Antimicrobial Stewardship

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Outline

- Reasons for urgency of Antimicrobial Stewardship Programs (ASPs)
- Understand the purpose, goals, and provide overview of our ASP
- Describe ASPs in key settings
- Summary and case studies
What is Antimicrobial Stewardship?

“The selection of the optimal antimicrobial agent, route of administration, dose, and duration to provide maximal clinical benefit, while minimizing unintended consequences.”
Why Antimicrobial Stewardship?

- Up to 50% of abx use is inappropriate
  - High quantity, poor quality
- Inappropriate & unnecessary abx use can lead to selection of resistant pathogens
- Antimicrobial resistance continues to increase
- Emergence of antimicrobial resistance leads to significant impact on pt morbidity & mortality, health care costs

Unnecessary Use of Antimicrobials in Hospitals

- Prospective observational study conducted in adult inpatients
- 576 (30%) of 1941 total antimicrobial days of therapy (DOT) deemed unnecessary

Most Common Reasons for Unnecessary DOT

- Duration of Therapy Longer than Necessary: 192 DOT
- Noninfectious or Nonbacterial Syndrome: 187 DOT
- Treatment of Colonization or Contamination: 94 DOT

How We Acquire Antibiotic Resistant Organisms in Hospitals

*Paterson DL. Clin Infect Dis 2006;42:S90-5*
12 Steps to Prevent Antimicrobial Resistance: Hospitalized Adults

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

Prevent Transmission
Use Antimicrobials Wisely
Diagnose & Treat Effectively
Prevent Infections

www.cdc.gov/drugresistance/healthcare
Antimicrobial Resistance Continues to Increase

1 = Staphylococcus aureus resistant to methicillin
2 = Enterococci resistant to vancomycin
3 = Pseudomonas aeruginosa resistant to imipenem
4 = Acinetobacter spp resistant to imipenem
5 = Candida spp resistant to fluconazole

Wenzel et al. Infect Cont Hosp Epi 2008;29:1012-8
Emergence of KPC Infections

Geographical Distribution of *Klebsiella pneumonia* carbapenemase (KPC) Infections

MMWR
Morbidity and Mortality Weekly Report
www.cdc.gov/mmwr

Guidance for Control of Infections with Carbapenem-Resistant or Carbapenemase-Producing *Enterobacteriaceae* in Acute Care Facilities

March 20, 2009 / Vol. 58 / No. 10
Antimicrobial Resistance at SJMH

Infection/Colonization Totals

- MRSA
- MICU MRSA
- C diff
- MICU C diff
- VRE
- ESBL
- MDR Ab
- MDR Pse

2010 MDRO
2011 MDRO
Antimicrobial Resistance at SJMH

SJAA IP HA Infection/Colonization Totals

- ESBL
- MDR Ab
- MDR Pse
- CRE/KPC

2010 GN MDRO
2011 GN MDRO
Costs of Antimicrobial Resistance

- The Chicago Antimicrobial Resistance Project
- 1391 high-risk adults hospitalized at one hospital in 2000
- Evaluated patients with antimicrobial-resistant infections
  - Attributable mortality: 6.5%
  - Excess hospital LOS: 6.4–12.7 days
  - Attributable medical costs: $18,588–$29,069 per patient
  - Societal costs: $10.7–$15.0 million for all patients at a single hospital

Antibacterials Approved by the FDA, 1983 - 2007

Impending Crisis of New Antibiotics

- Last new class of drugs active against GNB, in the 1970s, – “Trimethoprim”
- No new classes of antimicrobials in the foreseeable future
- No new drugs to deal with multi-resistant GNB until 2018
- WHO – “Antibiotic resistance” as one of major threats to human health

Evolving Resistance, The “ESKAPE” Organisms

- Enterococcus faecium
- Staphylococcus aureus
- Klebsiella pneumoniae
- Acinetobacter baumannii
- Pseudomonas aeruginosa
- Enterobacter species

Controlling Resistance?

