A Roadmap to Improve Antibiotic Use: Everyone Is an Antimicrobial Steward

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October 1, 2015
No Conflicts to Report

“IT IS TIME TO CLOSE THE BOOK ON INFECTIOUS DISEASES, AND DECLARE THE WAR AGAINST PESTILENCE WON”

-WILLIAM STEWART
SURGEON GENERAL
1965-1969
ANTIMICROBIAL STEWARDSHIP: WHY DO WE CARE?

CDC Antibiotic Resistance Threats

Urgent Threats
- C difficile
- Carbapenem-resistant Enterobacteriaceae
- Drug-resistant Neisseria gonorrhoeae

Serious Treats
- MDR Acinetobacter
- Drug-resistant Campylobacter
- Fluconazole-resistant Candida
- Vancomycin-resistant Enterococcus
- MRSA
- Other MDR organisms

Concerning Threats
- Vancomycin-resistant Staphylococcus aureus
- Erythromycin-resistant Group A Streptococcus
- Clindamycin-resistant Group B Streptococcus
Urgent Threats: Scope of the Problem

<table>
<thead>
<tr>
<th>Organism</th>
<th>Projected Cases</th>
<th>Projected Cost</th>
<th>Notes</th>
</tr>
</thead>
<tbody>
<tr>
<td>C. Difficile</td>
<td>250,000 Cases 14,000 Deaths</td>
<td>Greater than $1 Billion per year</td>
<td>New FQ-resistant strain</td>
</tr>
<tr>
<td>CRE*</td>
<td>9,000 Cases 600 Deaths</td>
<td>-</td>
<td>Primarily Klebsiella. 4% of acute care hospitals reported at least one case last year, and 18% LTACs</td>
</tr>
<tr>
<td>Drug-Resistant GC**</td>
<td>246,000 Cases</td>
<td>$235 Million per year</td>
<td>Pan-resistant organisms already circulating in Europe, Japan</td>
</tr>
</tbody>
</table>

Source: CDC Antibiotic Resistance Threats 2013

*Carbapenemase-resistant Enterobacteriaceae
**Neisseria gonorrhea
Antibiotic Resistance Emerges Shortly After Commercialization

Antibiotic resistance observed

Clatworthy et al. Nature Chemical Biology 2007

Antimicrobial Resistance: Scope of the Problem

- Antimicrobial resistance in both gram positive and gram negative organisms is widespread.
- Resistance develops quickly after introduction of novel antibacterial agents.
- Once resistance develops, it quickly spreads.

Geographical Distribution of Klebsiella pneumoniae carbapenemase (KPC) infections

CDC.Gov/Get Smart

MRSA = methicillin-resistant Staphylococcus aureus; VRE = Vancomycin-resistant enterococci; FQRP = Fluoroquinolone-resistant Pseudomonas aeruginosa
Spread of CRE Throughout the US...

... And the World

Spread of NDM-1 (New Delhi metallo-B-lactamase) worldwide
Pan-Resistant Gonorrhea: A Coming Plague

- Rates of Resistant Gonorrhea Are Increasing in the United States and Abroad
- In Europe, rates of decreased cephalosporin susceptibility already greater than 5% in most countries
- In the United States, rates of cephalosporin resistance are lower, but increasing
- In the next 10 years, the CDC estimates that pan-drug resistant gonorrhea will be the norm
- Ongoing campaign for new drugs, but nothing on the horizon

Antimicrobial Resistance Associated with Antibiotic Use, and Resistance Associated with Poor Patient Outcomes

<table>
<thead>
<tr>
<th>Pathogen and Antibiotic Exposure</th>
<th>Fold-Risk of Resistance</th>
</tr>
</thead>
<tbody>
<tr>
<td>Carbapenem Resistant Enterobacteriaceae and Carbapenems</td>
<td>15-X</td>
</tr>
<tr>
<td>ESBL-producing organisms and Cephalosporins</td>
<td>6-29-X</td>
</tr>
</tbody>
</table>

Meta-Analysis: Increased Use of Antibiotics Associated with Increased Rates of Antimicrobial Resistance

- Pooled odds ratio across many studies is 1.33
- Note that ALL studies demonstrate an effect of antibiotic use on resistance- the question is the magnitude of the effect.

