Antimicrobial Stewardship in the Emergency Department

Opportunities and Challenges for Rapid Molecular Diagnostics

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Objectives

- Overview of the importance of antimicrobial stewardship in the ED
- Discuss key strategies for antimicrobial stewardship in the ED
- Review recent studies on the potential role of rapid diagnostics to facilitate delivery of optimal antimicrobial therapy in the ED
- Outline future needs and limitations
Overview of Antimicrobial Stewardship

• Growing problem of antimicrobial resistance
• Inappropriate prescribing in a variety of healthcare settings
• Increased morbidity, mortality and healthcare cost
• Patient safety issue
  • adverse events
Overview of Antimicrobial Stewardship

• Collection of strategies—policies, guidelines, surveillance, data transparency, education, and evaluation
• Optimize antibiotic practices
• Improve healthcare outcomes
• Reduce cost
• Reduce resistance
Overview of Antimicrobial Stewardship: Why the ED?

- Nexus of community and hospital
- “Safety Net”
- 15% of ED visits result in antibiotic prescription
- Treat variety of conditions along the spectrum of severity
Overview of Antimicrobial Stewardship: Why the ED?

- Overuse of antibiotics for common ID problems (URI)
- Overuse of broad spectrum antibiotics (SSTI, UTI)
- Guideline adherence
- Unique challenges to ED necessitate ED tailored solution
Challenges for the ED

• High rates of ED crowding
• Rapid rate of patient turnover
• Quick decision-making
• Large/varied mix of providers working in shift-based scheduling format
• Diagnostic uncertainty
• Concern for poor outcomes
• Lack of patient follow-up
• Patient satisfaction
Approaches to AMS in the ED

• Engage ED clinicians in existing ASP
• Multidisciplinary collaboration
• Education
• Guidelines
• Audit and Feedback
• Clinical decision support
• Rapid Diagnostics
Clinician Education

• Active programs
• ED tailored educational messaging
• Multidisciplinary grand rounds
• Engagement of thought leaders from the ED
• Unlikely to lead to enduring changes without ongoing oversight
ED-Specific Guidelines

• Clinical practice guidelines
• Opportunity to tailor based on individual facility susceptibilities and formulary
• Provider education and feedback
• Clinical pathways
ED Pharmacist

- Recent literature suggests ED pharmacist can be key component of clinical care team
- Facilitate appropriate prescribing
- < 5% of EDs have one
- Define outcome measures for ASP in ED


Gaieski DF, Mikkelsen ME, Band RA, et al. Impact of time to antibiotics on survival in patients with severe sepsis or septic shock in whom early goal-directed therapy was initiated in the emergency department. Crit Care Med. 2010;38:1045-1053.
Clinical Decision Support

- Health information technology
- Handheld systems found to reduce antibiotic use and LOS in ICU
- CDSS reduces unnecessary antibiotic use in outpatient setting
- Widespread implementation slow
- **Ideal**: incorporate patient data at point of electronic prescribing
- Limit information overload

Antimicrobial Order Forms

- Facilitate implementation of guidelines
- Challenges include inconvenience and time burden
- Need to fit into ED workflow

Post-prescription Review

• Inpatient strategy
• Telephone follow-up
• Care coordination
• “Wait and see” approach
• Shorten duration of therapy
• Streamlining

Rapid Diagnostics for ASP

• Improving access to rapid diagnostics is cornerstone of IDSA effort to curb resistance
• Expanded laboratory capacity has important role in stewardship
• Rapid molecular tests with TAT ~1 hr
• Could be made available at POC
• Assess performance in ED setting
• Consider CLIA waiver
• Cost effectiveness
Potential ED Application of Rapid Diagnostics for MRSA

- Wound cultures not typically sent
  - Where results available > 2 days, treatment not changed
- Cultures useful for epidemiologic purposes not clinical care (TAT)
- Current IDSA guidelines
  - I & D with MRSA active empiric tx while awaiting culture results for complicated abscesses
- GeneXpert MRSA/SA SSTI assay could enable clinicians to choose narrower spectrum antibiotics
GeneXpert System

