Sustaining an Antimicrobial Stewardship

"Much needless expense, untoward effect, harm and disappointment can be prevented by better judgment in the use of antimicrobials."

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Objectives

- Describe ways in which to employ local microbiologic data
- Discuss the use of pharmacodynamic principles to optimize clinical outcomes
- Identify supplemental improvement strategies for antimicrobial stewardship
- Discuss modes of communication of stewardship processes and outcomes

Bad Bugs, No Drugs, No ESKAPE!

- Imparts utmost importance on antimicrobial stewardship programs
- It’s not just about streamlining anymore
- Multifaceted approach
  - Selection of appropriate antimicrobial
  - Dose optimization
  - Curative duration of administration
  - Minimization of toxicity
  - Minimization of conditions for selection of resistant strains

Antimicrobial Selection

- Hospital Mortality, %
  - Adequate
  - Inadequate

Initial Antimicrobial Treatment

Clinical Microbiology

- Critical role
  - Timely identification and susceptibility testing
  - Resistance surveillance
- Local antibiograms
  - Pathogen-specific susceptibility data
  - Location-specific susceptibility data
    - Inpatient vs. outpatient
    - ICU vs. ward
  - Adaptation of national guidelines

Local Trends in Antimicrobial Susceptibility

- S. aureus
  - Hospital-wide
  - ICU

- Gentamicin
- Piperacillin-tazobactam
- Tobramycin

Pip-taz = Piperacillin-tazobactam

Clinical Microbiology

- Critical role
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- Local antibiograms
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  - Location-specific susceptibility data
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Use of Local Microbiologic Data for Treatment of HAP

<table>
<thead>
<tr>
<th>Additional Antibiotic</th>
<th>Drugs</th>
<th>None</th>
<th>Ciprofloxacin</th>
<th>Gentamicin</th>
<th>Amikacin</th>
</tr>
</thead>
<tbody>
<tr>
<td>Piperacillin-tazobactam</td>
<td>80%</td>
<td>82%</td>
<td>81%</td>
<td>96%</td>
<td></td>
</tr>
<tr>
<td>Cefepime</td>
<td>81%</td>
<td>83%</td>
<td>82%</td>
<td>96%</td>
<td></td>
</tr>
<tr>
<td>Meropenem</td>
<td>82%</td>
<td>83%</td>
<td>83%</td>
<td>96%</td>
<td></td>
</tr>
</tbody>
</table>

*Data are presented as percentage susceptible to at least one antibiotic.

HAP = Hospital-acquired pneumonia

Don’t Miss a Strep....

- Choosing susceptibility panels for your automated system

- Considerations
  - Formulary
  - Breakpoint, MIC or MIC/Combo
  - Antibiogram
  - ESBL confirmation test
  - Inducible clindamycin screen

Pharmacokinetic/Pharmacodynamic Indices

- AUC: Area under the concentration-time curve
- Cmax: Maximum plasma concentration
- T>MIC: Time above MIC
- MIC: Minimum Inhibitory Concentration

**β-lactam Optimization Strategies**

1. Use of antibiotics with long half-life
2. Increasing the dose
3. Increasing the dosing frequency
4. Increasing the infusion duration

**Extended-Infusion of Meropenem**

![Graph showing concentration over time for Meropenem 500 mg infusion](image)

**Extended Infusions of Doripenem**

![Graph comparing 1 hour and 4 hour infusions](image)

**Review of Clinical Benefits**

- Meta-analysis
  - Continuous or extended infusions of β-lactams

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Odds Ratio (95% confidence interval)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Clinical cure</td>
<td>1.04 (0.74–1.46)</td>
<td>0.83</td>
</tr>
<tr>
<td>Mortality</td>
<td>1.00 (0.48–2.06)</td>
<td>1.00</td>
</tr>
</tbody>
</table>

- Conclusions
  - Use of continuous infusions leads to same results as higher dose antibiotic boluses

**Piperacillin-Tazobactam for Pseudomonas aeruginosa Infection: Clinical Implications of an Extended-Infusion Dosing Strategy**

- 194 patients
  - Extended infusions – 102 patients
  - Intermittent infusions – 92 patients
- APACHE score ≥ 17
- 14-day mortality
  - 12.2% extended infusions vs. 31.6% intermittent infusions
  - \( P = 0.04 \)

**Efficacy and safety of intravenous infusion of doripenem versus imipenem in ventilator-associated pneumonia: A multicenter, randomized study**

![Graph showing efficacy and safety comparison](image)
Pitfalls of Extended-Infusions

- Drug compatibility
- Infusion pump characteristics
  - Drug libraries
  - Programmable vs. non-programmable
  - Lock-outs
- Infusion volume
  - Infusion line dead space
  - Interruptions

Implementation of Extended Infusions

- Identify barriers
  - Systematic
  - Logistics
  - Infusion pump software
  - Personnel
- Extensive education
- CPOE utilization

Supplemental Strategies

- Information technologies
- CPOE
- Computer-assisted decision support
- Rapid molecular diagnostic testing
- Antimicrobial stewardship care bundles

“To Err is Human”

Computer-Assisted Support

- Reduction of:
  - Bug-drug mismatches
  - Overall antibiotic use
  - Excess antimicrobial dosages
  - Excessive-dose days
  - Allergy-drug mismatches
  - Drug-related side effects
  - Antimicrobial costs
  - Total hospital costs
  - Length of hospital stay