IMPACT OF ANTIMICROBIAL RESISTANCE ON CLINICAL OUTCOMES

MDR Enterobacteriaceae: Impact on Clinical Outcomes

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Patients with emergence of resistance</th>
<th>Patients without emergence of resistance</th>
<th>Value attributable to emergence of resistance</th>
<th>RR</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Death, a % of patients</td>
<td>26</td>
<td>13</td>
<td>...</td>
<td>5.02</td>
<td>.01</td>
</tr>
<tr>
<td>LOS, b days</td>
<td>30</td>
<td>19</td>
<td>9</td>
<td>1.47</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Hospital charges, d $US</td>
<td>79,323</td>
<td>40,406</td>
<td>29,379</td>
<td>1.51</td>
<td>&lt;.001</td>
</tr>
</tbody>
</table>

**NOTE.** LOS, length of hospital stay; RR, relative risk.
- a The following variables were included in the model: McCabe score, no. of comorbidities, and intensive care unit (ICU) stay.
- b The following variables were included in the model: McCabe score, ICU stay, and transfer from another hospital.
- c The RR for this outcome is also the multiplicative effect.
- d The following variables were included in the model hepatic disease, McCabe score, ICU stay, major surgery, and transfer from other hospital.

Source: Cosgrove CID 2006
**ESBL E. Coli and Klebsiella: Impact on Outcomes and Cost**

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Case patients (n = 33)</th>
<th>Control patients (n = 66)</th>
<th>RR (95% CI)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Death, a % of patients</td>
<td>15</td>
<td>9</td>
<td>...</td>
<td>...</td>
</tr>
<tr>
<td>LOS, b median days</td>
<td>11</td>
<td>7</td>
<td>1.73 (1.14–2.65)</td>
<td>.01</td>
</tr>
<tr>
<td>LOS, c median days</td>
<td>11</td>
<td>7</td>
<td>1.23 (0.81–1.87)</td>
<td>.34</td>
</tr>
<tr>
<td>Charge, c median US$</td>
<td>66,590</td>
<td>22,231</td>
<td>1.71 (1.01–2.88)</td>
<td>.04</td>
</tr>
</tbody>
</table>

**NOTE.** LOS, length of hospital stay; RR, relative risk.

a OR, 1.91 (95% CI, 0.49–7.42); P = .35.
b Controlling for APACHE II score at the time of infection.
c Controlling for APACHE II score and LOS before infection.

Source: Cosgrove CID 2006

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**Methicillin-Resistance In S. Aureus: Impact on Cost and Outcomes**

<table>
<thead>
<tr>
<th>Comparison</th>
<th>Death</th>
<th>Length of hospital stay after surgery</th>
<th>Charges</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Percentage of subjects who died</td>
<td>Total no. of days</td>
<td>No. of days attributable to MRSA</td>
</tr>
<tr>
<td>Control vs. MRSA SSI</td>
<td>OR</td>
<td>ME</td>
<td>P</td>
</tr>
<tr>
<td>Uninfected control subjects</td>
<td>11.4</td>
<td>&lt;.001</td>
<td>3.2</td>
</tr>
<tr>
<td>Patients with MRSA SSI</td>
<td>2.1</td>
<td>6.1</td>
<td>.01</td>
</tr>
<tr>
<td>(n = 121)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>MSSA SSI vs. MRSA SSI</td>
<td>3.4</td>
<td>.003</td>
<td>1.2</td>
</tr>
<tr>
<td>Patients with MSSA SSI</td>
<td>6.7</td>
<td>13.2</td>
<td></td>
</tr>
<tr>
<td>(n = 166)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Patients with MRSA SSI</td>
<td>20.7</td>
<td>29.1</td>
<td>118,414</td>
</tr>
<tr>
<td>(n = 121)</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**NOTE.** ME, multiplicative effect; MRSA, methicillin-resistant S. aureus; MSSA, methicillin-susceptible S. aureus.

