Antibiotic Stewardship

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Antimicrobial Stewardship

Objectives:
- Define antimicrobial stewardship and review models for antimicrobial stewardship programs
- The goals of effective antimicrobial stewardship: Appropriate antimicrobial use!
  - Decreased antibiotic resistance
  - Decreased toxicity
  - Decreased long term costs with appropriate therapy (a capitated, DRG-reimbursed world)
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• What is driving AS programs *NOW?*
  – Patient care issues: increasing MDR organisms; few new antimicrobials
  – Joint Commission Requirements (pt, safety)
  – Better microbiology/pharmacy/ID/IC information exchange and collaboration
  – Better understanding of PK/PD and development of resistance (the right dose, for the right organism, at the right tissue site, for the right duration)
  – Hospitals provided US Fed Govt incentive for electronic medical records: the switch is on!
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• A thorough, comprehensive, relevant plan:

  – IDSA And SHEA Guidelines For Developing An Institutional Program To Enhance Antimicrobial Stewardship

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• Multidisciplinary antimicrobial stewardship team
  – Infectious diseases physician
  – Clinical pharmacist with infectious diseases training
  – Clinical microbiologist
  – Information system specialist
  – Infection control professional/hospital epidemiologist

• Antimicrobial stewardship is a component of patient safety, a medical staff function
  – Usually *directed* by an infectious diseases physician or *co-directed* by an infectious diseases physician and a clinical pharmacist
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• Collaboration is Essential between:
  – Antimicrobial stewardship team
  – The hospital infection control committee (AS is not the same as IC)
  – Pharmacy and therapeutics committee
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- Collaboration is essential between
  - Hospital administration
  - Medical staff leadership
  - Medical staff

Antimicrobial stewards are not a new form of Police

Antimicrobial stewardship programs should function as Quality Assurance and Patient Safety programs (required by the Joint Commission (JCAHO))
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• The Infectious Diseases physician and the Director of Pharmacy require, from the hospital administration:
  – Adequate authority
  – Adequate compensation (or, for the pharmacy, allotment of time/resources)
  – Realistic outcomes measures for the program
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- Hospital administrative support for:
  - Infrastructure to measure and track antimicrobial use
  - Infrastructure to measure and track antibiotic resistance/nosocomial infections

Overall cost SAVINGS to the hospital!
Figure 1. Predicted mortality for patients with and without antimicrobial-resistant infection (ARI). APACHE, Acute Physiology and Chronic Health Evaluation.
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Figure 2. Projected cost savings if antimicrobial-resistant infection (ARI) rates were reduced from 13.5% to 10%.

Roberts RR et al. CID 2009;49:1175-84
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• Proactive strategies for the Program:
  – Prospective audit with intervention and feedback
  – Formulary preauthorization and restriction
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- Prospective audit of antimicrobial use with direct interaction and feedback to the prescriber by the ID physician or clinical pharmacist
  - It takes time, but it really works: TACTFULLY explain the prescribing physician how he/she is not complying with accepted standards... find out WHY they selected inappropriate antimicrobials/dosages; educate!
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• Ways to achieve the Goals of the Program
  – *Education* is considered to be an essential element of any program designed to influence prescribing behavior and can provide a foundation of knowledge that will enhance and increase the acceptance of stewardship strategies (A-III)
• However, education alone, without incorporation of active intervention, is only marginally effective in changing antimicrobial prescribing practices and has not demonstrated a sustained impact (B-II).
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- Ways to achieve the Goals of the Program
  - Guidelines and clinical pathways incorporating local microbiology and resistance patterns can improve antimicrobial utilization (A-I)
  - Guideline implementation can be facilitated through provider education and feedback on antimicrobial use and patient outcomes (A-III).
### Refer to Guidelines message:

<table>
<thead>
<tr>
<th>Order</th>
<th>Dose</th>
<th>Calc Dose</th>
<th>Dose Form</th>
<th>Route</th>
<th>Frequency</th>
<th>Recommended Regimen</th>
<th>Start Date</th>
<th>Start Time</th>
</tr>
</thead>
<tbody>
<tr>
<td>Option 1: SELECT BOTH ITEMS - 2 item(s)</td>
<td>Penicillin G IV 12 mg</td>
<td>mg</td>
<td>IV INFUSION</td>
<td>stat</td>
<td>Recommended regimen: q24h x 7-10 days</td>
<td>T</td>
<td>STAT</td>
<td></td>
</tr>
</tbody>
</table>

