Antimicrobial Stewardship Interventions in Acute Care Hospitals

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Disclosures

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Objectives

• Identify stewardship interventions that can be implemented in acute care facilities of varying sizes
• Describe factors associated with successful stewardship interventions

Goal
Provide a menu of interventions of various types and levels of complexity you can use to improve antibiotic use at your facilities along with some context on how to decide what to do
You Next Stewardship Committee Meeting

So we are supposed to improve antibiotic use?

Right. So what should we do?
How do you decide what to do?

CDC Core Elements
• Leadership Commitment
• Accountability
• Drug Expertise
• Action
• Tracking
• Reporting
• Education
Process Improvement - PDSA

**Plan**
- Establish a team
- What and why are we changing?
- What is current process?
- How will we change it?
- How will we measure improvement?

**Do**
- Initiate the change
- Consider a pilot if large scale change or resource intensive
- Measure results

**Act**
- What changes must be implemented for next cycle
- Review metrics and progress
- Determine if changes need to be made
- Summarize learnings

**Study**
- Review metrics and progress
- Determine if changes need to be made
- Summarize learnings
Process Improvement - DMAIC

**Define**
- Define and scope the problem
- Establish team

**Measure**
- Document processes
- Collect baseline data

**Analyze**
- Analyze data
- Identify root causes

**Improve**
- Generate and optimize solutions
- Implement

**Control**
- Maintain the improvement

**General Suggestions:**
- Get input from multiple sources
- Garner support from the C-suite
- Choose low hanging fruit
- Look at what others have done and if it worked – don’t reinvent the wheel
- Think about unintended consequences
- Engage IT early – CDS and measurement
Identify the Problem

- **Me:** “We seem to use vancomycin and P/T for everything these days. Is that really necessary?”
- **Resident:** “Well everyone is worried about sepsis. They might die. Plus it covers everything, so what’s the problem?”
- **Me:** “Have you seen the papers on the increased risk of renal failure?”
- **Resident:** “Oh sure; I guess we will just change to cefepime or meropenem.”
- **Me:** “That doesn’t seem to be ideal. Those agents are associated in increased risk of CDI, ESBL, and CRE.”
- **Resident:** “Hmmm, well maybe we could use daptomycin or linezolid instead of vancomycin.”
Vancomycin IV

Pip/Tazo
Is there really a problem?

Number of Patients Who Received Vancomycin and P/T on the Same Day 2013-2017
How Will We Measure Success?

26.5% received for >3 days

How will we measure success?
- Number who received both agents
- Duration of combination use
- Days of therapy / 1000 patient days
  - Vancomycin, P/T, cefepime, ertapenem, meropenem, ceftriaxone
Why is it Happening?

• Easy and comfortable
  • Broad spectrum
  • Included in many of our guidelines (and national guidelines)

• Sepsis initiative pushing for faster broad spectrum antibiotics

• ED often starts and team continues

• Misunderstanding regarding microbiology of specific infections and prevalence of resistant pathogens

• Not specifically captured by current ASP reviews
How will we fix it?

• Guidelines
  • Review guidelines with combination and adjust as appropriate

• Education
  • Educate on microbial etiology of various infectious syndromes and prevalence of MRSA and Pseudomonas
  • Develop vanco-P/T education and distribute in many venues

• ASP Activities
  • Create alert for vanco-P/T use and review patients on combination

• Work Flow – Clinical Decision Support
  • Create work cue tasks for team pharmacists that appears when patient on combination
  • Work with ED regarding antibiotic ordering mechanisms (<10% ordered via order sets)
Piperacillin-tazobactam Alternatives

Piperacillin-tazobactam (P/T) is one of the most common antibiotics used at Nebraska Medicine. It has a broad spectrum covering Streptococci, penicillin-sensitive Enterococci and Staphylococci, enteric gram negative rods, *Pseudomonas species*, and anaerobic bacteria. Recent data suggests its use, particularly in combination with vancomycin significantly increases the risk of acute kidney injury (AKI) even in patients at low risk for AKI. Rates of AKI approach 30% with combination use compared to 10% with vancomycin alone. While P/T is a highly effective antibiotic with many advantages, the consequences of AKI are substantial - resulting in significant patient harm and prolonged length of stay. With that in mind, we have produced the following guidance regarding use of combinations of vancomycin and P/T. Links to our clinical guidelines are included.

**General Recommendations:**

- **Vancomycin is overused** and should only be used when a significant risk for MRSA infection exists. Examples of appropriate use would include: Hospital or Ventilator-associated Pneumonia (HAP/VAP), Severe purulent skin and soft tissue or bone and joint infection, Sepsis presumed due to central venous catheter infection, and nosocomial sepsis of unknown etiology.