Source: Cosgrove CID 2006
C. DIFFICILE

Incidence of *C. Difficile* and Attributable mortality are increasing in US


Courtesy/ CDC Get Smart
Rates of *C. difficile* Increase with Increasing Antibiotic Use

**Figure 1**

Annual number of hospital discharges with enterocolitis caused by *Clostridium difficile* (ICD10 diagnosis code DA04.7) and annual consumption of fluoroquinolones and cephalosporins for human use, Denmark, 1997-2007

Source: [6]

Loes et al. Eurosurveillance 2009

**ANTIMICROBIAL STEWARDSHIP IN THE US: WHERE DO WE STAND?**
Fast Facts

- Antibiotic prescribing practices vary significantly by provider, hospital, and region of the country.
- Greater than 50% of all inpatients receive an antibiotic AND up to 50% of antibiotic use is inappropriate.
- Doctors in some hospitals prescribe three times the amount of antibiotics as doctors in other hospitals.
- 140,000 Emergency Room visits per year for adverse reactions to antibiotics.
- Reducing the use of high-risk antibiotics by 30% can lower the risk of C. Difficile by 26%.

Source: CDC Vital Signs

How Are We Doing?

Outpatient antibiotic use: U.S.A. compared to Europe (2004)
Defined Daily Dose / 1,000 Inhabitants per day

United States: 24.9
Europe: 19.0
We Need to Protect What We Have!

- Due in part to the intermittent nature of antimicrobial use (which makes antibiotics unattractive targets for pharmaceutical companies), development of new drugs is dwindling rapidly.
- At the same time that drug development is slowing, increasingly resistant organisms are circulating.

courtesy/CDC.gov

STEWARDSHIP IN GERIATRICS
Long-Term Care Facilities: A Major Source of Resistance and Antimicrobial Utilization

- At any given time 7-10% of residents receiving an antibiotic, frequently for prolonged periods
- 1.6-12 Antibiotic courses per 1000 patient days (on average)
- 50-70% will receive antibiotics in one year
  - Studies show between 25%-75% of systemic antibiotics inappropriate, and 60% of topical antibiotics inappropriate
  - Asymptomatic bactriuria a major driver of inappropriate utilization


Inherent Challenges

- Co-morbid conditions may obscure classic signs and symptoms of infectious diseases
- Fevers without a clear source are common
- Fever and leukocyte responses may be blunted
- Missing an infection has very high stakes
- Mental status changes can be difficult to quantify
- In LTACs, may have limited access to radiology and laboratory testing
- Culture data can be difficult to interpret due to common colonization

Case

HPI: 74 male with a history of diabetes, coronary artery disease 3-4 weeks s/p CABG x 4 vessels, fell overnight. He reports that he fell because his legs, which feel “heavy” got caught in his oxygen tubing while he was trying to walk to the bathroom on his down. Symptom screen is notable for shortness of breath when lying down as well as a dry cough.

VS: T98.0F, BP162/96, HR 102, RR 22 and pulse oximetry of 94% on 2L of O2 by nasal cannula.

Physical Exam: +Tachypnea, +tachycardia, +diffuse crackles, +bilateral lower extremity edema

Laboratory: WBC 8.0, 68% neutrophils. Cr 1.9 (pre-surg baseline ~1.2). The urinalysis shows 31 WBC, 15 RBC and 2+ bacteria on Gram stain.

Actions: The covering physician examines the patient, gets a chest film, checks a UA and culture (the patient has an indwelling urinary catheter) and starts the patient on empirically on moxifloxacin for coverage of “pneumonia.”

Follow up: The patient was transferred to the inpatient medicine service. He failed to improve with antimicrobial therapy, but felt significantly better after diuresis. He then developed C difficile infection, and required a prolonged inpatient stay before he was able to transfer back to the CLC to finish his rehabilitation.
DO ANTIMICROBIAL STEWARDSHIP PROGRAMS WORK?

Reducing Antimicrobial Use Improves Outcomes in Low-Risk ICU Patients


<table>
<thead>
<tr>
<th>Variable</th>
<th>Standard Therapy (N=42)</th>
<th>Experimental Therapy (N=39)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Regimen</td>
<td>Clinician discretion (all treated, 18 different drugs)</td>
<td>Ciprofloxacin 400 mg IV BID x 3 days</td>
</tr>
<tr>
<td>Treatment &gt;3 days</td>
<td>97%</td>
<td>28%</td>
</tr>
<tr>
<td>Antimicrobial Resistance</td>
<td>35%</td>
<td>15%</td>
</tr>
<tr>
<td>Length of Stay mean/median</td>
<td>14.7/9 days</td>
<td>9.4/4 days</td>
</tr>
<tr>
<td>Mortality (30 day)</td>
<td>31%</td>
<td>13%</td>
</tr>
<tr>
<td>Antimicrobial Cost (Mean/Total)</td>
<td>$640/$16,004</td>
<td>$259/$6484</td>
</tr>
</tbody>
</table>
Getting it Right Makes a Difference!