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<tr>
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<th>Dose</th>
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<th>Route</th>
<th>Frequency</th>
<th>Recommended Regimen</th>
<th>Start Date</th>
<th>Start Time</th>
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</thead>
<tbody>
<tr>
<td>Option 3: SELECT BOTH ITEMS - 2 item(s)</td>
<td>Ceftriaxone IV 1 g</td>
<td>mg</td>
<td>IV INFUSION</td>
<td>stat</td>
<td>Recommended regimen: q24h x 7-10 days</td>
<td>T</td>
<td>STAT</td>
<td></td>
</tr>
</tbody>
</table>

### Chest X-Ray

<table>
<thead>
<tr>
<th>Order</th>
<th>Sign/Symptom/Known Diagnosis</th>
<th>Clinical Question</th>
<th>Method</th>
<th>Schedule</th>
<th>Requested Date</th>
</tr>
</thead>
<tbody>
<tr>
<td>Option 1: XR Chest P.a.</td>
<td></td>
<td></td>
<td>Routine · Rad</td>
<td>T</td>
<td></td>
</tr>
</tbody>
</table>

### Ancillary

<table>
<thead>
<tr>
<th>Order</th>
<th>Indications</th>
<th>Schedule</th>
<th>PRN</th>
<th>PRN for</th>
<th>Priority</th>
<th>Requested/Start Date</th>
</tr>
</thead>
<tbody>
<tr>
<td>Option 1: ECG Routine (12 Lead</td>
<td>Adult 20 yrs or</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

### Laboratory

<table>
<thead>
<tr>
<th>Order</th>
<th>Specimen</th>
<th>Collection Date</th>
<th>Collection Time</th>
</tr>
</thead>
<tbody>
<tr>
<td>Culture Blood</td>
<td>#1 of 2 SPM</td>
<td>Mar-13,2009</td>
<td>STAT, Spm Collected</td>
</tr>
<tr>
<td>Culture Blood</td>
<td>#2 of 2 SPM</td>
<td>Mar-13,2009</td>
<td>STAT, Spm Collected</td>
</tr>
</tbody>
</table>
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Ways to achieve the Goals of the Program
- Antimicrobial order forms can be an effective component of antimicrobial stewardship (B-II) and can facilitate implementation of practice guidelines
- If forms are too simple… just ‘check the box,’ residents may just ‘check the box’ without thinking: is this best dose for MY patient? See “Dose Optimization”
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• Ways to achieve the Goals of the Program
  – *Streamlining or de-escalation* of empirical therapy on the basis of culture results and elimination of redundant combination therapy can more effectively target the causative pathogen, resulting in decreased antimicrobial exposure and substantial cost savings (A-II).
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- Ways to achieve the Goals of the Program
  - *Dose optimization* based on individual patient characteristics, causative organism, site of infection, and pharmacokinetic and pharmacodynamic characteristics of the drug is an important part of antimicrobial stewardship (A-II).
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• Ways to achieve the Goals of the Program
  – *Parenteral to oral conversion* of antimicrobials with excellent bioavailability, when the patient’s condition allows, can decrease the length of hospital stay and health care costs (AI)
  
• Development of clinical criteria and guidelines allowing switch to use of oral agents can facilitate implementation at the institutional level (A-III)

• Pediatrics is FAR AHEAD of adult medicine here…
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- *Health care information technology* in the form of electronic medical records (A-III), computer physician order entry (B-II), and clinical decision support (B-II) can improve antimicrobial decisions through the incorporation of data on patient-specific microbiology cultures and susceptibilities, hepatic and renal function, drug-drug interactions, allergies, and cost.
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• *Computer-based surveillance* can facilitate good stewardship by more efficient targeting of antimicrobial interventions, tracking of antimicrobial resistance patterns, and identification of nosocomial infections and adverse drug events (B-II).
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• Clinical microbiology laboratory
  – Provides patient-specific culture and susceptibility data
    • Can optimize individual antimicrobial management
    • Can assist infection control efforts
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- Process measures (did the intervention result in the desired change in antimicrobial use?)
- Outcome measures (did the process implemented reduce or prevent resistance or other unintended consequences of antimicrobial use?)

Both are useful in determining the impact of antimicrobial stewardship on antimicrobial use and resistance patterns (B-III)

…but measure the RIGHT outcomes, for patients
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**FIGURE 2** Impact of Prospective Audit With Intervention and Feedback

- a) IV antibiotic use down
- b) Costs down

But how did the PATIENTS do?