- **P/T is overused.** While it may be appropriate for nosocomial infections, most community-onset infections do not require coverage for *Pseudomonas*
  - The most common indications for P/T use at NM include: pneumonia, intra-abdominal infection, presumed sepsis, skin and soft tissue and bone and joint infections, and UTI
  - P/T use in SSTI and bone and joint infections and many cases of UTI is inappropriate

- **Just because a patient has “sepsis” doesn’t mean they need vancomycin and P/T**
  - Utilize institutional guidelines to assist with appropriate therapy choices based on the most likely organisms at each source
Acute Care Strategies

Infectious Diseases Society of America and the Society for Healthcare Epidemiology of America
Guidelines for Developing an Institutional Program to Enhance Antimicrobial Stewardship

Implementing an Antibiotic Stewardship Program:
Guidelines by the Infectious Diseases Society of America and the Society for Healthcare Epidemiology of America(18,126),(631,489)

Antimicrobial Stewardship Toolkit

http://www.jcrinc.com/antimicrobial-stewardship-toolkit/

http://www.cdc.gov/getsmart/healthcare/implementation/core-elements.html

IDSA/SHEA ASP Strategies

**Interventions**
- Restriction and pre-authorization
- Audit feedback
- Syndrome-focused practice guidelines
- Clinical decision support systems
- Education
- Decreased *C. difficile*-promoting antibiotics

**Other Strategies**
- PK monitoring
- Alternate dosing of beta-lactams
- IV to PO conversion
- Allergy assessment
- Duration of therapy

IDSA/SHEA Other ASP Activities

Microbiology
• Antibiograms
  • Stratified (source, location)
• Selective susceptibility reporting
• Rapid viral testing
• Rapid blood culture diagnostics
• Procalcitonin
• Fungal biomarker use

Special Populations
• Neutropenic fever guidance
• Antifungal use in immunocompromised
• LTCF interventions
• NICU
• Terminally ill

Take Action – Critical Access

• Policies
  • Require dose, duration, indication on all antibiotics
  • Facility specific treatment recommendations
  • Formulary restrictions

• Broad activities
  • Antibiogram creation and use
  • Focus on common syndromes – UTI, CAP, SSTI
    • Empiric choices
    • Appropriate diagnosis
    • Duration of therapy
Take Action – Critical Access

• Pharmacists
  • IV to PO conversion
  • Renal dosage adjustments
  • Redundant therapy
  • Drug-drug interactions
  • Review culture results for de-escalation

• Nurses
  • Ensure appropriate cultures obtained appropriately
  • Review culture results with physician
  • Inform pharmacist/physician regarding clinical response and ability take PO
  • Educate patient regarding antibiotic side effects and C. difficile
  • Time outs
Action: Restriction

• “You can’t have it.”
  • 88% of programs use restrictions in some form

• Examples
  • Meropenem is only carbapenem available on formulary
  • Daptomycin is only able to be ordered by ID physicians
  • Vancomycin stopped after 72 hours unless culture positive for MRSA

• Advantages
  • Minimal personnel needed, will decrease use

• Disadvantages
  • Restrictive, “squeezing the balloon”
Action: Pre-Authorization

- Preauthorization
  - “You can’t have it unless you meet our specific criteria”

- Example
  - Any patient started on piperacillin/tazobactam must be approved by ID fellow

- Advantages
  - Targeted, effective, feedback to clinicians

- Disadvantages
  - Painful, time consuming, info reliability, circumventing
Action: Audit and Feedback

- Process of reviewing patients who are receiving antibiotics and giving “unsolicited” advice

- Requirements
  - A process for identifying patients
  - Someone to do the reviewing and advising
    - Time and expertise

- Advantages
  - Customization, educational, no delays in therapy

- Disadvantages
  - Optional, time intensive
Mean carbapenem use (DOT/1,000 PD) was significantly lower in hospitals that restricted (shaded bars) versus did not restrict (open bars) carbapenems ($p = 0.04$)
Impact of a Hospital-Based Antimicrobial Management Program on Clinical and Economic Outcomes

Primary Intervention was **Pre-Authorization**

Audit and Feedback

• Single center ICU patients on 3rd or 10th day of broad-spectrum therapy audit/feedback from ID pharmacist
  • Monthly DOT/1000 PD decreased 644→503 (∧=0.0054)
  • No increase in mortality

• Inpatients with suspected infection randomized to usual care vs. audit/feedback by ID MD and microbiologist
  • 89% acceptance rate
  • No difference in mortality

<table>
<thead>
<tr>
<th></th>
<th>Control (N=125)</th>
<th>Intervention (N=127)</th>
<th>P-Value</th>
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<tbody>
<tr>
<td>LOS from randomization (days)</td>
<td>9</td>
<td>5.7</td>
<td>&lt;0.001</td>
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<tr>
<td>Antibiotic Costs ($)</td>
<td>2683</td>
<td>2078</td>
<td>0.038</td>
</tr>
<tr>
<td>Lab and Radiology Costs ($)</td>
<td>3293</td>
<td>2496</td>
<td>0.032</td>
</tr>
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</table>

How to Select Cases for Restriction, Pre-Authorization or Audit and Feedback

• High cost agents
• Broad-spectrum agents (eg. FQs, Pip/Tazo)
• High use agents (facility dependent)
• High risk of adverse effects (eg. aminoglycosides)
• Novel agents
• Site of infection (eg. UTI)
• Resistance profiles (eg. MDROs, MRSA)
• Double coverage of organisms (eg. anaerobes)
Action: Time Out