- System combines on-board sample preparation with:
- Real-time PCR amplification
- Detection of targeted nucleic acid sequences
- Delivers answers from unprocessed samples
Implementation of a molecular assay to improve SSTI outcomes in the ED

- Dual site RCT (GW and JHH ED)
- N=250
- Patients 18 and older presenting with community-acquired abscess
- Excluding:
  - Retreatment for same abscess
  - Post-procedure infection
Aim 1: Feasibility/ Performance

- Determine proportion of MRSA and MSSA in wound specimens (infection) & nares and inguinal specimens (colonization)
- Compare to standard culture
- Performance characteristics
- Assess for pathogen concordance
- Calculate TAT
- Evaluate acceptability
Aim 2: Clinical Outcomes

- Determine the impact of new assay on key outcome measures:
  - Non beta-lactam antibiotic use
  - Guideline adherence
### Preliminary Results: Patient Characteristics

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Frequency (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Patient and Treatment Characteristics (N=20)</strong></td>
<td></td>
</tr>
<tr>
<td>Mean age</td>
<td>37 years</td>
</tr>
<tr>
<td>Gender</td>
<td>55% Male</td>
</tr>
<tr>
<td>Race</td>
<td>85% Black</td>
</tr>
<tr>
<td>Comorbidities (diabetes mellitus, renal disease, immunosuppression, IDU)</td>
<td>30% (15% HIV, 10% DM)</td>
</tr>
<tr>
<td>Prior history of abscess or MRSA</td>
<td>65%</td>
</tr>
<tr>
<td>Antibiotic use in the prior 6 months</td>
<td>35%</td>
</tr>
<tr>
<td>Provider suspected MRSA</td>
<td>55%</td>
</tr>
<tr>
<td>Presenting with multiple abscesses</td>
<td>15%</td>
</tr>
<tr>
<td>Abscess location</td>
<td>Buttock/perineum 50%, Extremities 20%</td>
</tr>
<tr>
<td>Disposition</td>
<td>100% discharged home</td>
</tr>
<tr>
<td>MRSA positive wound culture</td>
<td>40%</td>
</tr>
<tr>
<td>MSSA positive wound culture</td>
<td>5%</td>
</tr>
<tr>
<td>Wound culture negative for <em>S. aureus</em></td>
<td>55%</td>
</tr>
</tbody>
</table>
## Preliminary Results: Treatment Patterns

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Frequency (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Pilot Data (N=20)</strong></td>
<td></td>
</tr>
<tr>
<td>Wound MRSA positive by GeneXpert®</td>
<td>40%</td>
</tr>
<tr>
<td>Antibiotics prescribed to patients that were found to be MRSA positive</td>
<td>100% non-beta lactam</td>
</tr>
<tr>
<td>Antibiotics prescribed to patients that were found to be MRSA negative</td>
<td>63% no antibiotic use</td>
</tr>
</tbody>
</table>
### Performance at Point of Care (Wound Specimens)

<table>
<thead>
<tr>
<th>Pilot Data and RCT Data* (N=37)</th>
<th>Standard Culture</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>MRSA +</td>
</tr>
<tr>
<td><strong>GeneXpert®</strong></td>
<td></td>
</tr>
<tr>
<td>MRSA +</td>
<td>14</td>
</tr>
<tr>
<td>MRSA -</td>
<td>0</td>
</tr>
</tbody>
</table>

- Sensitivity = **100%** (95% CI = 73-100%)  NPV = **100%**
- Specificity = **100%** (95% CI = 82-100%)  PPV = **100%**

<table>
<thead>
<tr>
<th>Pilot Data and RCT Data* (N=37)</th>
<th>Standard Culture</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>MSSA +</td>
</tr>
<tr>
<td><strong>GeneXpert®</strong></td>
<td></td>
</tr>
<tr>
<td>MSSA +</td>
<td>4</td>
</tr>
<tr>
<td>MSSA -</td>
<td>2</td>
</tr>
</tbody>
</table>

- Sensitivity = **67%** (95% CI = 24-94%)  NPV = **94%**
- Specificity = **100%** (95% CI = 86-100%)  PPV = **100%**
Preliminary Conclusions

