Syndrome Specific Interventions: SSTI and Pneumonia

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10/31/17
“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
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.
# Skin and Soft-Tissue Infections Requiring Hospitalization at an Academic Medical Center: Opportunities for Antimicrobial Stewardship


Timothy C. Jenkins,1,4 Allison L. Sabel,2,3 Ellen E. Sarcone,2,4 Connie S. Price,1,4 Philip S. Mehlert,2,4 and William J. Burman1,4

Retrospective analysis of 322 SSTI

*Staphylococcus aureus* or Streptococci isolated from 97% cultures

(only pathogens in >70%)

<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>
</tr>
<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>
</tr>
<tr>
<td>Median Duration Therapy (days)</td>
<td>11</td>
<td>14</td>
<td>14</td>
</tr>
</tbody>
</table>

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Opportunities for Improvement

### Utilization of Imaging in SSTI

<table>
<thead>
<tr>
<th>Imaging</th>
<th>Cellulitis (N=66)</th>
<th>Cutaneous Abscess (N=103)</th>
<th>SSTI with Complicating Factors (N=153)</th>
<th>Yield of Image for Deep Infection</th>
</tr>
</thead>
<tbody>
<tr>
<td>Any imaging</td>
<td>94%</td>
<td>69%</td>
<td>86%</td>
<td>4%</td>
</tr>
<tr>
<td>Plain film</td>
<td>94%</td>
<td>69%</td>
<td>86%</td>
<td>1%</td>
</tr>
<tr>
<td>Ultrasound</td>
<td>42%</td>
<td>14%</td>
<td>26%</td>
<td>0.3%</td>
</tr>
<tr>
<td>CT image</td>
<td>9%</td>
<td>15%</td>
<td>17%</td>
<td>2%</td>
</tr>
<tr>
<td>MRI</td>
<td>8%</td>
<td>3%</td>
<td>9%</td>
<td>1%</td>
</tr>
<tr>
<td>CT or MRI</td>
<td>17%</td>
<td>17%</td>
<td>24%</td>
<td>NR</td>
</tr>
</tbody>
</table>

SSTI Intervention

- Multidisciplinary guideline
- Diagnosis
  - When and what labs to order
  - Discouraged use of swab cultures and imaging
- Treatment
  - Discouraged gram negative and anti-anaerobic agents
  - Empiric vancomycin only
  - Transition to oral therapy at 48-72 hours
  - Duration of therapy 7 days
- Implementation
  - Created order set
  - Educated using peer champions
  - Audit-feedback to departments by champions

Measure the Impact

Exposure to Antimicrobial Classes by Time Period

- Broad Aerobic Gram-Negative Activity: Baseline period 80%, Intervention period 60% (P<0.001)
- Anti-pseudomonal Activity: Baseline period 10%, Intervention period 5% (P=0.02)
- Broad Anaerobic Activity: Baseline period 20%, Intervention period 10% (P<0.001)

Duration of Therapy by Time Period

- <10 days: Baseline period 20%, Intervention period 10% (P<0.001)
- 10-14 days: Baseline period 30%, Intervention period 30% (P=0.83)
- >14 days: Baseline period 50%, Intervention period 60% (P<0.001)

Clinical outcomes no difference pre- and post-intervention

- Clinical failure → 7.7% vs. 7.4% (P=0.93)
- Rehospitalization → 7.7% vs. 5.1% (P=0.33)
- Median length of hospital stay → 4 vs. 4 (P=0.43)

SSTI Issues to Consider

• Specific Infection Being Treated – Cellulitis vs. Abscess

• I&D primary therapy
  • Multiple, immune suppressed, can’t drain, systemic symptoms, rapid spread or severe, lesions size?? = antibiotics
  • Targeting MRSA unless you know different
    • Mild-Moderate = TMP/SMX, doxycycline, clindamycin
    • Severe = Vancomycin, linezolid, daptomycin
• Duration therapy 5-7 days
Should we give antibiotics after incision and drainage?