CDC Get Smart with Antibiotics

- All antimicrobial orders need:
  - Dose
  - Duration (stop date)
  - Indication
- Get cultures before starting
- Once the culture data comes back, take an antimicrobial time-out: Reassess therapy

http://blogs.cdc.gov/safehealthcare/?p=1026; accessed 3/2/11
Action: Indication and Duration

• Why indication??
  • Prompt prescriber to consider appropriate indication/duration
  • Communication
  • Analyze use patterns
    • Drug or indication

• How is the data entered?
  • Computerized
  • Form
  • Level of detail
  • Use of other/fever/sepsis

• Why duration??
  • Prompt consideration of planned duration for infection
  • When combined with indication can be evaluated for appropriateness

• How to implement
  • Pre-specified based on indication
  • Ordering physician specified
  • Pre-set for all
  • Short duration for certain agents (form of restriction)
Required Indication and Duration
Is Indication Data Accurate?

Accuracy of Physician Entered Indication Compared with Expert Review (N=396)

<table>
<thead>
<tr>
<th>Indication</th>
<th>Accuracy at Time of Order</th>
<th>Accuracy at 48-72 Hours</th>
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<tbody>
<tr>
<td>All Indications</td>
<td>100</td>
<td>80</td>
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<tr>
<td>Pneumonia</td>
<td>100</td>
<td>90</td>
</tr>
<tr>
<td>Bacteremia/Sepsis</td>
<td>100</td>
<td>80</td>
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<tr>
<td>GU-UTI</td>
<td>90</td>
<td>60</td>
</tr>
<tr>
<td>SSTI</td>
<td>80</td>
<td>60</td>
</tr>
<tr>
<td>GI-Peritonitis</td>
<td>50</td>
<td>30</td>
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Antibiotic Time Outs

• CDC and Joint Commission advocate
• Make inherent sense but
  • Little data to demonstrate their impact
  • Little data on how to make them effective
• Single-center, 2 IM wards developed targeted checklist
  • Carbapenems, moxifloxacin, P/T, vancomycin
  • Senior residents reviewed patients twice per week
• Antibiotics adjusted in 12.5% (189/1513) audits
  • Mostly change dose, duration and on initial audit
  • Decreased moxifloxacin and carbapenem use with 46% decrease in drug cost

**Antimicrobial Time Out Process**

**Timing:** Utilize on all patients started on antimicrobials. Initial time out to occur ≤72 hours after antimicrobials initiated. Repeat 48 hours after initial time out. If transfer from ICU, perform within 24 hours of acceptance. Suggested to be performed with any changes in subsequent antibiotic regimen.

**Review:** Antimicrobials (indication, dose and frequency), culture results, clinical indicators of infection (WBC, procalcitonin, imaging, vital signs), and renal function

**Determine role of antimicrobials:** For each agent, determine if it is **empiric**, **definitive therapy**, or **prophylaxis**.

- **Empiric** – Suspected source of infection but no definitive pathogen identified (cultures pending) OR source of infection unclear
- **Definitive** – Specific pathogen identified OR confirmed source of infection but no or negative culture data
- **Prophylaxis** – Antimicrobials provided to prevent infection

Discuss with team regarding recommendations. Refer to clinical pathways and reference tables for guidance.

**Document interaction with iVent.**

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**Definitive Therapy Algorithm**

- **Evaluate Culture**
  - Is culture data available?]
    - Yes
    - No
- **Evaluate Spectrum**
  - Is the agent active against the pathogen(s)? Is this the most narrow spectrum therapy possible?
- **Evaluate Agent**
  - Are the dose and frequency correct? Can the agent be changed to PO?
- **Evaluate Duration**
  - How long has the patient been on active antimicrobials? What is the appropriate duration of therapy for this infection? Has an adequate course of antibiotics been completed?

**Typical Duration of Therapy**

- Skin/soft tissue infections: 5-7 days
- CAP/HAP/HAP/VAP: 5-7 days
- Complicated UTI and pyelonephritis:
  - Levofoxacin: 5-7 days
  - Beta-lactams and TMP/SMX: 10-14 days
- Simple UTI
  - TMP-SMX: 3 days
  - Nitrofurantoin: 5 days
  - Fosfomycin: 1 dose

**Prophylaxis**

- Is prophylaxis indicated for this condition?
  - Yes
  - No
- Is this the correct agent, dose, route, and frequency?
  - Stop Antibiotic
Time Out Trial

Other Outcomes

- No difference in antibiotic use (DOT/1000PD)
  - IV levofloxacin DOT lower (31 TO vs. 49 US DOT/1000PD)
- IV to PO conversion higher
- Ratio PO to IV DOT significantly higher in TO (1.28 vs. 0.57, P=0.032)
- No differences in clinical outcomes
Daily Antibiotic Therapy Checklist

Current Therapy:

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<thead>
<tr>
<th>Drug</th>
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<th>Route</th>
<th>Frequency</th>
<th>Start Date</th>
<th>End Date</th>
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<tr>
<td>Drug 2</td>
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<td>Drug 3</td>
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Parameters for Review:

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<tr>
<td>Day 1</td>
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<td>Yes/No/Unclear</td>
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</table>

Reason(s) for Adjusting Antibiotic Regimen:

- Yes, due to bug drug mismatch
- Yes, narrower spectrum agent can be used
- Yes, due to adverse drug reactions, toxicity, or interaction

Recommended New Antibiotic Regimen:

<table>
<thead>
<tr>
<th>Drug</th>
<th>Date</th>
<th>Route</th>
<th>Frequency</th>
<th>Date of Change</th>
</tr>
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<tbody>
<tr>
<td>Drug 1</td>
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</tr>
<tr>
<td>Drug 2</td>
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<tr>
<td>Drug 3</td>
<td></td>
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</tbody>
</table>
Syndromic Stewardship: Shifting Focus

“Antimicrobial stewardship interventions have been proven to improve individual patient outcomes, reduce the overall burden of antibiotic resistance, and save healthcare dollars.” CDC Website

www.cdc.gov/getsmart/healthcare/evidence
Action: Syndromic Stewardship

- Stewardship activities focusing on improving care for a specific infectious syndrome
  - SSTI, UTI, pneumonia, asymptomatic bacteriuria, etc.
- Addresses multiple aspects of care (bundled)
- Allows to address key decision points where choices can go wrong
  - Is this an infection?
  - What infectious syndrome is it?
  - How should I evaluate this infection using lab and imaging?
  - How should I choose empiric therapy?
  - How should I adjust therapy based on subsequent data?
  - How long should I continue therapy?
  - What can be done to prevent the infection?
Advantages of Syndromic Focus

- Multidisciplinary
- Improve diagnostic activities
- Improve therapeutic activity (empiric, definitive, duration)
- Targeted education and improved messaging
- Prevention

Reasons that Antimicrobial Courses Were Not Appropriate According to Accuracy of Provider Initial Diagnosis

<table>
<thead>
<tr>
<th>Accuracy of Provider Initial Diagnosis</th>
<th>Antimicrobial Course Appropriate</th>
<th>Incorrect Drug</th>
<th>Incorrect Dose</th>
<th>Incorrect Duration</th>
<th>Other</th>
<th>Antimicrobial Not Indicated</th>
</tr>
</thead>
<tbody>
<tr>
<td>Correct (n = 291)</td>
<td>181 (62)</td>
<td>81 (28)</td>
<td>5 (2)</td>
<td>43 (15)</td>
<td>1 (0)</td>
<td>10 (3)</td>
</tr>
<tr>
<td>Correct, but sign or symptom rather than a syndrome or disease (n = 31)</td>
<td>2 (7)</td>
<td>6 (19)</td>
<td>1 (3)</td>
<td>1 (3)</td>
<td>1 (3)</td>
<td>25 (81)</td>
</tr>
<tr>
<td>Incorrect (n = 156)</td>
<td>6 (4)</td>
<td>21 (14)</td>
<td>1 (1)</td>
<td>5 (3)</td>
<td>0 (0)</td>
<td>131 (84)</td>
</tr>
<tr>
<td>Indeterminate (n = 22)</td>
<td>2 (9)</td>
<td>4 (18)</td>
<td>0 (0)</td>
<td>7 (32)</td>
<td>0 (0)</td>
<td>11 (50)</td>
</tr>
</tbody>
</table>

NOTE. Percentages sum to >100% because some courses involved multiple errors.

Retrospective analysis of 322 SSTI
*S. aureus* or Streptococci isolated from 97% cultures

<table>
<thead>
<tr>
<th>Antimicrobial</th>
<th>Cellulitis (N=66)</th>
<th>Cutaneous Abscess (N=103)</th>
<th>SSTI with Complicating Factors (N=153)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Vancomycin</td>
<td>79%</td>
<td>73%</td>
<td>73%</td>
</tr>
<tr>
<td>Cefazolin</td>
<td>20%</td>
<td>20%</td>
<td>17%</td>
</tr>
<tr>
<td>Beta-lactam/Beta-lactamase inhibitor</td>
<td>53%</td>
<td>65%</td>
<td>66%</td>
</tr>
<tr>
<td>Clindamycin</td>
<td>26%</td>
<td>18%</td>
<td>33%</td>
</tr>
<tr>
<td>Levoﬂoxacin</td>
<td>11%</td>
<td>5%</td>
<td>14%</td>
</tr>
<tr>
<td>Gram-positive therapy only</td>
<td>38%</td>
<td>33%</td>
<td>17%</td>
</tr>
<tr>
<td>Broad-spectrum Gram-negative therapy</td>
<td>61%</td>
<td>67%</td>
<td>80%</td>
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<tr>
<td>Anaerobic therapy</td>
<td>74%</td>
<td>73%</td>
<td>83%</td>
</tr>
<tr>
<td>Three or more antibiotics</td>
<td>52%</td>
<td>40%</td>
<td>48%</td>
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<tr>
<td>Median Duration Therapy (days)</td>
<td>11</td>
<td>14</td>
<td>14</td>
</tr>
</tbody>
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SSTI Intervention