- Novel POC assay for SSTIs demonstrated excellent performance for MRSA with mean TAT of 82 min
- Ease of use by non-lab personnel
- GeneXpert test could be used for clinical decision-making in ED
  - reduce unnecessary antibiotic use
- Additional study needs to be conducted to assess
  - How and for which ED patients to implement rapid molecular testing
  - Cost effectiveness
Rapid MRSA Testing in ED for Hospitalized Patients

- Talan et al, IDSA 2011
- Retrospective blinded review
- Admitted adults with complicated SSTI
- **Phase I**: Baseline
- **Phase II**: ED use of rapid test, MD education
- **Phase III**: PharmD direction
<table>
<thead>
<tr>
<th></th>
<th>Phase I n/total (%)</th>
<th>Phase II n/total (%)</th>
<th>Phase III n/total (%)</th>
<th>p-value†</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>All Patients</strong></td>
<td>31/53 (58)</td>
<td>31/50 (62)</td>
<td>28/62 (45)</td>
<td>0.16</td>
</tr>
<tr>
<td><strong>MRSA</strong></td>
<td>1/15 (7)</td>
<td>2/13 (15)</td>
<td>0/19 (0)</td>
<td>0.44</td>
</tr>
<tr>
<td><strong>Non-MRSA</strong>**</td>
<td>30/38 (79)</td>
<td>29/37 (78)</td>
<td>28/43 (65)</td>
<td>0.17</td>
</tr>
</tbody>
</table>

*Treatment with vancomycin, linezolid, daptomycin and TMP/SMX were considered inappropriate for Non-MRSA
** Non-MRSA includes those with no growth and contaminants
† Chi-square and Fishers exact p-values comparing Phase I and Phase III patients
Figure 2. Days of inappropriate antibiotics* among non-MRSA patients by study phase

Median Days

IQR

Phase I

Phase II

Phase III

p=0.04 **

*For phase I, median days of inappropriate antibiotics after admission, and for phase II & III, median days of inappropriate antibiotics after PCR results available

**Mann-Whitney Test p-value comparing Phases I and III
Management of Sexually Transmitted Infections

- Clinical judgment inadequate for appropriate treatment of STI in ED
  - Leads to over/underuse of antibiotics
- Screening not performed in ED due to diagnostic and time constraints
- Poor follow up necessitates treatment at point of care
- Increasing concern regarding resistance
- Public health implications

Management of Sexually Transmitted Infections

- Gonorrhea and chlamydia most common notifiable diseases in ED
  - Positivity rates in ED sufficient to be cost effective for screening
  - ED follow up difficult
  - Delay treatment pending lab results or treat presumptively
- Incorrect treatment can lead to:
  - infected future partners
  - lack of follow up or unnecessary tx
  - patient stress from improper diagnosis

GC-Chlamydia: Cepheid Xpert CT/NG

- Near POCT can reduce time from testing to treatment
- Improve overall treatment rate
- Prevent complications
- Overall assay success 99.6%
- 97-100% sensitive and specific for urine versus endocervical specimens for males and females
- Cost effectiveness likely based on modeling

Huang et al, Comparative effectiveness of a rapid point of care test for detection of Chlamydia trachomatis among women in a clinical setting. Sex transmit Infect, 2012
Patient Pathway

ED/OBGYN, Sexual Health Clinic

Patient exam → Collect sample → Meds (sympt) → Patient leaves

Send-out

Sample arrives lab → Sample results available

Clinician contacts patient → Public Health Reportable

Partner notification

0 → 2hr → 24hr → 48hr → 72hr

In many institutions, results for CT/NG testing can take 24hrs - 1 week
Clinical Impact of delayed confirmation

- Most Clinician’s prefer evidence based treatment for CT/NG²
  - Direct impact on positive patient experience and patient satisfaction
  - Repeat visits are costly and frustrating
- >20% of patients screened cannot be reached in follow up²
  - Spread infection to future partners
  - Complications from untreated infection
  - Resource intensive patient follow-up
- Antibiotic stewardship
  - PID and Chlamydia have different treatment and follow up requirements
  - NG strains are showing increasing antibiotic resistance

