Antimicrobial Stewardship – A Multi-Disciplinary Approach

“The Path of Least Resistance”
Founded in 1898, and affiliated with what is now New York-Presbyterian Hospital since 1927, Weill Cornell Medical College is among the top-ranked clinical and medical research centers in the country.
Mentoring

• A mentor is someone whose hindsight can become your foresight!

Rationale for Antibiotic Stewardship

• Antibiotic resistance is among the greatest public health threats today

• Estimated 2 million infections and 23,000 deaths/year in the US

• Infections with pathogens resistant to 1\textsuperscript{st}-line antibiotics often require treatment with alternative antibiotics that can be both expensive and toxic

• Antibiotic-resistant infections often lead to increased health care costs and, more importantly, increased M&M
Rationale (continued)

• Most important modifiable risk factor for antibiotic resistance is …..

• Approximately 50% of outpatient antibiotic prescribing is probably inappropriate including antimicrobial selection, dosing, or duration (in addition to unnecessary antibiotic prescribing) \(^1,2\)

• ≥ 30% of outpatient antibiotic prescriptions in the US are unnecessary \(^3\)

Definition and Purposes

• Antibiotic stewardship is the effort to:
  – Measure antibiotic prescribing
  – Improve antibiotic prescribing by clinicians and use by patients such that antibiotics are only prescribed and used when needed
  – Minimize misdiagnoses or delayed diagnoses leading to underuse of antibiotics
  – Ensure that the right dose, drug, and duration are selected when an antibiotic is needed

• Antibiotic stewardship can be used in all health care settings in which antibiotics are prescribed and is the basis of efforts aimed at improving patient safety and slowing the spread of antibiotic resistance
Benefits of Antimicrobial Stewardship

- Improved patient outcomes
- Reduced adverse events including *Clostridium difficile* infection
- Improvement in antibiotic susceptibility rates to targeted agents
- Optimization of resource utilization across the continuum of care (reduced costs)
Policy Statement on Antimicrobial Stewardship by SHEA, the IDSA, and PIDS\(^4\)- Model

- Creation of multidisciplinary inter-professional antimicrobial stewardship team that is physician-directed
- Team members should include, but are not limited to:
  - A physician (ideally with antimicrobial stewardship training)
  - A pharmacist
  - A clinical microbiologist
  - An infection preventionist
- A formulary limited to non-duplicative antibiotics with demonstrated clinical need
- Institutional guidelines for management of common infectious syndromes
- Periodic distribution of facility-specific antibiograms indicating the rates of relevant antibiotic susceptibilities for key pathogens

\(^4\)Infection Control and Epidemiology. 2012. 33:322-327.
Model (continued)

• Additional interventions to improve the use of antimicrobials including those designed to detect and eliminate:
  – Multi-drug regimens with unnecessarily redundant antimicrobial spectra
  – Antibiotic therapy for management of non-bacterial syndromes or cultures that represent contamination or routine colonization
  – Empiric regimens that are either inadequately or excessively broad-spectrum for infection syndromes
  – Regimens that do not adequately treat infections caused by culture-confirmed pathogens
  – Processes to measure and monitor antimicrobial use
Ten Key Points for the Appropriate Use of Antibiotics in Hospitalized Patients

Consensus from the Antimicrobial Stewardship and Resistance Working Groups of the International Society of Chemotherapy

1. Get appropriate microbiological samples before antibiotic administration and carefully interpret the results: “in the absence of clinical signs of infection, colonization rarely requires antimicrobial treatment” (“Get the bug!!” – Dr. Alex Vandevelde)

2. Avoid the use of antibiotics to “treat” fever: Investigate the root cause of fever and treat only significant bacterial infections (“Fever is not a ceftriaxone-deficiency syndrome.” – Dr. John Nelson)

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Key Points (continued)

3. When indicated, start empirical antibiotic treatment **AFTER** taking cultures, tailoring it to the site of infection, risk factors for MDR bacteria, and local microbiology and susceptibility patterns (e.g., do not report/prescribe tigecycline for UTIs caused by CRE)

4. Prescribe drugs at their optimal dose, mode of administration, and for the appropriate length of time, adapted to each clinical situation and patient characteristics

5. Use antibiotic combinations only in cases where evidence suggests some benefit
Key Points (continued)

6. When possible, avoid antibiotics with a higher likelihood of promoting drug resistance or HAIs, or use them only as a last resort

7. Drain the infected foci quickly and remove all potentially or proven infected devices: Control the infection source

8. Always try to de-escalate/streamline antibiotic treatment according to the clinical situation and the microbiological results; Switch to the oral route as soon as possible

9. Stop antibiotics as soon as a significant bacterial infection is unlikely

10. Do not work alone: Set up teams to include an ID specialist, clinical microbiologist, hospital pharmacist, infection control practitioner or hospital epidemiologist; ensure compliance with policies and guidelines
Other considerations

- The non-clinical use of antibiotics (animal feed, etc.) and their massive release into the environment may exert the most relevant pressure in the emergence and selection of antibiotic-resistant bacteria.