• Multidisciplinary guideline
• Focused on diagnosis and treatment
  • Lab utilization
  • Empiric therapy
  • Duration therapy

• Implementation
  • Created order set
  • Educated using peer champions
  • Audit-feedback to departments by champions

Measure the Impact

Exposure to Antimicrobial Classes by Time Period

Duration of Therapy by Time Period

• Clinical outcomes no difference pre- and post-intervention
  • Clinical failure $\rightarrow$ 7.7% vs. 7.4% (P=0.93)
  • Rehospitalization $\rightarrow$ 7.7% vs. 5.1% (P=0.33)
  • Median length of hospital stay $\rightarrow$ 4 vs. 4 (P=0.43)

Examples of Syndromic Efforts at NM

- Pneumonia
- UTI
- Skin/soft tissue infection
- Diabetic Foot Infection
- Exacerbation COPD
- *C. difficile* infection
- *Staph aureus* bacteremia
- Sepsis

[www.nebraskamed.com/asp](http://www.nebraskamed.com/asp)
Action: IV to PO

• IV to PO conversion of highly bioavailable agents
  • Fluoroquinolones, metronidazole, fluconazole, linezolid, rifampin, TMP/SMX
  • Benefits = cheaper, shorter stays, lines out, patient preference

• Pharmacist lead conversion of IV levofloxacin to oral
  • Clinically stable and taking oral medications and nutrition

• Pre vs. post intervention (P<0.05)
  • IV duration 3.5 days less
  • LOS 3.5 days shorter
  • Costs $3,300 less

• Consider mechanisms
  • Pharmacy policy, calls, notes, reminders

Action: Dose Adjustment

Clinical Outcomes for Patients Treated with Aminoglycoside or Vancomycin with and without a Pharmacist-led Antimicrobial Stewardship Program

Action: Antibiotic Allergy Assessment

• Antibiotic allergy noted 13-15% patients
• Impacts
  • Clinical care - associated with 50% decrease in odds of receiving effective surgical prophylaxis
  • Outcomes - increased LOS, ICU admission, number of antibiotics used, mortality in non-surgical patients
  • Cost - 63% increase in hospital antibiotic costs; 38% higher cost in discharge regimen with PCN allergy
• Implementing PCN allergy skin testing at a hospital found only 1 of 146 hospitalized patients with PCN allergy developed a reaction
  • Changes in antibiotic regimens after skin testing saved estimated $82,000 per year
• Interventions
  • Desensitization protocols, graded challenge, education, improved documentation

Mild Reaction
(Examples: itching, minor rash (not hives), maculopapular rash)

OR
Documented intolerance/side effect

Gell and Coombs Type I Reaction
(Examples: anaphylaxis, angioedema, wheezing, laryngeal edema, hypotension, or hives/urticaria)

OR
Unknown reaction without mucosal involvement, skin desquamation, or organ involvement

Gell and Coombs Type II - IV Major Reactions
(Examples: serum sickness, SJS, TEN, DRESS syndrome, or hemolytic anemia)

Use any generation cephalosporin (full dose)

OR
If non-allergic adverse event (e.g., nausea, diarrhea, fainting), use different agent in same class

AND/OR
Consult Infectious Disease

Previously Tolerated Beta-Lactam

Utilizing Previously Tolerated Beta-Lactam

Use 3rd or 4th generation cephalosporins or carbapenems by graded challenge

OR
Use guideline-appropriate non-beta-lactam agent (table 3)

OR
Consult Infectious Disease

Utilizing Different Agent than Beta-Lactam Previously Tolerated

Use guideline-appropriate non-beta-lactam agent (table 3)

OR
Ampicillin

OR
Consult Infectious Disease

NO Previous Beta-Lactam Tolerance

Reaction Occurred Greater than or Equal to 10 Years Ago

Use guideline-appropriate non-beta-lactam agent (table 3)

OR
Ampicillin

OR
Consult Infectious Disease

Reaction Occurred Within 10 Years

Use guideline-appropriate non-beta-lactam agent (table 3)