### Accuracy

#### Self-Collected Vaginal Swab

<table>
<thead>
<tr>
<th></th>
<th>CT</th>
<th>NG</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sensitivity</td>
<td>99.5%</td>
<td>100%</td>
</tr>
<tr>
<td>Specificity</td>
<td>99.1%</td>
<td>99.9%</td>
</tr>
</tbody>
</table>

#### Urine

<table>
<thead>
<tr>
<th></th>
<th>CT</th>
<th>NG</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sensitivity</td>
<td>98.1%</td>
<td>94.4%</td>
</tr>
<tr>
<td>Specificity</td>
<td>99.8%</td>
<td>99.9%</td>
</tr>
</tbody>
</table>

#### Endocervical Swab

<table>
<thead>
<tr>
<th></th>
<th>CT</th>
<th>NG</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sensitivity</td>
<td>96.0%</td>
<td>100%</td>
</tr>
<tr>
<td>Specificity</td>
<td>99.6%</td>
<td>99.9%</td>
</tr>
</tbody>
</table>

#### Urine

<table>
<thead>
<tr>
<th></th>
<th>CT</th>
<th>NG</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sensitivity</td>
<td>98.5%</td>
<td>98.3%</td>
</tr>
<tr>
<td>Specificity</td>
<td>99.8%</td>
<td>99.9%</td>
</tr>
</tbody>
</table>

All performance results at 95% confidence interval. For details, refer to Package Insert.
Clinical performance characteristics of the Xpert® CT/NG Assay were determined in a multi-site prospective investigational study at 36 US and UK institutions by comparing the Xpert CT/NG Assay to a patient infected status (PIS) algorithm based on results from two currently marketed NAAT tests.
Public Health Impact of CT/NG

- **Screening**
  - <50% of men and women visiting a GP get screened for CT
  - 50% reduction in PID incidence with proactive screening

- **Long-term impact (modeling based)**
  - 26% Screened <25 yrs + 20% Partner Notification
  - Reduction in prevalence of Chlamydia by year
    - 1yr: 29%
    - 5yrs: 68%
    - 10yrs: 82%

- **Reporting**
  - Better reporting can help ensure improved resource allocation for testing & treatment
  - Improvements can flag positive or negative trends earlier to prompt programs to counter negative trends

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1 NICE Guidance: Revised rapid review of evidence for the effectiveness of screening for genital chlamydial infection in sexually active young women and men
Patient Collected Vaginal Swabs

The sample of choice

Archived Webinars:

Cepheid Xpert CT/NG: An exciting and promising new point-of-care rapid test to address the epidemic of Chlamydia and Gonorrhea

Presenter: Dr. Charlotte A. Gaydos

Hear Dr. Charlotte Gaydos discuss Cepheid’s Xpert CT/NG test, a promising new rapid test to address the epidemic of Chlamydia and Gonorrhea.

Chlamydia trachomatis (CT) infection is the most common bacterial sexually transmitted infection (STI) in the United States, with >2,800,000 new cases estimated to occur annually. In 2010, 1.3 million cases were reported to the CDC. Neisseria gonorrhoeae (NG) is the second most prevalent bacterial STI with an estimated 700,000 infections occurring annually, and with 309,341 cases reported in 2010. Both of these infections can result in pelvic inflammatory disease (PID), which can cause serious and costly sequelae (infertility, ectopic pregnancy, and chronic pelvic pain) in women.

<table>
<thead>
<tr>
<th>Specimen Type Preference</th>
<th>Percent</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cervical</td>
<td>15.4%</td>
</tr>
<tr>
<td>Vaginal</td>
<td>50.9%</td>
</tr>
<tr>
<td>Urine</td>
<td>33.7%</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>How Easy or Hard to Collect Vaginal Swab</th>
<th>Percent</th>
</tr>
</thead>
<tbody>
<tr>
<td>Very Easy</td>
<td>62.0%</td>
</tr>
<tr>
<td>Easy</td>
<td>33.7%</td>
</tr>
<tr>
<td>OK</td>
<td>4.0%</td>
</tr>
<tr>
<td>Hard</td>
<td>0.0%</td>
</tr>
<tr>
<td>Very Hard</td>
<td>0.3%</td>
</tr>
</tbody>
</table>
Respiratory Virus Testing