- A combination of BOTH
  - Effective antimicrobial stewardship program
  - Comprehensive infection control program

- Have been shown to limit the emergence and transmission of antibiotic resistant bacteria

Antimicrobial Stewardship Works

Impact of a Reduction in the Use of High-Risk Antibiotics on the Course of an Epidemic of *Clostridium difficile*-Associated Disease Caused by the Hypervirulent NAP1/027 Strain

Antimicrobial Stewardship Reduces Costs

Clinical outcomes better with antimicrobial stewardship program

Antimicrobial Stewardship Program Goals

- Ensure appropriate antimicrobial use
  - Optimal selection, dose, duration
- Reduce or attenuate advancing antimicrobial resistance
- Improve patient outcomes and reduce adverse events related to antimicrobials
  - Decrease *Clostridium difficile* infection
  - Decrease morbidity and mortality
  - Decrease length of stay
- Decrease healthcare expenditures and antimicrobial costs

Ohl CA. *Seminar Infect Control* 2001;1:210-21
Antimicrobial Stewardship Interventions

- Prospective audit with intervention and feedback
- Formulary restriction and preauthorization
- Educations
- Streamlining and de-escalating
- Dose optimization
- Guidelines and clinical pathways
- Parenteral to oral conversion

Role of the Infection Preventionist

- Daily activities of IPs/HEs vital for ASP
- Implementation of evidenced-based practice and prevention care bundles (hand hygiene, isolation precautions, environmental cleaning, etc)
- No transmission of infection = Avoidance of abx
Role of the Infection Preventionist

- Identification and surveillance of MDROs
- Monitoring and reporting of trends of MDROs
- Promote high compliance with hand hygiene
- Track and analyze trends in antimicrobial resistance
- Educate multidisciplinary rounding teams about NHSN surveillance definitions of HAIs
- Partners for accountability – share findings with and progress to stakeholders and providers

SJMH Antimicrobial Stewardship Program

- Focus on restricted abx
  - New starts, duration

- Interventions
  - Approve
  - Stop abx
  - Change/Narrow abx
  - Obtain ID Consult
  - Against ASP advice
## SJMH Animicrobial Stewardship Program

### ANTIBIOTIC STEWARDSHIP - Intervention

**Instructions:** Click on the **MAROON** headers to sort the table. Currently you can click on Encounter, Start Date, and Patient Name.

- Dates must be in the MM/DD/YYYY format.
- Times must be in military time format (HH:MM) with values between 00:00 and 23:59.

**Legend:**
- Approved >= 7 Days
- Acknowledgement Needed: +
- Self Follow Up Reminder: +
- Add/View Comments: +

<table>
<thead>
<tr>
<th>Patient Name/Encounter</th>
<th>Unit/Room</th>
<th>Generic Drug</th>
<th>Start Date</th>
<th>Attending/Ordering</th>
<th>Intervention Date</th>
<th>Intervention Time</th>
<th>Intervention</th>
</tr>
</thead>
</table>

**Intervention Options:**
- Approved
- Get ID Consult
- Change Dose
- Stop Antibiotics
- (Narrow)-Change Antibiotics
- Other:

**Submit**

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If you have any questions or need further assistance, please contact the SJMH Animicrobial Stewardship Program.
Outcomes from SJMH ASP

Interventions (n = 510)

- Approved: 323 (64%)
- Narrow Change: 94 (18%)
- Against ASP Advice: 5 (1%)
- ID Consist: 27 (5%)
- Stsep: 61 (12%)
Demographic and clinical characteristics and outcomes of patients pre-ASP compared to patients post-ASP