- We are now facing the threat of a lack of effective agents to treat some infections: Recent bacteremic patient, transferred to NYP from Saudi Arabia with an *E. coli* harboring an NDM, VIM, and IMP (three different carbapenemases) as well as a TEM. Isolate was resistant to all agents tested (including ceftazidime-avibactam) except for polymyxin B (patient in renal failure). Expired
IDSA Evidence-Based Guidelines for Implementing an Antibiotic Stewardship Program

1. Recommend preauthorization and/or prospective audits with feedback

2. Cannot rely solely on didactic educational materials

3. Suggest that ASPs develop and implement facility-specific guidelines for common infectious syndromes and develop a plan for their dissemination

4. Recommend implementation of interventions to improve antibiotic use and clinical outcomes that target patients with specific clinical syndromes
Implement facility-specific guidelines for common infectious syndromes

- Guidelines are published and available on Medical Center Infonet
- Can be accessed on smart phones
- Reviewed by Subcommittee on Antimicrobial Usage on an annual basis
- Blood culture guidelines for BioFire panels drafted by CMIDCC (which has representation of the clinical microbiologists, Pharm D's with ID training, and a complement of interested ID physicians including the two Hospital Epidemiologists who oversee the institution’s ASP)
TITLE: COMMUNITY-ACQUIRED PNEUMONIA (CAP) EMPIRIC MANAGEMENT OF ADULT PATIENTS

GUIDELINES:

- These guidelines serve to aid clinicians in the diagnostic work-up, assessment of severity of illness, empiric antimicrobial treatment, and follow-up of adult patients with community-acquired pneumonia (CAP).
- These guidelines have been developed based on published literature including the most recent CAP guidelines and expert clinical opinions. The recommendations serve as a guide and clinicians are encouraged to use clinical judgment to manage all cases.

PURPOSE:

To develop guidelines for the use of appropriate antimicrobials for adult patients with CAP and provide guidance on IV to PO conversion.

APPLICABILITY:

Prescribers and pharmacists

PROCEDURE:

1. Initial approach (See algorithm)
   A. Diagnostic studies
   B. Patient stratification
      1) Severity of illness score
         a. CURB-65 criteria (confusion, uremia, respiratory rate, low blood pressure, age ≥ 65 years)
         b. Pneumonia PORT Severity Index Score (PSI)
      2) Patients with asthma have increased risk of complications and may require hospital admission.
   C. Need for hospitalization
      1) In general, patients with CURB-65 scores <2 or PSI Risk Class I and II may be managed as outpatients.
      2) Providers should assess patient’s clinical condition, follow-up, and home environment as part of this decision.
   D. Need for admission to an intensive care unit

2. Empiric antimicrobial therapy (See algorithm)
   A. Outpatient therapy
   B. Inpatient antimicrobial therapy
1) Risk factors - Initial therapy should be individualized where appropriate based on antimicrobial history, recent hospitalizations, immune status, and culture history.
   C. Non-ICU admission
   D. ICU-admission
   E. Every effort should be made to initiate antimicrobial therapy as soon as possible
   F. **Antimicrobial therapy should always be de-escalated to target culture and susceptibility data when available**

3. IV to PO Conversion (See algorithm)
   A. Patients should be switched from IV to PO therapy when they are hemodynamically stable, improving clinically, able to ingest medications, and have a normally functioning gastrointestinal tract.
   B. Recommendations for oral conversion are provided based on initial IV therapy. The choice of oral antimicrobials may be influenced by results of microbiologic studies. Narrow spectrum agents should be utilized when possible.
   C. Recommendations have been made to convert intravenous ceftriaxone (a third generation IV cephalosporin) to cefuroxime (an oral second-generation cephalosporin). If a specific pathogen is identified, therapy should be modified accordingly.

4. Discharge (See algorithm)
   A. Prior to discharge, all patients should be screened for influenza vaccination during influenza season, pneumococcal vaccination, and the need for smoking cessation counseling.3-5 (A list of steps taken to carry out the policy. A “How To” guideline for executing the policy.)