- Viral etiology responsible for three quarters of respiratory infections
- 50% of antibiotics are unnecessary
- Typically adults not tested for viruses
- Children more frequently tested upon hospital admission
- Influenza: sensitivity ranges from 10-75% for RIDTs, specificity 50-100%
- RSV under-diagnosed

Ginocchio, strengths and weaknesses of FDA-approved/cleared diagnostic Devices for the molecular detection of respiratory pathogens, CID 2011; 52(suppl 4)
Respiratory Virus Testing

- Respiratory testing with multiplex technologies daily with <24 hour TAT to provide clinical value
- Technologies targeted to outpatients
  - Inpatients sicker and more likely to receive antibiotics
- Primary outcomes include cost and improved patient management
  - decreased length of stay
  - decreased antibiotic use
  - decreased ancillary test ordering

Respiratory Virus Testing in Adults

- Brittain-Long et al, 2011
- RCT of 447 adult patients with ARTI
- NP and OP swab analysis
- Open-label treatment protocol
- 4.5% of patients in test group received antibiotics compared to 12.3% in control group (p=0.0005)
- No significant difference for outcomes between groups

Brittain Long et al, access to a polymerase chain reaction assay method targeting 13 respiratory viruses can reduce antibiotics: a randomized controlled trial. BMC Medicine 2011; 9:44
### Table 2 Antibiotic prescription at initial visit (and within 48 hours of initial visit) for adult patients with acute respiratory tract infection, according to randomisation group (rapid result vs. delayed result)

<table>
<thead>
<tr>
<th>Antibiotic prescription</th>
<th>Rapid result (n = 202)</th>
<th>Delayed result (n = 204)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Initial antibiotic treatment, n (%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>At initial visit</td>
<td>9 (4.5)</td>
<td>25 (12.3)</td>
<td>0.005&lt;sup&gt;a&lt;/sup&gt;</td>
</tr>
<tr>
<td>After 24 to 48 hours</td>
<td>2 (1.0)</td>
<td>4 (2.0)</td>
<td></td>
</tr>
<tr>
<td>β-lactam&lt;sup&gt;b&lt;/sup&gt;</td>
<td>4 (2.0)</td>
<td>13 (6.4)</td>
<td>-</td>
</tr>
<tr>
<td>Tetracycline</td>
<td>4 (2.0)</td>
<td>8 (3.9)</td>
<td>-</td>
</tr>
<tr>
<td>Macrolide</td>
<td>1 (0.5)</td>
<td>3 (1.5)</td>
<td>-</td>
</tr>
<tr>
<td>Quinolone</td>
<td>-</td>
<td>1 (0.5)</td>
<td>-</td>
</tr>
</tbody>
</table>

| Patient demographics at initial antibiotic treatment, n (%) | | | |
|---|---|---|
| Body temperature ≥38.5°C, n (%) | - | 4 (33.3<sup>a</sup>) | - |
| CRP level ≥50 mg/L, n (%) | 2 (8.3<sup>d</sup>) | 10 (67.0<sup>e</sup>) | <0.001<sup>a</sup> |
| Duration of illness ≤5 days, n (%) | 3 (1.5) | 12 (12.4<sup>a</sup>) | 0.02<sup>a</sup> |
| Duration of illness > 5 days, n (%) | 6 (5.4) | 13 (12.1) | - |
| Patients with virus detected, n (%) | | | |
| Antibiotics prescribed | 3 (3.3<sup>b</sup>) | 11 (12.1<sup>b</sup>) | 0.03<sup>a</sup> |
| Patients with *Mycoplasma pneumoniae* detected, n (%) | | | |
| Antibiotics prescribed, n | 2<sup>h</sup> | 2<sup>h</sup> | - |
| Patients with *Chlamydia pneumoniae* detected, n (%) | | | |
| Antibiotics prescribed, n | 1<sup>i</sup> | - | - |