Antimicrobial Stewardship Programs Reduce Resistance

Interventions: Antibiotic prescription and prior authorization, control of perioperative fluoroquinolone use.
Antimicrobial Stewardship Programs Reduce Rates of *C. difficile* Infection

<table>
<thead>
<tr>
<th>Study of subgroup</th>
<th>log (Risk ratio)</th>
<th>SE</th>
<th>Weight</th>
<th>IV, Random, 95% CI</th>
<th>Risk ratio</th>
<th>IV, Random, 95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ellingson 2012</td>
<td>-0.37</td>
<td>0.393</td>
<td>5.0%</td>
<td>0.69 [0.32, 1.49]</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Fowler 2007</td>
<td>-1.05</td>
<td>0.372</td>
<td>12.3%</td>
<td>0.35 [0.17, 0.73]</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Frank 2001</td>
<td>-0.029</td>
<td>0.522</td>
<td>1.6%</td>
<td>1.01 [0.37, 2.89]</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Gulhar 2009</td>
<td>-1.65</td>
<td>0.522</td>
<td>3.6%</td>
<td>0.19 [0.07, 0.53]</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Jones 1997</td>
<td>-0.4</td>
<td>0.205</td>
<td>8.1%</td>
<td>0.67 [0.45, 1.00]</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ludom 1999</td>
<td>-0.731</td>
<td>0.177</td>
<td>8.7%</td>
<td>0.45 [0.34, 0.69]</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Malani 2013</td>
<td>-0.753</td>
<td>0.275</td>
<td>7.2%</td>
<td>0.47 [0.28, 0.78]</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Miller 2009</td>
<td>-1.361</td>
<td>0.432</td>
<td>13.8%</td>
<td>0.26 [0.13, 0.51]</td>
<td></td>
<td></td>
</tr>
<tr>
<td>O’Connor 2004</td>
<td>-1.164</td>
<td>0.567</td>
<td>3.2%</td>
<td>0.31 [0.10, 0.95]</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Price 2010</td>
<td>-0.661</td>
<td>0.082</td>
<td>10.1%</td>
<td>0.52 [0.44, 0.61]</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Rehove 2002</td>
<td>-3.372</td>
<td>3.438</td>
<td>0.7%</td>
<td>0.03 [0.00, 0.37]</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Schön 2011</td>
<td>0.034</td>
<td>0.103</td>
<td>9.8%</td>
<td>1.03 [0.85, 1.27]</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Starks 2008</td>
<td>-0.986</td>
<td>0.309</td>
<td>6.3%</td>
<td>0.37 [0.23, 0.60]</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Stone 1998</td>
<td>-0.546</td>
<td>0.253</td>
<td>7.3%</td>
<td>0.58 [0.35, 0.95]</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Tadepato 2011</td>
<td>-1.079</td>
<td>0.272</td>
<td>6.9%</td>
<td>0.34 [0.20, 0.58]</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Thomsa 2002</td>
<td>-0.798</td>
<td>0.1986</td>
<td>8.3%</td>
<td>0.45 [0.31, 0.68]</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Total (95% CI): 100.0% 0.48 [0.38, 0.62]

Heterogeneity: Test: $I^2 = 0.14$ ($C^2 = 63.27, df = 15 (P = 0.00001)$; $I^2 = 76$

Test for overall effect: $Z = 3.94$ ($P = 0.00001$)

CDC Get Smart Campaign
Antimicrobial Stewardship Programs Reduce Costs

Antimicrobial Stewardship Programs in Geriatrics
- ID Consult service offered in long-term care facility
- Pre-post intervention (36 months pre, 18 months post)
- Antibiotic use decreased significantly
- Trends in C. difficile incidence reversed