5. Algorithm
IDSA Evidence-Based Guidelines for Implementation of Program

5. Recommend interventions designed to reduce the use of antibiotics associated with a high risk of CDI

6. Suggest use of strategies to encourage prescribers to perform routine review of antibiotic regimens to improve antibiotic prescribing (antibiotic time-outs; stop orders)

7. Suggest incorporation of computerized clinical decision support at the time of prescribing (example) ......
Microbiology and Laboratory Diagnostics

14. Suggest development of stratified antibiograms over solely non-stratified antibiograms to assist in developing guidelines for empiric therapy (overall, ICU vs. non-ICU, ED, OP, urine, blood, lower respiratory, for specific resistant organisms (e.g., CRE), PEDS)

15. Suggest use of selective and cascade reporting of AST results (ampicillin-sulbactam only on ampicillin-resistant strains; tobramycin and/or amikacin only on gentamicin resistant strains; 2nd and 3rd generation cephalosporins only on cefazolin/cephalothin resistant strains, etc.) NOTE: Always, however, report resistance. Many KPC-producing *Klebsiella pneumoniae* are tobramycin and/or amikacin resistant
<table>
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<tr>
<th>Organism</th>
<th>No. Strains</th>
<th>AMK</th>
<th>AMP</th>
<th>CFZ</th>
<th>CRO</th>
<th>CIP</th>
<th>GEN</th>
<th>IPM</th>
<th>PTZ</th>
<th>TET</th>
<th>SXT</th>
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</thead>
<tbody>
<tr>
<td>K. pneumoniae (All)</td>
<td>1163</td>
<td>63</td>
<td>R</td>
<td>44</td>
<td>48</td>
<td>46</td>
<td>74</td>
<td>64</td>
<td>53</td>
<td>84</td>
<td>46</td>
</tr>
<tr>
<td>K. pneumoniae (Extended-spectrum cephalosporin resistant)</td>
<td>233</td>
<td>30</td>
<td>R</td>
<td>0</td>
<td>0</td>
<td>6</td>
<td>48</td>
<td>100</td>
<td>0</td>
<td>84</td>
<td>3</td>
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<td>K. pneumoniae (Carbapenem-resistant)</td>
<td>361</td>
<td>5</td>
<td>R</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>28</td>
<td>0</td>
<td>0</td>
<td>82</td>
<td>0</td>
</tr>
<tr>
<td>K. pneumoniae (Not resistant to extended-spectrum cephalosporins or carbapenems)</td>
<td>569</td>
<td>100</td>
<td>R</td>
<td>84</td>
<td>99</td>
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16. Suggest use of rapid viral testing for respiratory pathogens to reduce use of inappropriate antibiotics


FilmArray decreased the time to diagnosis of influenza compared to conventional methods (median turnaround times of 1.7 h versus 7.7 h, respectively; P = 0.015); FilmArray also decreased the time to diagnosis of non-influenza viruses (1.5 h versus 13.5 h, respectively; P < 0.0001). Multivariate logistic regression found that a diagnosis of influenza by FilmArray was associated with significantly lower odds ratios (ORs) for admission (P = 0.046), length of stay (P = 0.040), duration of antimicrobial use (P = 0.032), and number of chest radiographs (P = 0.005), when controlling for potential confounders.
IDSA Evidence-Based Guidelines
Microbiology Issues (cont’d.)

17. Suggest rapid diagnostic testing in addition to conventional culture and routine reporting on blood specimens if combined with ASP support and interpretation.
Impact of RT-PCR for Rapid Identification of Staphylococcal Bacteremia

- Retrospective, interventional cohort study evaluated inpatients with blood cultures positive for GPC/clusters in pre-PCR vs. post-PCR implementation periods
- MRSA results (in both groups) were phoned to the patient’s floor within 60 minutes to assure implementation of Infection Control precautions
- Post PCR implementation, the microbiology laboratory batched PCR testing (twice daily - Monday through Friday and once daily on weekends)
- Results other than MRSA were only reported in the medical record (without additional interventions)
Impact of RT-PCR for Rapid Identification of Staphylococcal Bacteremia

- 68 and 58 patients with *S. aureus* bacteremia from the pre- and post-PCR periods met inclusion criteria
- Time to organism identification (ID) was significantly reduced post-PCR implementation (mean 13.2 hours; 95% confidence interval 10.5 to 15.9 hours; p < 0.0001), but time to optimal antibiotic Rx was not significantly reduced
- Authors concluded that implementation of the PCR assay demonstrated the potential to improve appropriate antibiotic use based upon clinically meaningful and statistically significant reductions in time to microbiologic ID, but to optimize this potential benefit processes must be optimized and additional interventions initiated to facilitate providers’ use of the data
Implementation of Rapid Multiplex Diagnostic Panels from Blood Cultures

• Do we call the Gram stain, then the report of the rapid panel? Or, just one phone call?
• To which healthcare provider should we phone the result? Nurse or physician?
• If no antimicrobial stewardship team is present, how do we ensure that the antibiotics are being appropriately tailored?
• Do we have to call the daytime pharmacists for every case?
FilmArray Blood Culture Identification Panel Testing – Broadcast Message

What is changing?