<sup>a</sup>x<sup>2</sup> test; <sup>b</sup>phenoxymethylpenicillin or amoxicillin with or without clavulanic acid or loracarbef; <sup>c</sup>four (33.3%) of twelve patients; <sup>d</sup>two (8.3%) of twenty-four patients; <sup>e</sup>10 (67.0%) of 15 patients; <sup>f</sup>three (3.3%) of ninety-one patients and 12 (12.4%) of 97 patients, respectively; <sup>g</sup>three (3.3%) of ninety-one patients and 11 (12.1%) of 91 patients, respectively; <sup>h</sup>one patient received antibiotics within 24 hours and the other within 48 hours in each group, for a total of two patients in each group as indicated in table; <sup>i</sup>patient received antibiotics within 48 hours.
Table 3 Results (multiple detections not included) of multiplex real-time polymerase chain reaction assays of all included patients in order of frequency and by randomisation group (rapid vs. delayed result group)

<table>
<thead>
<tr>
<th>Detected pathogens</th>
<th>All patients, n (%)</th>
<th>Rapid result group, n (%)</th>
<th>Delayed result group, n (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Influenza A virus</td>
<td>56 (13.8)</td>
<td>31 (15.3)</td>
<td>25 (12.3)</td>
</tr>
<tr>
<td>Rhinovirus</td>
<td>40 (9.9)</td>
<td>24 (11.9)</td>
<td>16 (7.8)</td>
</tr>
<tr>
<td>Coronavirus (all subtypes)</td>
<td>29 (7.1)</td>
<td>11 (5.4)</td>
<td>18 (8.8)</td>
</tr>
<tr>
<td>Coronavirus OC43</td>
<td>16 (3.9)</td>
<td>4 (2.0)</td>
<td>12 (5.9)</td>
</tr>
<tr>
<td>Coronavirus NL63</td>
<td>11 (2.7)</td>
<td>5 (2.5)</td>
<td>6 (2.9)</td>
</tr>
<tr>
<td>Coronavirus 229E</td>
<td>2 (0.5)</td>
<td>2 (1.0)</td>
<td>-</td>
</tr>
<tr>
<td>Respiratory syncytial virus</td>
<td>18 (4.4)</td>
<td>6 (3.0)</td>
<td>12 (5.9)</td>
</tr>
<tr>
<td>Influenza B virus</td>
<td>14 (3.4)</td>
<td>7 (3.5)</td>
<td>7 (3.4)</td>
</tr>
<tr>
<td>Metapneumovirus</td>
<td>14 (3.4)</td>
<td>6 (3.0)</td>
<td>8 (3.9)</td>
</tr>
<tr>
<td>Parainfluenzavirus types 1 through 3</td>
<td>7 (1.7)</td>
<td>4 (2.0)</td>
<td>3 (1.5)</td>
</tr>
<tr>
<td>Mycoplasma pneumoniae</td>
<td>7 (1.7)</td>
<td>5 (2.5)</td>
<td>2 (1.0)</td>
</tr>
<tr>
<td>Adenovirus</td>
<td>4 (1.0)</td>
<td>2 (1.0)</td>
<td>2 (1.0)</td>
</tr>
<tr>
<td>Enterovirus</td>
<td>1 (0.2)</td>
<td>-</td>
<td>1 (0.5)</td>
</tr>
<tr>
<td>Chlamydia pneumoniae</td>
<td>1 (0.2)</td>
<td>1 (0.5)</td>
<td>-</td>
</tr>
<tr>
<td>No pathogen found</td>
<td>215 (53.0)</td>
<td>105 (52.0)</td>
<td>110 (54)</td>
</tr>
<tr>
<td>Total, N (%)</td>
<td>406 (100)</td>
<td>202 (100)</td>
<td>204 (100)</td>
</tr>
</tbody>
</table>
Respiratory Virus testing in Pediatric Patients

- *Mahoney et al, 2009*
- 661 pediatric patients entered into decision tree model
- Lowest cost for Xtag RVP alone
- $291 saved to replace status quo of DFA+SVC (> 500K per year saved for four hospitals from 1820 pediatric inpatients)