OR
Ampicillin

OR
Consult Infectious Disease
Action: Antibiograms

• Utility
  • Track resistance trends
  • Choose empiric therapy

<table>
<thead>
<tr>
<th>Organism</th>
<th>Antibiotic name</th>
<th>Number</th>
<th>%S</th>
</tr>
</thead>
<tbody>
<tr>
<td>Proteus mirabilis</td>
<td>Ampicillin</td>
<td>175</td>
<td>89.7</td>
</tr>
<tr>
<td>Proteus mirabilis</td>
<td>Ampicillin/Sulbactam</td>
<td>175</td>
<td>96</td>
</tr>
<tr>
<td>Proteus mirabilis</td>
<td>Piperacillin/Tazobactam</td>
<td>175</td>
<td>100</td>
</tr>
<tr>
<td>Proteus mirabilis</td>
<td>Cefazolin*</td>
<td>139</td>
<td>94.2</td>
</tr>
<tr>
<td>Proteus mirabilis</td>
<td>Cefuroxime</td>
<td>175</td>
<td>98.3</td>
</tr>
<tr>
<td>Proteus mirabilis</td>
<td>Ceftazidime</td>
<td>169</td>
<td>100</td>
</tr>
<tr>
<td>Proteus mirabilis</td>
<td>Ceftriaxone</td>
<td>175</td>
<td>98.3</td>
</tr>
<tr>
<td>Proteus mirabilis</td>
<td>Cefepime</td>
<td>175</td>
<td>99.4</td>
</tr>
<tr>
<td>Proteus mirabilis</td>
<td>Aztreonam</td>
<td>175</td>
<td>93.7</td>
</tr>
<tr>
<td>Proteus mirabilis</td>
<td>Ertapenem</td>
<td>175</td>
<td>99.4</td>
</tr>
<tr>
<td>Proteus mirabilis</td>
<td>Meropenem</td>
<td>175</td>
<td>100</td>
</tr>
<tr>
<td>Proteus mirabilis</td>
<td>Amikacin</td>
<td>175</td>
<td>100</td>
</tr>
<tr>
<td>Proteus mirabilis</td>
<td>Gentamicin</td>
<td>175</td>
<td>91.4</td>
</tr>
<tr>
<td>Proteus mirabilis</td>
<td>Tobramycin</td>
<td>175</td>
<td>92.6</td>
</tr>
<tr>
<td>Proteus mirabilis</td>
<td>Levofloxacin</td>
<td>175</td>
<td>81.1</td>
</tr>
<tr>
<td>Proteus mirabilis</td>
<td>Trimethoprim/Sulfamethoxazole</td>
<td>175</td>
<td>76.6</td>
</tr>
<tr>
<td>Proteus mirabilis</td>
<td>Tetracycline</td>
<td>175</td>
<td>2.3</td>
</tr>
</tbody>
</table>
Antibiograms and Practice Guidelines

- For sepsis and pneumonia, routine use of vancomycin + piperacillin/tazobactam + ciprofloxacin
- Developed combination antibiogram
- Implemented new treatment guidelines for sepsis

---

<table>
<thead>
<tr>
<th>Suspected Source of Infection</th>
<th>Suggested Antibiotics</th>
</tr>
</thead>
<tbody>
<tr>
<td>Unknown (includes catheter related</td>
<td>Vancomycin IV per pharmacy consult (initial 25mg/kg loading dose)</td>
</tr>
<tr>
<td>bloodstream infection)</td>
<td>PLUS EITHER</td>
</tr>
<tr>
<td></td>
<td>Piperacillin/tazobactam 4.5g IV q8h, infused over 4 hours OR Cefepime 1 gm IV q6hr</td>
</tr>
<tr>
<td></td>
<td>+/-</td>
</tr>
<tr>
<td></td>
<td>Tobramycin 7 mg/kg IV EIAD</td>
</tr>
</tbody>
</table>

---

| Percentage Susceptible to ciprofloxacin or aminoglycosides if resistant to one of the following beta-lactams |
|---------------------------------------------------------------|---------------------------------------------------------------|---------------------------------------------------------------|
| If resistant to piperacillin/tazobactam                      | Pseudomonas aeruginosa | Escherichia coli | Klebsiella oxytoca   |
| Ciprofloxacin                                                | 28% | 17% | 35% |
| Gentamicin                                                   | 52% | 71% | 100% |
| Amikacin                                                     | 76% | 92% | 100% |
| Tobramycin                                                   | 88% | 63% | 96% |
| If resistant to cefepime                                     | (n=52) | (n=11) | (n=6) |
| Ciprofloxacin                                                | 39% | 0% | 17% |
| Gentamicin                                                   | 42% | 82% | 100% |
| Amikacin                                                     | 77% | 91% | 100% |
| Tobramycin                                                   | 89% | 70% | 100% |
Effect of combination antibiogram & new guideline implementation

52.7% decrease in IV ciprofloxacin use (79.8 DOT → 37.7 DOT)
47.9% increase in IV tobramycin use (11.9 DOT → 17.6 DOT)
| Pathogen              | Isolate Tested | Ampicillin | Ampicillin/Sulbactam | Piperacillin/Tazobactam | Cefazolin | Cefepine | Cefotaxim | Ceftriaxone | Cefuroxime | Aztreonam | Eraperam | Meropenem | Amikacin | Gentamicin | Tobramycin | Ciprofloxacin | Levofloxacin | Trimethoprim/Sulfonamide | Nitrofurantoin | Tetracyclines |
|-----------------------|----------------|------------|----------------------|-------------------------|-----------|----------|----------|------------|------------|-----------|----------|----------|----------|----------|-----------|-----------|----------------|----------------|----------------|---------------------|----------------|---------------|
| *Escherichia coli*    | 111            | 53         | 59                   | 99                      | 86        | 98       | 92       | 98         | 97         | 91        | 100      | 100      | 100      | 91        | 91        | 58           | 59           | 76             | 99             | 77            |
| *Klebsiella pneumoniae* | 41             | --         | 78                   | 98                      | 93        | 98       | 95       | 98         | 93         | 98        | 98       | 95       | 95       | 93        | 63        | 83           |               |                |                |
| *Proteus mirabilis*   | 41             | 98         | 98                   | 100                     | 100       | 100      | 100      | 100        | 100        | 100       | 75       | 75       | 75       | 75        | 50        | 75           |               |                |                |
| *Pseudomonas aeruginosa* | 31            | --         | --                   | 97                      | --        | 97       | --       | 97         | --         | 84        | --       | 90       | 100      | 74        | 77        | 71           | 71           | --             | --             | --            |