Source: Jump et al. ICHE. 2012

Antimicrobial use decreased in LTAC
- C. difficile incidence trend in LTAC reversed
SPECIFIC INTERVENTIONS

12 Steps to Prevent Antimicrobial Resistance: Hospitalized Adults

12. Break the chain
11. Isolate the pathogen
10. Stop treatment when cured
  9. Know when to say "no" to vancomycin
  8. Treat infection, not colonization
  7. Treat infection, not contamination
  6. Use local data
  5. Practice antimicrobial control
  4. Access the experts
  3. Target the pathogen
  2. Get the catheters out
  1. Vaccinate

Prevent Transmission
Use Antimicrobials Wisely
Diagnose & Treat Effectively
Prevent Infections
Evidence-Based Interventions

- Infectious diseases approval/implementation of antimicrobial restrictions
- 48-72 hour review of antibiotic order for ongoing need and possibility of de-escalation
- Review of all patients on multiple antibiotics for necessity (“double coverage”)
- Review of safety and dosing
- Intravenous to oral conversions
- Cycling of first-line antimicrobials
- Implementation of evidence-based guidelines and order sets
- Consider procalcitonin program, rapid respiratory viral screens, Strep pneumo urine antigen

Electronic Monitoring of Antimicrobial Use One Effective Means for Improving Outcomes while Reducing Costs

- Implementation of an electronic monitoring and feedback system decreased antimicrobial use by 10% compared to pre-intervention levels.*
- Rates of *C difficile*, MRSA, and VRE all decreased after the intervention.
- Total cost savings >$1.7 million dollars per year.

*Nowak at el. Am J Health Syst Pharm. 2012
Preventing C. Difficile: Evidence-Based Options

- About 75% of patients who develop C. difficile do not have an indication for antimicrobial therapy*
- Approximately 60% of patients continue antimicrobial therapy after C. difficile diagnosis.
- Continuing antimicrobials is associated with increased length of stay and increased mortality, compared to patients in which other antimicrobials are stopped**
- Tetracyclines may be associated with lower risk- and perhaps even improved outcomes in C. difficile.
- Decreasing antibiotic use and prioritizing tetracyclines may be two targets for antimicrobial stewardship interventions.

*Srigley et al. AJIC 2013. **Harpe et al. Pharmacotherapy 2012

### Adjusted Risk of C. Difficile Infection in Patients Receiving Doxycyline versus Ceftriaxone

<table>
<thead>
<tr>
<th></th>
<th>Unadjusted HR (95% CI)</th>
<th>P Value</th>
<th>Adjusted HR (95% CI)</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, per year</td>
<td>1.01 (0.99–1.03)</td>
<td>.18</td>
<td>1.01 (0.99–1.03)</td>
<td>.26</td>
</tr>
<tr>
<td>Gender</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Female</td>
<td>ref</td>
<td>ref</td>
<td>ref</td>
<td>ref</td>
</tr>
<tr>
<td>Male</td>
<td>0.57 (0.31–1.03)</td>
<td>.06</td>
<td>0.53 (0.29–0.99)</td>
<td>.05</td>
</tr>
<tr>
<td>Race</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Nonwhite</td>
<td>ref</td>
<td>ref</td>
<td>ref</td>
<td>ref</td>
</tr>
<tr>
<td>White</td>
<td>1.67 (1.46–1.91)</td>
<td>.001</td>
<td>1.79 (1.48–2.11)</td>
<td>.001</td>
</tr>
<tr>
<td>Charlson index, per point</td>
<td>1.01 (0.92–1.12)</td>
<td>.77</td>
<td>1.04 (0.95–1.14)</td>
<td>.39</td>
</tr>
<tr>
<td>Admission diagnosis</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Nonsurgical</td>
<td>ref</td>
<td>ref</td>
<td>ref</td>
<td>ref</td>
</tr>
<tr>
<td>Surgical</td>
<td>1.81 (1.77–1.90)</td>
<td>.08</td>
<td>1.90 (1.84–1.96)</td>
<td>.81</td>
</tr>
<tr>
<td>Admission diagnosis</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pneumonia</td>
<td>...</td>
<td>...</td>
<td>0.22 (0.03–1.69)</td>
<td>.15</td>
</tr>
<tr>
<td>Time before CRO, per day</td>
<td>1.02 (1.00–1.04)</td>
<td>.09</td>
<td>0.97 (0.93–1.02)</td>
<td>.25</td>
</tr>
<tr>
<td>Inpatient status, per day</td>
<td>11.7 (5.25–25.9)</td>
<td>&lt;.001</td>
<td>15.1 (7.33–30.6)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>CRO, per day of use</td>
<td>1.03 (0.93–1.13)</td>
<td>.58</td>
<td>0.92 (0.84–1.02)</td>
<td>.11</td>
</tr>
<tr>
<td>DOXY, per day of use</td>
<td>0.67 (0.48–0.90)</td>
<td>.008</td>
<td>0.73 (0.56–0.96)</td>
<td>.03</td>
</tr>
<tr>
<td>Additional antibiotics, per day of use</td>
<td>1.04 (1.02–1.07)</td>
<td>&lt;.001</td>
<td>0.99 (0.96–1.03)</td>
<td>.73</td>
</tr>
</tbody>
</table>