CPOE

- Improved compliance with treatment guidelines
- Reduction of:
  - Antimicrobial prescribing errors
  - Antimicrobial costs
  - Length of hospital stay
  - Improved antimicrobial use

Computer-assisted Management Program for Antifungicides at LDS

<table>
<thead>
<tr>
<th>Variable</th>
<th>Penicillin Fos (N=50)</th>
<th>Amphotericin B (N=50)</th>
<th>Difference</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>No of different antibiotic agents treated</td>
<td>23.9 ± 7.2</td>
<td>19.3 ± 7.2</td>
<td>4.6</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Duration of antibiotic therapy (days)</td>
<td>14 ± 5.2</td>
<td>14 ± 5.2</td>
<td>0.0</td>
<td>&gt;0.05</td>
</tr>
<tr>
<td>No. of antibiotic agents</td>
<td>1.0 ± 0.5</td>
<td>1.0 ± 0.5</td>
<td>0.0</td>
<td>&gt;0.05</td>
</tr>
<tr>
<td>No. of patients receiving antibiotics</td>
<td>40 (80.0%)</td>
<td>40 (80.0%)</td>
<td>0.0</td>
<td>&gt;0.05</td>
</tr>
<tr>
<td>Length of stay in ICU (days)</td>
<td>4 ± 2.2</td>
<td>4 ± 2.2</td>
<td>0.0</td>
<td>&gt;0.05</td>
</tr>
</tbody>
</table>

ADVISE Program

![Graph showing statistical significance](image)

**Proprietary Informatics**

- Diverse functions
  - Hospital epidemiology
  - Antimicrobial stewardship

- Programs available
  - TheraDoc
  - SafetySurveillor
  - BD Protect
  - Quality Compass
  - Health Evaluation through Logical Processing (HELP)

**Computer-Assisted Stewardship**

- Institution specific
- Implementation is challenging
  - Technology
  - Identification and participation of users
  - Functionality
  - Time
    - Installation
    - Validation
- Cost

**Rapid Molecular Testing**

- Multiplex detection recently made available
  - Clinical outcome improvement
    - Decreasing time to identification
    - Provision of therapy
      - Earlier
      - More effective
  - Evaluation of clinical outcomes and economic impact

**Rapid PCR S. aureus Blood Culture Test**

![Graph showing comparison](image)
Economic Impact of MRSA PCR

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Pre-PCR period</th>
<th>Post-PCR period</th>
<th>p*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hospital costs by department</td>
<td>(n = 74)</td>
<td>(n = 62)</td>
<td></td>
</tr>
<tr>
<td>Pharmacy, mean (SD)</td>
<td>$15,716 ± 21,271</td>
<td>$262 ± 1,194</td>
<td>.81</td>
</tr>
<tr>
<td>Microbiology laboratory, mean USD ± SD</td>
<td>$686 ± 10,230</td>
<td>561 ± 687</td>
<td>.13</td>
</tr>
<tr>
<td>Room and board</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>ICU, mean USD ± SD</td>
<td>$27,207 ± 25,777</td>
<td>17,737 ± 21,404</td>
<td>.03</td>
</tr>
<tr>
<td>Non-ICU, mean USD ± SD</td>
<td>$12,620 ± 13,491</td>
<td>10,117 ± 10,932</td>
<td>.24</td>
</tr>
<tr>
<td>Other*, mean USD ± SD</td>
<td>$14,842 ± 10,012</td>
<td>16,430 ± 20,077</td>
<td>.02</td>
</tr>
<tr>
<td>Total hospital costs, mean USD ± SD (n = 144)</td>
<td>$90,051 ± 50,076</td>
<td>48,350 ± 50,076</td>
<td>.00</td>
</tr>
</tbody>
</table>


Rapid Viral Testing

- Wake Forest University Baptist Medical Center
- Implementation of viral multiplex PCR
- 2009/2010 influenza season with H1N1
- Immunocompromised patients with pneumonia
  - 10-15% viral
  - Respiratory syncytial virus (RSV)
  - Human metapneumovirus
- Rapid de-escalation of antibiotic therapy if possible

Antimicrobial Stewardship Care Bundles

- Current care bundles include antibiotics
  - “100K lives campaign”
- The missing care bundles
  - Antibiotics for treatment in acute settings
  - Antibiotics as surgical prophylaxis
  - Incorporation into antimicrobial stewardship programs


Implementation of Stewardship Care Bundles

- Quality indicators
  - Documentation of treatment rationale
  - Collection of appropriate cultures
  - Appropriate empiric antimicrobial selection
  - Appropriate deescalation

<table>
<thead>
<tr>
<th>Indicator</th>
<th>Control Phase</th>
<th>Intervention Phase</th>
<th>p*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Documented indication for antibiotic therapy</td>
<td>75 (90) (97)</td>
<td>90 (94) (90)</td>
<td>.12</td>
</tr>
<tr>
<td>Appropriate culture</td>
<td>75 (90) (97)</td>
<td>90 (94) (90)</td>
<td>.06</td>
</tr>
<tr>
<td>Appropriate empirical therapy</td>
<td>67 (84) (89)</td>
<td>90 (94) (90)</td>
<td>.01</td>
</tr>
<tr>
<td>Appropriate deescalation</td>
<td>42 (57) (61)</td>
<td>90 (94) (90)</td>
<td>.01</td>
</tr>
<tr>
<td>All indications combined</td>
<td>133 (89) (92)</td>
<td>90 (94) (90)</td>
<td>.00</td>
</tr>
</tbody>
</table>


Communication

- Education, education, education
- Reports
- Community stewardship
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