**Percent Clinical Cure**

<table>
<thead>
<tr>
<th></th>
<th>Placebo</th>
<th>TMP-SMX</th>
<th>Clindamycin</th>
</tr>
</thead>
<tbody>
<tr>
<td>Talan, et al (N=1265)</td>
<td><img src="73.6" alt="73.6" /></td>
<td><img src="80.5" alt="80.5" /></td>
<td><img src="83.1" alt="83.1" /></td>
</tr>
<tr>
<td>Daum, et al (N=786)</td>
<td><img src="68.9" alt="68.9" /></td>
<td><img src="81.7" alt="81.7" /></td>
<td><img src="83.1" alt="83.1" /></td>
</tr>
</tbody>
</table>

- **Placebo vs. TMP-SMX 2 DS tabs BID**
- **Clindamycin 300mg TID**


Do we need to worry about MRSA in Cellulitis?

- Two multicenter RCT evaluating addition of TMP-SMX to beta-lactam in uncomplicated cellulitis
  - No abscess, immunosuppression, PVD, device present
- All treated with cephalexin and randomized TMP-SMX OR placebo
  - Various dosing regimens
    - Weight-based high dose cephalexin and TMP-SMX for 7-14 days
    - Traditional cephalexin and high dose TMP-SMX for 7 days

<table>
<thead>
<tr>
<th>Outcomes</th>
<th>Pallin, et al. (N=146)</th>
<th>Moran, et al. (N=496)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Clinical Cure Rate</td>
<td>85% vs. 82% (95%CI, -9.3%-15%, P=.66)</td>
<td>83.5% vs. 85.5% (95%CI, -9.7%-5.7%, P=.5)</td>
</tr>
<tr>
<td>Adverse Events</td>
<td>49% vs. 53% (P=.62)</td>
<td>41.1% vs. 36.3%, P=NS)</td>
</tr>
</tbody>
</table>

Moran GJ.  *JAMA.*  2017;317:2088-96
Abscess and Cellulitis Summary

• Treat based on infectious syndrome
  • Non-purulent cellulitis → treat for strep using beta-lactam
    • Use high doses in obese or severe edema
  • Abscess → drainage alone may be adequate but increasing evidence benefit from treatment
  • Purulence present → treat for MRSA
    • Mild-Moderate = TMP/SMX or Doxy (or Clinda??)
      • Recent trials suggested no difference between TMP-SMX and Clindamycin in outcomes
    • Severe = Vancomycin or others
• Complicated infections = same as purulent infections
• Don’t routinely cover gram-negatives/anaerobes
  • Use with necrotizing fasciitis and severe DFI

Pneumonia (CAP, HCAP?, HAP, VAP)

Ventilator-Associated Pneumonia: Overdiagnosis and Treatment Are Common in Medical and Surgical Intensive Care Units

• Only 41.6% of 231 possible VAP cases determined to be VAP
• Antibiotics continued beyond day 3 in 76% without VAP (1183 DOT)

**Pneumonia Opportunities**

• Diagnostics
  • Procalcitonin
  • Blood and sputum culture
  • Viral and MRSA PCR
  • Urine antigens

• Treatment
  • When to treat for MDROs and use combination therapy
  • De-escalation
  • Duration of therapy

• Prevention including vaccines

Procalcitonin

- Most specific biomarker for bacterial infection currently available
- Rapidly rises (~6 hr after insult) and has a half life of 24 hours
- Multicenter, non-inferiority, randomized trial of adults with LRTI presenting to ED
  - PCT levels at admission and if antibiotics started on day 3, 5, 7

- Decreased
  - Absolute abx starts -12.2%
  - Mean duration therapy -34.8% (-3 days)
  - Abx side effects 28.1% vs. 19.9%
  - 30-day adverse events 18.9% vs. 15.4%

Diagnostic Testing Opportunities

• Blood cultures not needed in everyone
• Sputum cultures only obtained in half of patients
• Timing less than ideal
  • Gram-stain and culture can identify 80% Pneumococcal pneumonias if obtained within 12 hours of antibiotics\(^1\)
  • Median time to sputum culture = 11 hours after antibiotics\(^2\)
• Urine antigens can provide useful data
  • 474 CAP cases with 75 cases pneumococcal pneumonia diagnosed by antigen only and antibiotics adjusted in 41 based on this data\(^3\)
• Nasal MRSA PCR testing
  • NPV ranging 84% to 99%\(^4,5\)

Retrospective, observational, single-center analysis adult CAP/HCAP over 2 years (N=521)
- MDRO = MRSA, Pseudomonas, ESBL GNR, CRE, Acinetobacter, Stenotrophamonas
- 3.8% overall → 5.9% HCAP, 1.9% CAP