Mahoney et al, Cost analysis of multiplex PCR testing for Diagnosing respiratory virus infections, J of Clin Micr 2009; 47(9)
Pros and Cons of FDA Cleared NAAT for Respiratory Pathogens in ED Setting

- Extensive analytical and clinical validation
- Simple to use fully automated platforms
- Lack of tests for non-viral targets
- Specimen collection
- TAT
- Reimbursement
**Clostridium Difficile Colitis**

- High rate *c. difficile* infection in recent pediatric ED study (12%)
- Community acquired strains
- RT-PCR for *C. diff* more affordable, conduct tests locally
- Multiplex testing has problem with clinical interpretation
- Directly assay for pathogen at time obtaining specimen is ideal for acute care setting

**Role of molecular diagnostics in the management of infectious disease emergencies.**

Klein et al, diarrhea etiology in children’s hospital ED: a prospective cohort study, CID 2006; 43
**C. difficile: Recent Literature**

- *Shin et al, 2012*
- *C. diff* infection growing concern, increased prevalence of hospital and community strains
- Existing methods insensitive & time consuming
- **Xpert *C. difficile* assay:**
  - Real time multiplex PCR to detect toxigenic strains and distinguish 027/Nap1/B1 strain
  - 253 loose stool specimens collected
  - Xpert CD assay found to be 100% sensitive, 94.6% specific compared to VIDAS CDAB 40.8% sensitive and 98% specific

*Shin et al, evaluation of the Xpert clostridium difficile assay for the diagnosis of Clostridium Difficile infection, Annals of Laboratory Medicine, 2012, 32:355-58*
ASP and Diagnostics in the ED

• Goal is to optimize treatment outcomes for individual patients
• Decrease emergence and spread of antimicrobial resistance
• Example: current CAP guidelines do not recommend culture for bacterial pathogens
  • important role in HAP/VAP
• Challenges: determining colonization versus infection, poor quality sputum specimens

Tenover FC, Potential impact of rapid diagnostic tests on improving antimicrobial use. Annals of the New York Academy of Sciences, 2010
**Virology, Oncology and CLIA-Waived Portfolios**

- Entry into New High Volume and/or High Value Markets

**Nine New Tests Targeted in US, Bringing Total to 25**

- MDRO, Norovirus, HIV, HCV, HBV, BCR/ABL Monitor V2, Monitor Bladder CA, Dx Bladder CA, CLIA-Waived Vaginitis
Rapid Diagnostic Testing in the ED

- Failure of clinical judgment and currently available diagnostic testing
- Need quick and accurate data
- Costs not only consideration
- Hospital LOS
- Societal benefits

Rapid Diagnostics in ED: Benefits

- Tremendous opportunity for infectious disease diagnosis and management
- Major benefit of molecular assays is simplicity and minimal hands on time
- Equal or better performance to (direct) culture based approach
- Direct specimen testing
- Opportunities for future research and targeted interventions
Rapid Diagnostic Testing in the ED: Limitations

• False positives and false negatives
• Limit of detection
• Practical issues:
  • Clinician buy-in
  • Clinical significance/interpretation
  • TAT
  • POCT
  • Training of personnel
• Cost

Rapid Diagnostic Testing in the ED: Future Needs

- PCR currently supplements but can’t replace culture for high risk clinical scenarios
- Limited susceptibility info
- False positives
- Need 24 hours service for immediate analysis
- Role for automated systems

Pletz et al, Will PCR based diagnostics improve outcome in septic patients? A clinical view
The future of PCR diagnostics for antimicrobial stewardship?

- Institutional resources, manpower, cost effectiveness must be considered
- Automated platforms save substantial amounts of time and labor
- Direct monetary costs not only consideration
  - Infections averted
  - Hospital stay
  - Antimicrobial resistance
  - Links to public health and infection control (data management, epidemiologic surveillance, outbreak investigation)
Rapid diagnostics in ED: Summary

- Tremendous opportunity for targeting use of antibiotics and improving diagnosis in ED
- Limitations to be addressed:
  - Turn around time
  - Clinician and patient buy in
  - Cost
- Opportunities for future research and targeted interventions
Questions?
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