Doernberg et al. CID 2012

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Targeting Post-Operative Antibiotics

- Despite multiple studies demonstrating no harm to post-procedural antibiotics, it is still common practice in some specialties.
- Randomized controlled trial of patients with acute cholecystitis (an active infection) demonstrated no benefit to post-operative antibiotics.

Regimbeau et al. JAMA 2014
Procalcitonin to Guide Therapy (ED)

- Multi-center, non-inferiority randomized controlled trial in emergency departments.
- Patients with lower respiratory tract illness assigned to administration of antibiotics based on a procalcitonin algorithm or according to usual practice.
- Composite outcome (death, ICU admission, disease-specific complications, recurrent infection requiring antibiotic treatment).
- Non-inferiority cut-off of 7.5%
- Control group with fewer adverse events (not statistically significant)
- Lower duration of antibiotic exposure in the PCT group (5.7 days versus 8.7 days)

Source: Schuetz et al. JAMA 2009.

Procalcitonin Group: Fewer Antibiotic Days, Fewer Adverse Events, Lower Lengths of Stay

Table 3. Antibiotic Exposure, Adverse Effects, and Length of Hospital Stay

<table>
<thead>
<tr>
<th></th>
<th>PCT Group</th>
<th>Control Group</th>
<th>Relative Mean Change or Ratio Difference, % (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>No patients</td>
<td>[n = 471]</td>
<td>[n = 488]</td>
<td></td>
</tr>
<tr>
<td>Antibiotic exposure, mean (SD), d</td>
<td>5.7 (3.1)</td>
<td>5.7 (3.9)</td>
<td>-0.0 (-43.7 to 8.7)</td>
</tr>
<tr>
<td>Antibiotic prescription rate, No. (%)</td>
<td>539 (74.6)</td>
<td>600 (81.7)</td>
<td>-12.2 (-18.3 to -6.1)</td>
</tr>
<tr>
<td>Adverse effect rate from antibiotics, No. (%)</td>
<td>133 (16.9)</td>
<td>160 (22.5)</td>
<td>-27.2 (-37.7 to -16.7)</td>
</tr>
<tr>
<td>Duration in patients with adverse effects, median (IQR), d</td>
<td>3 (1-7)</td>
<td>4 (0-10)</td>
<td>2.7 (-3.8 to 10.2)</td>
</tr>
<tr>
<td>Length of hospital stay, mean (SD), d</td>
<td>5.4 (0-13)</td>
<td>16.8 (5-13)</td>
<td>-5.6 (-10.2 to -1.0)</td>
</tr>
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</tbody>
</table>

Source: Schuetz et al. JAMA 2009.
Procalcitonin to Guide Therapy (ICU)

- Multicenter, randomized controlled trial
- Patients assigned to the procalcitonin arm received antibiotics based on algorithm
- Control arm usual care
- End-point: Mortality at 1 and 2 months (non-inferiority analysis) and antibiotic use (superiority analysis)


Procalcitonin Versus Control

- Study met non-inferiority end-point for mortality (no difference)
- Also met superiority end-point for antibiotic use