☑ Effective immediately, the Clinical Microbiology Service will begin testing blood cultures that have flagged as positive using a new molecular multiplex amplification technique. This will provide a more rapid identification of pathogens and detection of certain antibiotic resistance genes. As a result, two phone calls will be placed by the microbiology laboratory to the relevant HCP. The first call will inform the HCP that the culture is positive and provide the Gram stain results, as is current practice. The second call will communicate organism identification and antibiotic resistance gene information, if applicable.
FilmArray Blood Culture Identification Panel Testing Broadcast Message (continued)

- The first aerobic blood culture bottle that becomes positive with a given bacterial morphotype on Gram stain (e.g., gram-positive cocci in clusters). **NOTE:** Subsequent blood cultures collected from a given patient exhibiting an organism with the same morphology on Gram stain will not be tested.

- Test results will be reported as either: “Organism not identified by Film Array testing”, or specifically list the organism detected as well as any associated antibiotic resistance genes. Full antimicrobial susceptibility testing results will follow in 48–72 hours for most organisms.
What additional actions should be considered?

- It is strongly suggested that upon receipt of the information provided from the Film Array testing, HCP’s refer to the “Antimicrobial Recommendations Based on Rapid identification of Organisms from Blood Cultures in Adults” NYP/Weill Cornell Medical Center guidelines which can be found on the Infonet under the Infectious Diseases Division web page. [http://infonet.nyp.org/ID/Pages/index.aspx](http://infonet.nyp.org/ID/Pages/index.aspx)

- **Test Availability:** The assay will be performed 24 hours/day, 7 days/week and results can be expected in approximately two hours from detection of growth in blood cultures.
TITLE: ANTIMICROBIAL RECOMMENDATIONS BASED ON RAPID IDENTIFICATION OF ORGANISMS FROM BLOOD CULTURES IN ADULTS – WEILL CORNELL MEDICAL CENTER

GUIDELINE:

• These guidelines should be used to assist with antimicrobial selection in adult patients based on rapid identification of organisms isolated from blood cultures. These recommendations are based upon local antimicrobial susceptibility testing results for organisms from patients with bloodstream infections. Rapid testing identifies select gram-positive, gram-negative, and yeast pathogens and predicts resistance to select agents based on the detection of resistance genes for vancomycin (van A/B) in enterococci, methicillin (mecA) in *Staphylococcus aureus*, and carbapenems (KPC) in *Enterobacteriaceae*. These data will be available within 2-3 hours of the Gram-stain result and should be used to optimize antimicrobial therapy. Antimicrobial susceptibility testing results will be available in approximately 48 hours.
GUIDELINES (continued)

PURPOSE:
• To assist in the initiation of active antimicrobial treatment in patients with bloodstream infections.

APPLICABILITY:
• All prescribers

PROCEDURE:
☐ The following are generally recommended therapies based on previously characterized bloodstream isolates at Weill Cornell Medical Center. However, these recommendations may need to be modified based on the following: The patient’s previously positive cultures and susceptibilities, if available

☐ Clinical judgment and severity of illness. If patient is clinically improving on current therapy, it may not be necessary to escalate therapy based on the recommendations below

☐ Certain infections (e.g., intra-abdominal) are often polymicrobial and clinical judgment should be used when deciding whether or not to narrow therapy to only cover a single organism from blood cultures

☐ Please contact the Infectious Diseases service with questions and consider consultation for serious and/or multidrug-resistant infections
IDSA Evidence-Based Guidelines for Implementation

Microbiology and Laboratory Diagnostics – continued

18. In adults in ICUs with suspected infection, suggest use of serial procalcitonin testing to decrease antibiotic use.

19. In patients with hematologic malignancy at risk of contracting invasive fungal disease, suggest incorporating nonculture-based fungal markers to optimize antifungal use.