--- Denotes organism has intrinsic resistance to this antimicrobial

--- Nitrofurantoin is reported for urine sources only

1. Nitrofurantoin is reported for urine sources only

**Summary for Gram-Negative Organisms**

During the 2-year period between January 2015 and December 2016, a total of 111 *E. coli* were identified, making it the most commonly identified Gram-negative pathogen. Antibiotic susceptibilities of these *E. coli* can be summarized as follows:

1. Oral antibiotics with the highest susceptibilities (in descending order) were:
   a. Nitrofurantoin (99%)
   b. Cefuroxime (91%)
   c. Cephalexin (86%, as indicated by cefazolin susceptibility)
   d. Trimethoprim/sulfamethoxazole (76%)

2. Susceptibilities of antibiotics available only in intravenous formulation (e.g., ceftriaxone) exceed 90%, except:
   a. Ampicillin/sulbactam (59%)
   b. Cefazolin (86%)

Antibiotic susceptibility data can be useful for guiding selection of empiric antibiotic therapy for residents in whom culture and susceptibility data from the past few months are not available.
**Action: Rapid Identification of Pathogens**

**Numerous** new rapid diagnostic technologies currently approved and near approval

- **SeptiFast Test**
- **MGRADE**
- **QuickFISH™**
- **PNA FISH®**
- **T2 Biosystems**
- **BIOFIRE**
- **MALDI-TOF**
- Chromogenic agars
- Latex agglutinations

- **14-20 hours**
- **12-24 hours**
- **24-48 hours**
- **72-96 hours**

**Sepsis**

**Bacteremia identified**

**Growth of Organism**

**Full ID and Susceptibility**
Rapid Identification of \textit{S. aureus} and Methicillin-resistance from Blood Cultures

Impact of introduction of Cepheid Xpert MRSA/SA PCR combined with ID call to clinician in \textit{S. aureus} and coagulase-negative staphylococcal bacteremia

\begin{figure}[h]
\centering
\includegraphics[width=\textwidth]{chart.png}
\caption{Mean time to switch and stop for \textit{S. aureus} and coagulase-negative staphylococci.}
\end{figure}

Decreased LOS 4.5 to 6.2 days and costs $8,300 to $21,000

<table>
<thead>
<tr>
<th>Pathogen Detected</th>
<th>Preferred Therapy</th>
<th>Comments (susceptibility data from 2016)</th>
</tr>
</thead>
</table>
| **Enterococcus genus**  
  van A/B negative  
  van A/B positive = VRE | Vancomycin 15 mg/kg Q12h  
  Linezolid 600mg q12h | Linezolid slightly more active in VRE  
  Linezolid 89-94% susceptible (85% blood)  
  Daptomycin 87-90% susceptible (90% blood) |
| **Staphylococcus aureus**  
  mecA negative = MSSA  
  mecA positive = MRSA | Oxacillin 2g q4h  
  Vancomycin 15 mg/kg Q12h | Cefazolin 2g q8h is an alternative  
  Daptomycin is an alternative to vancomycin |
| **Staphylococcus genus with negative S. aureus PCR**  
  Blood Culture (BCx) result:  
  1 of 2 BCX positive | Consider withholding or discontinuing therapy as likely contaminant, do not need to routinely draw repeat BCX | In severely ill patients consider starting/continuing therapy until more definitive results return |
| 2 of 2 BCX positive  
  mecA negative  
  mecA positive | Oxacillin 2g q4h  
  Vancomycin 15 mg/kg Q12h | Cefazolin 2g q8h is an alternative |
| **Streptococcus pyogenes**  
  (Group A Strep) and  
  Streptococcus agalactiae  
  (Group B Strep) | Penicillin 3 million units q4h or  
  Ampicillin 2g IV q4h or  
  Cefazolin 2g IV Q8h | Beta-hemolytic strep are routinely susceptible to penicillin  
  Vancomycin in severe beta-lactam allergy |
| **Streptococcus pneumoniae**  
  **Source of Infection:**  
  Pneumonia  
  CNS Infection | Penicillin 3 million units q4h or  
  Ampicillin 2g IV q4h  
  Ceftriaxone 2g q24h + Vancomycin 15 mg/kg Q12h | Continue vancomycin until susceptibilities return |
| **E. coli** | Ceftriaxone 2g q24 OR  
  Piperacillin/tazobactam 4.5 g q8h  
  (consider with history of resistance, recurrent UTI, recent FQ exposure, or recent hospital stay) | **Community-onset (CO):**  
  Ceftriaxone 86-96% susceptible  
  91-96% CO susceptible (91% blood)  
  78-85% NO susceptible (78% blood)  
  Pip/tazo: 94-98% susceptible  
  95-98% CO susceptible (97% blood)  
  64-95% NO susceptible (94% blood)  
  **Nosocomial-onset (NO):**  
  Piperacillin/tazobactam 4.5 g q8h OR Ertapenem 1g q24h  
  Ceftriaxone: 78-97% susceptible  
  92-97% CO susceptible (92% blood)  
  78-92% NO susceptible (78% blood)  
  Levofloxacin: 69-84% susceptible (75% blood)  
  80-84% CO susceptible  
  69-74% NO susceptible  
  Ertapenem: 100% susceptible |
| **Serratia marcescens** | Cefepime 1g q6h | Cefepime: 91-95% susceptible  
  Levofloxacin: 97-100% susceptible  
  Ertapenem: 97-100% susceptible |
| **Enterobacter cloacae** | Meropenem 500mg Q6h | Meropenem: 100% susceptible  
  Levofloxacin: 97-99% susceptible  
  Cefepime: 78-87% susceptible (87% blood)  
  Ertapenem: 79-86% susceptible (87% blood)  
  Pip/tazo: 73-85% susceptible (85% blood) |
| **Proteus spp** | Ceftriaxone 2g q24h | 97-100% susceptible (100% blood) |
Decreased mortality with Rapid Diagnostics