STARTING AN ANTIMICROBIAL STEWARDSHIP PROGRAM: KEY ELEMENTS AND PERSONNEL

### CDC Checklist: Summary of Core Elements

**Leadership Commitment**: Dedicating necessary human, financial and information technology resources

**Accountability**: Appointing a single leader responsible for program outcomes. Experience with successful programs show that a physician leader is effective

**Drug Expertise**: Appointing a single pharmacist leader responsible for working to improve antibiotic use.

**Action**: Implementing at least one recommended action, such as systemic evaluation of ongoing treatment need after a set period of initial treatment

**Tracking**: Monitoring antibiotic prescribing and resistance patterns

**Reporting**: Regular reporting information on antibiotic use and resistance to doctors, nurses and relevant staff

**Education**: Educating clinicians about resistance and optimal prescribing

Source: CDC.Gov/Core Elements of AS

### Infectious Diseases Pharmacists Are a Key Element of Successful Antimicrobial Stewardship Programs

- Study comparing two hospitals, one with dedicated ID pharmacist, the other without
- Quality of care measures for infectious disease management significantly better in hospital with dedicated ID pharmacist support.

<table>
<thead>
<tr>
<th></th>
<th>Hospital A (ID Pharmacist)</th>
<th>Hospital B (No ID Pharmacist)</th>
<th>P-Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Indication for Antibiotic Therapy Documented</td>
<td>189/190 (99.5%)</td>
<td>95/100 (95%)</td>
<td>0.02</td>
</tr>
<tr>
<td>Collection of Appropriate Cultures</td>
<td>113/176 (64.2%)</td>
<td>82/100 (82%)</td>
<td>0.0023</td>
</tr>
<tr>
<td>Appropriate Empiric Therapy</td>
<td>184/190 (96.8%)</td>
<td>87/100 (87%)</td>
<td>0.022</td>
</tr>
<tr>
<td>Therapy Modification within 24 hours of Laboratory Results</td>
<td>124/143 (86.7%)</td>
<td>37/51 (72.6%)</td>
<td>0.029</td>
</tr>
<tr>
<td>Discontinuation of Therapy when Infection Ruled Out</td>
<td>37/48 (77.1%)</td>
<td>11/33 (33.3%)</td>
<td>0.0002</td>
</tr>
<tr>
<td>IV to PO Conversion Completed</td>
<td>97/120 (80.8%)</td>
<td>41/67 (61.2%)</td>
<td>0.0052</td>
</tr>
<tr>
<td>Any Streamlining Activity</td>
<td>165/182 (90.7%)</td>
<td>47/95 (49.5%)</td>
<td>&lt;0.0001</td>
</tr>
</tbody>
</table>

Courtesy/Clegg, Pepe, Fugit, Bessesen 2014
Antimicrobial Stewardship Program

Benefits:
• Improved patient outcomes
• Reduced rates of antimicrobial resistance
• Reduced rates of C difficile infection
• Reduced cost

Harms:
• Requires dedicated personnel, including both pharmacy and infectious diseases support

Everyone Has a Role in Antimicrobial Stewardship

• Improving antimicrobial prescribing practices requires a community approach
• Requires involvement of many services— including physicians, pharmacists, microbiologists, and administrators
• The Bottomline: Anyone can improve antimicrobial use

Every Pediatrician Can Be an Antimicrobial Steward.
JAMA Pediatrics, 2003
Simple Steps to Reduce Antibiotic Use

- Do not prescribe antibiotics over the phone!
  - Most antibiotic prescriptions given without ever seeing the patient. And most of these are inappropriate.
- Choose antibiotics carefully
  - Fosfomycin for lower UTI (especially with resistance!)
  - Consider doxycycline for CAP/SSTI when possible
- Increase access to ID services
- Improve the provider to patient ratio
  - Higher ratios associated with more antibiotic use
- Utilize emerging diagnostics
  - Procalcitonin to guide antibiotic use
  - Rapid respiratory viral screens to diagnose respiratory infections
- Obtain fewer cultures
  - Treat the patient, not the culture
  - What you don’t know can’t hurt you!


Attention to Antimicrobial Stewardship Increasing

- January 24, 2014: VA published a new directive, mandating an antimicrobial stewardship program in all VA medical centers
- September 19, 2014: President Obama signed an executive order, “Combating Antibiotic Resistant Bacteria”

Courtesy/NBC News
THANK YOU!

QUESTIONS?