- galactomannan
- 1-3-β-D-glucan (PCP)
- T2Candida
NYP/WCMC T2Candida Approach

• Patient Selection Criteria

The T2Candida Panel will be on restricted orders in the ICU, and can only be placed by the physician if:

[1] suspected candidemia or deeply invasive candidiasis

[2] before initiation of antifungal therapy

[3] persistently febrile neutropenic patient

[4] sepsis syndrome
Additional T2Candida Guidance

• Physician preference to order one T2Candida test at two different times on the same patients

• Physician preference to order T2Candida test in addition to all other tests

• Outcomes (T2 positive or T2 negative for fungemia) and the impact on antifungal and antibacterial therapy to be documented for quality of care

• If T2 is positive for candidemia and conventional blood cultures are negative for bacteremia, consider careful antibiotic de-escalation in non-neutropenic, non-HSCT patients
IDSA Evidence-Based Guidelines for Implementation of Program

• Series of recommendations regarding measurements to assess impact of ASP to include:
  – Days of therapy
  – Antibiotic costs based upon prescriptions or administration rather than purchasing data
  – Impact on syndrome-specific interventions

• Specific populations:
  – Suggest development of facility-specific guidelines for fever and neutropenia in hematology-oncology patients
  – Suggest interventions to improve appropriate prescribing of antifungal treatment in immunocompromised patients
  – Suggest implementation of AS strategies to ↓ unnecessary antibiotic use in nursing homes and skilled nursing facilities
<table>
<thead>
<tr>
<th>Yeasts</th>
<th>Treatment</th>
<th>Notes</th>
</tr>
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</table>
| *Serratia marcescens*  
*(See Carbapenem resistant Enterobacteriaceae above if KPC positive)* | Cefepime IV 2 g q8h  
*If severe PCN-allergy:* Levofloxacin IV 750 mg q24h | • Cefepime: adjust for renal insufficiency  
Levofloxacin: adjust for renal insufficiency; caution in those at risk for QTc prolongation |
| *Candida albicans*     | Micafungin 100mg IV daily then fluconazole IV/PO 6 mg/kg/day             | • If patient not in an ICU and is clinically stable, fluconazole may be considered as initial therapy (instead of micafungin)  
• If micafungin started initially, may de-escalate to fluconazole once patient is clinically stable  
• Fluconazole: adjust for renal insufficiency |
| **Candida glabrata**   | Micafungin 100mg IV$^1$ daily then fluconazole IV/PO 12 mg/kg/day        | • De-escalate to fluconazole in patients if:  
A) Patient is clinically stable and not in an ICU AND  
B) Isolate is SDD (susceptible dose-dependent) to fluconazole or patient lacks risk factors for fluconazole-resistance (e.g. history of fluconazole-resistant isolates, exposure to azole, heme-malignancy, or HIV)  
• Fluconazole: adjust for renal insufficiency |
| *Candida krusei*       | Micafungin 100mg IV daily                                               | • Fluconazole: adjust for renal insufficiency |
| *Candida parapsilosis* | Micafungin 100mg IV$^1$ daily then fluconazole IV/PO 6 mg/kg/day         | • If patient not in an ICU and is clinically stable, fluconazole may be considered as initial therapy (instead of micafungin)  
• If micafungin started initially, may de-escalate to fluconazole once patient is clinically stable  
• Fluconazole: adjust for renal insufficiency |
| *Candida tropicalis*   | Micafungin 100mg IV daily then fluconazole IV/PO 6 mg/kg/day             | • If patient not in an ICU and is clinically stable, fluconazole may be considered as initial therapy (instead of micafungin)  
• If micafungin started initially, may de-escalate to fluconazole once patient is clinically stable  
• Fluconazole: adjust for renal insufficiency |
IDSA Evidence-Based Guidelines for Implementation of Program

Special populations (continued)

- Suggest stewardship interventions to reduce inappropriate antibiotic use and/or resistance in NICUs
- Suggest that ASPs provide support to clinical care providers in decisions related to antibiotic treatment
Conclusions

• ASP interventions should be implemented based upon facility-specific assessments of need and resources

• Every healthcare facility is able to perform stewardship and it is of great importance both to the specific facility and to overall public health

• To accomplish this, efforts must my multi-disciplinary in nature taking advantage of (and relying upon) the expertise of physicians, ideally with antimicrobial stewardship training, pharmacists, clinical microbiologists, and infection preventionists

• This is truly the path of least resistance
THANK YOU FOR YOUR PRESENTATION, JENKINS. HOWEVER, I DON'T THINK WE CAN RESPONSIBLY APPROVE YOUR DISSEMINATION. YOUR INSIGHTS ON TROWELS, WHILE INFORMATIVE, WERE HARDLY GROUND-BREAKING.
Questions