<table>
<thead>
<tr>
<th></th>
<th>Period 1 N=372</th>
<th>Period 2 N=344</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (yr)</td>
<td>64.8 (±15.7)</td>
<td>62.5 (±18.4)</td>
<td>0.08</td>
</tr>
<tr>
<td>Charlson Comorbidity Count, median (IQR)(\dagger)</td>
<td>1 (0-2)</td>
<td>1 (1-2)</td>
<td>0.08</td>
</tr>
<tr>
<td>Length of stay, median (IQR)(\dagger) days</td>
<td>8.0 (4-8)</td>
<td>7.0 (4-7)</td>
<td>0.44</td>
</tr>
<tr>
<td>Males</td>
<td>168 (45.2)</td>
<td>171 (49.7)</td>
<td>0.22</td>
</tr>
<tr>
<td>Race (white)</td>
<td>313 (84.1)</td>
<td>299 (86.9)</td>
<td>0.29</td>
</tr>
<tr>
<td>ICU stay*</td>
<td>115 (30.9)</td>
<td>94 (27.3)</td>
<td>0.29</td>
</tr>
<tr>
<td>Ventilator use*</td>
<td>103 (27.7)</td>
<td>46 (13.4)</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Receipt of &gt; 1 target antimicrobial</td>
<td>47 (12.6)</td>
<td>51 (14.8)</td>
<td>0.39</td>
</tr>
<tr>
<td>Death within 30 days</td>
<td>77 (20.7)</td>
<td>55 (16.0)</td>
<td>0.11</td>
</tr>
<tr>
<td>Readmitted within 30 days</td>
<td>76 (20.4)</td>
<td>69 (20.1)</td>
<td>0.87</td>
</tr>
<tr>
<td>C. difficile infection</td>
<td>46 (12.4)</td>
<td>20 (5.8)</td>
<td>&lt;0.01</td>
</tr>
</tbody>
</table>

\(\dagger\)IQR is defined as the mathematical difference between the 75\(^{th}\) and the 25\(^{th}\) percentile.

*Within 2 days of admission.
Multivariable analysis for association of ASP and patient outcomes

<table>
<thead>
<tr>
<th>Model Covariates</th>
<th>Death within 30 days</th>
<th>R</th>
<th>Readmission within 30 days</th>
<th>R</th>
<th>C. difficile Infection</th>
<th>R</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, Race, Sex, ICU Stay‡, Vent Use‡, 2nd abx*, CCC**</td>
<td>0.77 (0.50-1.18)</td>
<td>0.23</td>
<td>0.95 (0.63-1.42)</td>
<td>0.80</td>
<td>0.46 (0.25-0.82)</td>
<td>&lt;0.01</td>
</tr>
</tbody>
</table>

†Within 2 days of admission.
*At least 2 target antimicrobials prescribed
**Charlson Comorbidity Count
Flow Diagram of Outcomes from ASP

- 455 patient encounters on target antibiotic (June 1, 2008 – May 31, 2009)
  - 372 initial patient encounters
    - 295 alive
      - 68 readmitted
        - 29 CDI
    - 77 died
  - 440 patient encounters on target antibiotic (July 1, 2009 – June 30, 2010)
  - 344 initial patient encounters
    - 289 alive
      - 65 readmitted
        - 16 CDI
    - 55 died

- 510 separate antibiotic orders
  - 323 appropriate
  - 94 de-escalated
  - 61 denied
  - 27 ID consult
  - 5 against ASP advice

## Antimicrobial Costs by Fiscal Year

<table>
<thead>
<tr>
<th></th>
<th>Fiscal year 2009</th>
<th>Fiscal year 2010</th>
<th>Percent change</th>
</tr>
</thead>
<tbody>
<tr>
<td>Antimicrobial agents total costs</td>
<td>$1,503,748</td>
<td>1,274,837</td>
<td>-15.2 (-$228,911)</td>
</tr>
<tr>
<td>Total patient days</td>
<td>147,955</td>
<td>144,783</td>
<td></td>
</tr>
<tr>
<td>Antimicrobial costs per patient day</td>
<td>$10.16</td>
<td>$8.81</td>
<td>-13.3</td>
</tr>
<tr>
<td>(average)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Targeted antimicrobial agents</td>
<td>$462,404</td>
<td>$297,851</td>
<td>-35.6 (-$164,553)</td>
</tr>
</tbody>
</table>