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a) IV antibiotic use down
b) C diff disease down
TABLE 1. Assessment Tool Used to Classify the Quality of Studies of Antimicrobial Stewardship Programs in Pediatric Settings

<table>
<thead>
<tr>
<th>Measures of Quality</th>
<th>Study Parameters Assessed</th>
<th>Composite Scores</th>
</tr>
</thead>
<tbody>
<tr>
<td>Study clarity (reproducibility)</td>
<td>Adequate descriptions of inclusion/exclusion criteria, intervention(s), outcome(s) measures, statistical analyses</td>
<td>Sufficient clarity: No inadequate or unspecified parameters and ≤2 partially inadequate parameters. Insufficient clarity: ≥1 Inadequate parameter and &gt;2 partially inadequate parameters</td>
</tr>
<tr>
<td>Internal validity (degree of bias)</td>
<td>Potential sources of bias: Subject selection, baseline characteristics of control and intervention groups, investigator bias, detection bias, attrition bias, compliance with intervention, adequacy of statistical analyses</td>
<td>Low risk of bias: No inadequate or unspecified parameters and ≤1 partially inadequate parameter. Medium risk of bias: ≤1 Inadequate parameter or unspecified OR ≤2 partially inadequate parameters. High risk of bias: ≥2 Inadequate or unspecified parameters OR ≥3 partially inadequate parameters</td>
</tr>
</tbody>
</table>
Antimicrobial Stewardship

<table>
<thead>
<tr>
<th>Type of Intervention (n)</th>
<th>Clinical Setting</th>
<th>Primary Outcomes Measured</th>
<th>Antimicrobial Resistance Measured (n)</th>
<th>Study Findings</th>
<th>Moderate to High Risk of Bias (n)</th>
<th>Major Sources of Bias</th>
</tr>
</thead>
<tbody>
<tr>
<td>General education (8)</td>
<td>6 outpatient</td>
<td>Antibiotic prescribing rates</td>
<td>1</td>
<td>8 improved prescribing rates</td>
<td>8</td>
<td>Selection bias, Attrition bias</td>
</tr>
<tr>
<td></td>
<td>2 inpatient</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Dynamic education (4)</td>
<td>2 outpatient</td>
<td>Antibiotic prescribing rates, prescribing errors</td>
<td>0</td>
<td>2 decreased antibiotic use</td>
<td>3</td>
<td>Selection bias, Attrition bias</td>
</tr>
<tr>
<td></td>
<td>2 inpatient</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Parent education (4)</td>
<td>4 outpatient</td>
<td>Antibiotic prescribing rates</td>
<td>0</td>
<td>2 decreased antibiotic use</td>
<td>3</td>
<td>Selection bias, Contamination bias</td>
</tr>
<tr>
<td></td>
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<td></td>
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<td></td>
<td></td>
</tr>
<tr>
<td>Restrictive methods (6)</td>
<td>5 ICU</td>
<td>Colonization and infection rates with resistant pathogens</td>
<td>6</td>
<td>3 reduced resistance</td>
<td>4</td>
<td>Selection bias, Contamination bias</td>
</tr>
<tr>
<td>Ancillary tests (6)</td>
<td>4 NICU</td>
<td>Clinical outcomes, antibiotic use</td>
<td>0</td>
<td>6 decreased antibiotic use</td>
<td>3</td>
<td>Inadequate controls</td>
</tr>
<tr>
<td></td>
<td>2 inpatient</td>
<td></td>
<td></td>
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</tbody>
</table>
# Antimicrobial Stewardship

Table 3. Recommendations to Improve Study Designs to Assess Antimicrobial Stewardship

<table>
<thead>
<tr>
<th>Potential Flaws in Study Quality</th>
<th>Potential Solutions</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lack of generalizability</td>
<td>Use multiple sites with diverse patient acuity and demographics, standardize data collection to allow comparison of design and findings among studies</td>
</tr>
<tr>
<td>Inadequate preintervention data collection</td>
<td>Study at least 3 preintervention and 3 postintervention data points for interrupted time series analysis, implement prolonged baseline data collection (up to 2 yr) to identify secular trends.</td>
</tr>
<tr>
<td>Attrition of participants</td>
<td>Improve/reinforce follow-up of participants</td>
</tr>
<tr>
<td>Contamination between study groups</td>
<td>Separate interventions or study groups geographically</td>
</tr>
<tr>
<td>Compliance with interventions</td>
<td>Monitor compliance with interventions via computerized methods</td>
</tr>
<tr>
<td>Selection bias among participants</td>
<td>Describe patient characteristics including age, comorbidities, socioeconomic status, describe prescriber characteristics such as age, level of training</td>
</tr>
</tbody>
</table>

Patel SJ et al. PIDJ 2007;26:531-537
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• The time is NOW to establish your program
• Organize and lead your team (with an ID pharmacist, if you have one) WITH salary and resource from Hospital Admin
• GOOD LUCK!