- OR 0.66 (95% CI .54-.80)

- Significant decrease in
  - Gram positives (OR 0.73; .55-.97)
  - Gram negatives (OR 0.51; .33-.78)
  - With stewardship (OR 0.64; .51-.79)

- Non-significant without stewardship

Shortened time to effective therapy 5 hours and LOS 2.5 days
**Action: Procalcitonin**

Biomarker of bacterial infection: Specific for bacterial infection, correlates with disease severity, rapid rise (6-12 hours), predictable rate of decline, not impaired by immunosuppression

- Numerous RCT in lower respiratory tract infection and sepsis
- Patient level meta-analysis with 6708 patients, 26 trials, 12 countries
- RCT involving any RTI in any setting
  - URTI 8%, CAP 44%, HAP 8%, VAP 6%, bronchitis 9%, COPD exacerbation 19%
  - Clinic 15%, ED 49%, ICU 36%
- Decreased antibiotic duration 2.4 days

### Clinical Outcomes

<table>
<thead>
<tr>
<th></th>
<th>Adjusted OR (95% CI), P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>30-day Mortality</td>
<td><strong>0.83 (0.7-0.99), p=0.037</strong></td>
</tr>
<tr>
<td>Treatment Failure</td>
<td>0.90 (0.80-1.01), p=0.068</td>
</tr>
<tr>
<td>Length of ICU Stay, days</td>
<td>0.39 (-0.81-1.58), p=0.524</td>
</tr>
<tr>
<td>Length of Hospital Stay, days</td>
<td>-0.19 (-0.96-0.58), p=0.626</td>
</tr>
<tr>
<td>Antibiotic-related Side Effects</td>
<td><strong>0.68 (0.57-0.82), p&lt;0.0001</strong></td>
</tr>
</tbody>
</table>

Efficacy and Safety of PCT Guidance in Patients with Suspected or Confirmed Sepsis: a Systematic Review and Meta-Analysis

- 10 RCT of PCT use in sepsis (N=3489)
- Adherence 47-93%
- Abx stopping cutoffs varied but most commonly 0.5 or 80-90% decline from peak

Antibiotic Duration

Efficacy and Safety of PCT Guidance in Patients with Suspected or Confirmed Sepsis: a Systematic Review and Meta-Analysis

- 10 RCT of PCT use in sepsis (N=3489)
- Adherence 47-93%
- Abx stopping cutoffs varied but most commonly 0.5 or 80-90% decline from peak

Mortality

Conclusions

• Use your team and data to develop a plan
• Implement with a plan to monitor effectiveness
• Choose from well established solutions
  • Target the root of the problem
  • Customize to your facility
  • Don’t be afraid to adjust what you are doing
1. Go to -- https://asap.nebraskamed.com

2. Click here

3. Click here

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Question 1

• All of the following are key components of quality improvement activities except
  1. Establish a team responsible for improvement
  2. Measure outcomes associated with the improvement
  3. Secure outside expertise to develop the plan
  4. Understand and analyze the process when developing an improvement plan
Question 2

• All of the following are strategies which have been shown to improve clinical outcomes in acute care hospitals
  1. Antibiotic time outs
  2. Use of rapid diagnostic technology in bacteremia
  3. Procalcitonin use
  4. Renal dose adjustment by pharmacists