Incidence and mortality of CDI are increasing in US


<table>
<thead>
<tr>
<th>HAI</th>
<th>Target Population</th>
<th>Start Date</th>
</tr>
</thead>
<tbody>
<tr>
<td>CLABSI</td>
<td>ICUs</td>
<td>Jan 2011</td>
</tr>
<tr>
<td>SSI</td>
<td>Colon and abdominal hysterectomy procedures</td>
<td>Jan 2012</td>
</tr>
<tr>
<td>CAUTI</td>
<td>ICUs</td>
<td>Jan 2012</td>
</tr>
<tr>
<td>MRSA Bacteremia Lab ID Event</td>
<td>Facility-wide</td>
<td>Jan 2013</td>
</tr>
<tr>
<td><em>C. difficile</em> Lab ID Event</td>
<td>Facility-wide</td>
<td>Jan 2013</td>
</tr>
<tr>
<td>HCP Influenza Vaccination</td>
<td>Acute care hospitals</td>
<td>Jan 2013</td>
</tr>
</tbody>
</table>
National Efforts on Antimicrobial Stewardship

- SHEA Task Force
- CDC Get Smart Campaign
  [www.cdc.gov/getsmtart/](http://www.cdc.gov/getsmtart/)
- JTC National Patient Safety Goals
  (NPSG) 07.03.01
- California Senate Bill 739
LTACs: The Perfect Storm

- Admit complex pts with acute care needs (ventilation weaning, wound care, IV abx)
- Mean duration of 25 days
- Pts with multiple co-morbidities, at risk for colonization with MDROs
- High rates of HAI s
- Implicated in various regional outbreaks of MDROs

Stewardship in the LTAC

- 60 bed unit in Dallas, Tx
- Weekly chart reviews: ID doc and director of pharmacy
  - Left nonbinding recs in chart
- 15 month intervention period
  - 21% decrease in mean monthly abx use (DDDs/1000 pt days)
  - 28% reduction in mean monthly abx cost/pt day ($29 to $20.8)

Pate, et al Infect Cont Hosp Epi 2012;33:405-08.
Stewardship in the LTAC

- Limitations: no data on outcomes
- Effective stewardship possible with limited resources
Stewardship at Transitions of Care

- All pts to get parenteral abx seen by ID prior to d/c at Cleveland Clinic
- 244 CoPat consultations
  - 175 (72%) approved
  - 66 (28%) avoided
  - 11% consults avoided abx
- Targeting pts at transitions of care (hospital to community) is an AS strategy

Future Steps

- Develop systems for appropriate abx use
  1. All orders should have dose, duration, indication
  2. When placing orders, need micro cultures
  3. Abx timeouts in 24 – 48 hrs
- Lead quality initiatives related to abx use (i.e. SCIP)
- Increase collaboration between IP and AS
- Develop ASPs in LTCFs and LTACs
Surgical Care Improvement Project (SCIP)  
Infection-Prevention Measures

<table>
<thead>
<tr>
<th>Individual SCIP measures</th>
</tr>
</thead>
<tbody>
<tr>
<td>INF-1: patients who received prophylactic antibiotics within 1 h prior to surgical incision (2 h if receiving vancomycin)</td>
</tr>
<tr>
<td>INF-2: patients who received prophylactic antibiotics recommended for their specific surgical procedure</td>
</tr>
<tr>
<td>INF-3: patients whose prophylactic antibiotics were discontinued within 24 h after surgery end time (48 h for coronary artery bypass graft surgery or other cardiac surgery)</td>
</tr>
<tr>
<td>INF-4: cardiac surgery patients with controlled 6 AM postoperative blood glucose level (( \leq 200 \text{ mg/dL} ) ( \leq 11.1 \text{ mmol/L} ))</td>
</tr>
<tr>
<td>INF-6: surgery patients with appropriate surgical-site hair removal with clippers or depilatory or those not requiring surgical-site hair removal</td>
</tr>
<tr>
<td>INF-7: colorectal surgery patients with immediate postoperative normothermia (first recorded temperature was ( \geq 96.8^\circ \text{F} ) within first 15 minutes after leaving the operating room)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Composite Measures</th>
</tr>
</thead>
<tbody>
<tr>
<td>S-INF-Core: patient data on all 3 original SCIP measures: INF-1, INF-2, and INF-3</td>
</tr>
<tr>
<td>S-INF: all patients with ( \geq 2 ) recorded SCIP infection-prevention measures in a single visit (any combination of INF-1, INF-2, INF-3, INF-4, INF-6, and INF-7)</td>
</tr>
</tbody>
</table>

Summary

- Primary mission of ASPs is patient safety
- ASPs help assure the appropriate use of antimicrobial therapy
- ASPs can improve pt outcomes, reduce tx costs, & reduce or slow the development of resistant organisms
- A multidisciplinary team approach is essential
Case # 1

- 83 year old male s/p AAA repair
- Extubated in PACU and tx to the 2000 unit
- 4 days later, develops respiratory distress, SICU tx, and reintubation.

