting cultures
- Breakpoints interpretation/implementation
- Antibiogram preparation and interpretation
    - Preparation and analysis of cumulative susceptibility testing at least annually
        - CLSI Doc M39-A provides guideline for preparation
            - Include only species with at least 30 isolates
            - Include diagnostic (not surveillance) isolates
            - Include 1st isolate/patient
            - Include only drugs **routinely** tested
            - Calculate %S (do not include %I)
- Evaluation of resistance trends

Why doesn't every institution have an antimicrobial stewardship team?

- Funding Issues
    - Limited resources available
        - May computer with other programs (e.g. infection control)
    - Overall antimicrobial stewardship program costs are not well-described in most studies
    - Proof of sustained benefit is lacking for most interventions
- Implementation Issues
    - Lack of direction in the guidelines for smaller, non-academic institutions

- Guidelines don't address outpatient or long term care facilities
- Fear of being labeled "Antibiotic Police"
- Programs may be perceived as self-serving (endorsed by those with the most gain)
- No endorsement by QA groups or accreditation organizations

New Guidelines for the Prevention of Early-Onset Group B Streptococci Disease
What's A Lab To Do?
Roberta B. Carey Ph.D.
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2010 Guidelines: Collection and Transport

- Type of swab acceptable for antenatal screening vaginal/rectal swabs only; cervical swabs or perianal/perirectal not acceptable
- Recommend use of non-nutritive transport media-e.g. Amies or Stuart's (with or without charcoal)
- Group B Streptococcus (GBS) viability declines over 1-4 days at high temperatures, refrigerate if dealy before processing

2010 Guidelines: Culture

- Remove swab from transport media and inoculate selective borht medium
  - TransVag broth
    - Incubate 18-24 hours at 35-37 C and subculture to sheep blood agar (SBA), Columbia agar with colistin/Nalidixic acid (CNA)or chromagar
  - LIM broth
    - Incubate 18-24 hours at 35-37 C and subculture to BAP,CNA or chromagar
  - Selective enrichment broth
    - Incorporates chromogenic pigments for the detection of GBS using color detection
      - Examples: Strep B carrot broth or Granada Biphasic broth
    - Monitor for color change
- Chromogenic Media
  - Studies show majority agars and broth equal to or better than SBA/CNA and LIM broth for GBS recovery
    - Added advantage of detection within 24 hours
    - Positives do not require confirmation by latex agglutination
- Non- hemolytic GBS
  - Approximately 4% of invasive GBS isolates are non-0hemolytic
  - Chromogenic broths do not detect non-hemolytic GBS
  - Most chromogenic agars do not detect non-hemolytic GBS

    - Need to subculture all negative chromogenic media if they don't detect non-hemolytic isolates
- Optional Direct Broth Testing
    - Detection of GBS can be determined directly from broth media using latex agglutination, probes or nucleic acid amplification tests (NAAT) such as PCR.

2010 Guidelines: Nucleic Acid Amplification Tests

- Recommendation for PCR antepartum testing (antepartum before labor begins)
    - For identification of GBS from enrichment broth
    - Not to replace culture
- Recommendations for PCR for intrapartum (woman in labor)
    - NAAT may be performed on patients with unknown GBS status and no risk factors who present at triage or labor/delivery
    - For clinical utility test results should be reported within 2 hours and PCR testing should be available 24/7

PCR Assays Available

Assay	**GeneOhm**	**Smart GBS**	**GeneXpert**
Hands on time	18 min	25 min	2-3 min
Total Test Time	70 min	75 min	$\leq$ 80 min
Complexity	High	High	Moderate
External Controls	yes	Yes	No
Cost	$18-26	$18-26	$40-45

PCR Tests Performance
Based on Manufacturing Package Insert

Test	% Sensitivity	% Specificity
BD GeneOhm Strep B	94%	96%
Cepheid Smart GBS	85%	97%
Cepheid Xpert GBS	92%	90%

2010 Guidelines: GBS Bacteriuria

- GBS can cause symptomatic and asymptomatic UTI
- GBS bacteriuria is a marker for heavy genital tract colonization and these women should receive IAP
- Laboratories should report significant concentrations ($\geq 10^4$ cfu/ml) of GBS bacteriuria in pregnant women
- Report $\geq 10^4$ GBS in pure culture or in the presence of a second organism (*E.coli* and GBS)

2010 Guidelines: Antimicrobial Susceptibility Testing (AST)

- Specimen requisitions for GBS testing should identify the patient at high risk for anaphylaxis as penicillin allergic and antibiotic susceptibility testing for clindamycin and erythromycin should be ordered
- CLSI M100-S21 performance Standards recommend using
    - Disk diffusion
    - Broth microdilution
        - FDA-cleared/approved commercial system may also be used
    - Testing for inducible clindamycin resistance
        - D Zone of other validated test

Summary of Key Changes

- **Vaginal/Rectal Culture**
    - Expand swab options
    - Option to use chromogenic broths and agars
    - Option to use antigen detection, probe NAAT from broth
    - Direct plating can accompany broth inoculation (not replace)
- **Molecular ID Tests**
    - Not recommended for routine 36-37 week antenatal screening
    - Recommended direct testing for women with no risk factors and no prenatal screening
    - Recommended for use on broth enriched cultures to ID GBS
- **Urine Culture Screening**
    - Report GBS at $\geq 10^4$ CFU/ml in pregnant women
- **AST**
    - Test for inducible clindamycin resistance when women is at high risk for anaphylaxis due to penicillin allergy

CDC Website For GBS : http://www.cdc.gov/groupb