"Once you start you can’t stop"
- Patients with HCAP at VA hospitals over 4 years (N=9319)
  - >50% received both anti-MRSA and Pseudomonas abx
    - 6.7% had MRSA, 4.8% had Pseudomonas
  - Only 28.3% had any de-escalation by hospital day 4
- De-escalation safe and beneficial
  - Early antibiotics discontinuation in VAP with negative BAL safe with fewer superinfections and MDR pathogens
  - De-escalation was protective in multivariate analysis of hospital mortality in severe sepsis/septic shock (N=628) → OR 0.55 (0.32-0.98), P = 0.022
Case #1

- 80yo female with LVAD
- Developed cellulitis around LVAD insertion site, fever, lethargy
- WBC remained normal throughout hospital stay
- Started empirically on daptomycin 4 mg/kg/day but had not failed PO ABX outpatient or received any IV ABX
- Prescriber rationale for ABX choice: want to be more aggressive due to risk of infection traveling to heart
- Blood culture prior antibiotic remained negative; wound culture grew MRSA sensitive to clindamycin, levofloxacin, TMP/SMX, vancomycin
- Patient discharged home on TMP/SMX
Questions

What would be the best way to approach the issue?

Would a formulary restriction be best in this scenario?

What is the best way to approach the physician who is overly aggressive treating this cellulitis?
Case #2

- 39yo male presented to ED with diagnosis of sepsis
- Weight = 91.1kg, BMI 31 kg/m²
- PMHx: COPD, CAD, HTN, tobacco use
- Labs: Scr 0.7, CrCl >100 ml/min, WBC 12.6
- In ED, received pip/tazo 3.375g x 1, vancomycin 1.5g x 1
- Upon admission, continued pip/tazo 3.375g IV q8h, vancomycin 1.5g q8h for necrotizing fasciitis
- Vanco trough prior to 4th dose 42.9 (8/17); dose held and re-dosed on 8/18
- Discharged 8/18, readmitted 8/19 with renal failure, likely due to vancomycin toxicity
Questions

Does your facility allow >4g/day of vancomycin doses for empiric therapy?

What incidence of renal toxicity have you seen with combination pip/tazo and vancomycin?

Does your facility have guidelines for vancomycin dosing in obese patients?
Incidence of Vancomycin Nephrotoxicity in Obese Patients

- Retrospective review compared vancomycin nephrotoxicity based on degree of obesity
- Dosing protocol
  - Loading dose: variable
  - Maintenance dose: 15 mg/kg actual body weight (2 g/dose max)
  - Frequency: q12h if CrCl 60-120 ml/min; q24h if CrCl 30-60 ml/min

- Rate of nephrotoxicity: 8.7% non-obese; 14.3% Class I-II obesity; 26.3% Class III obesity
- ~35% in each group on pip/tazo
- Predictors: Obesity (OR 2.99), trough >20, concomitant pip/tazo therapy (OR 3.55), ICU stay, duration of therapy

Nephrotoxicity from Vancomycin + Piperacillin/Tazobactam Therapy (VPT)

- Meta-analyses
  - 14 studies: VPT vs. vanco alone (aOR 3.11)
  - 15 studies: VPT vs vanco +/- other beta-lactam (OR 3.6)

- Individual studies
  - VPT vs. vanco + cefepime:
    - 29% vs. 11%
  - VPT vs. vanco + cefepime:
    - 2.18x more likely to cause AKI
  - VPT vs. vanco alone:
    - aOR 2.48
  - VPT as independent risk factors for AKI in 4 studies
    - OR ranged from 5.36 to 2.61
## Risk Factors Associated Vancomycin Nephrotoxicity

<table>
<thead>
<tr>
<th>Vancomycin Exposure Variables</th>
<th>Loading dose</th>
<th>Total daily dose</th>
<th>AUC</th>
<th>Trough level</th>
<th>Duration</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patient-Specific Factors</td>
<td>Obesity</td>
<td>Severity of illness</td>
<td>ICU residence</td>
<td>Chronic kidney disease</td>
<td>Concurrent nephrotoxin exposure</td>
</tr>
</tbody>
</table>

Questions??