Further evaluation:
- New infiltrate on CXR
- WBC 26.5
- Tmax 101.9
Case # 1

- Started on Cefepime and Vancomycin.
- Has PCN allergy (rash).
- After 1 wk, WBC decreased to 13.7
- Final culture & sensitivities from sputum show:
  - Direct Smear: Moderate neutrophils, GNB
  - Culture (Final): *Enterobacter aerogenes*
### Enterobacter aerogenes

<table>
<thead>
<tr>
<th>Drug</th>
<th>MIC</th>
<th>INT</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ampicillin/Sulb</td>
<td>8</td>
<td>R</td>
</tr>
<tr>
<td>Ampicillin</td>
<td>16</td>
<td>R</td>
</tr>
<tr>
<td>Aztreonam</td>
<td>&lt;=1</td>
<td>S</td>
</tr>
<tr>
<td>Cefazolin</td>
<td>&gt;=64</td>
<td>R</td>
</tr>
<tr>
<td>Cefepime</td>
<td>&lt;=1</td>
<td>S</td>
</tr>
<tr>
<td>Ceftriaxone</td>
<td>&lt;=1</td>
<td>S</td>
</tr>
<tr>
<td>Ciprofloxacin</td>
<td>&lt;=0.25</td>
<td>S</td>
</tr>
<tr>
<td>Gentamicin</td>
<td>&lt;=1</td>
<td>S</td>
</tr>
<tr>
<td>Meropenem</td>
<td>&lt;=0.25</td>
<td>S</td>
</tr>
<tr>
<td>Piper/Tazobac</td>
<td>&lt;=4</td>
<td>S</td>
</tr>
<tr>
<td>Tobramycin</td>
<td>&lt;=1</td>
<td>S</td>
</tr>
<tr>
<td>Trimeth-Sulfa</td>
<td>&lt;=20</td>
<td>S</td>
</tr>
</tbody>
</table>
Case # 1

- Pt received 72 hours of Cefepime/Vancomycin
- Readdress abx regimen given cx results

A. Continue Cefepime and Vancomycin
B. Continue Cefepime. D/C Vancomycin.
C. De-escalate Cefepime to a different abx. D/C Vancomycin.
Case # 1
Take Home Points

- Antibiotic Timeout (reasons for abx use)
- Streamlining and de-escalating
- Duration for abx course
- Clear plans when transitions of care (tx to/from ICUs/discharge summaries/ECFs)
Case # 2
Case # 2

- 88 y/o male, hx of dementia, presented with confusion/weakness
- Recent stay at an ECF, presented with foley
- WBC 13.4
- Started on Ceftriaxone → Cefepime/Vancomycin
- Blood cx: ¾ CNS
- Urine cx: alpha hemolytic streptococcus
- U/A 57 WBC, + LE
Case # 2

- No fevers, exam significant for L knee effusion/pain
- ID c/s stopped all abx
- Underwent arthrocentesis → Pseudogout
- A few days later, started on IV flagyl for CDI
- Changed over to PO flagyl
- D/C back to ECF
Case # 2

- While at ECF, receives ertapenem for ESBL E. Coli bacteriuria, and then nitrofurantoin for VRE bacteriuria
- Presents 1 month from previous admission with abdominal pain, diarrhea, lethargy, WBC 15.9
- Started on IV ceftriaxone/flagyl
- Seen by ID
Case # 2

A. Add po Vancomycin
B. D/C Ceftriaxone, add po Vancomycin.
C. Change abx to Zosyn
D. No treatment
Case # 2

- Severe CDI
- Pt eventually goes on hospice despite maximal medical tx for a wk
Case # 2
Take Home Points

- Aware of adverse effects of abx including CDI, MDRO, etc
- Improved abx use improves pt outcomes
- AS through continuum of care is critical