Preserving bacterial susceptibility
Implementing Antimicrobial Stewardship Programs
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Impact of Antibacterial Resistance

• Each year an estimated 1.7 million patients in U.S. hospitals acquire an infection resulting in 100,000 deaths\(^1\)

• This results in an additional $6.5 billion in health care expenditures\(^2\)

ESCAPE Pathogens

- ESCAPE: Describes the most critical drug resistant pathogens:
  - E = *Enterococcus faecium*
  - S = *Staphylococcus aureus*
  - C = *Clostridium difficile*
  - A = *Acinetobacter baumannii*
  - P = *Pseudomonas aeruginosa*
  - E = *Enterobacteriaceae* (*E. coli* infection more numerous than *Klebsiella* and *Enterobacter* combined)
### Hospital and Societal Costs of Antimicrobial-Resistant Infections

<table>
<thead>
<tr>
<th>organism</th>
<th>Mean cost (USD) per patients</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Health-care acquired</td>
</tr>
<tr>
<td><strong>E</strong> VRE</td>
<td>$73,481</td>
</tr>
<tr>
<td><strong>S</strong> MRSA</td>
<td>$60,984</td>
</tr>
<tr>
<td><strong>A</strong> Acinetobacter</td>
<td>$111,062</td>
</tr>
<tr>
<td>resistant to amikacin or imipenem</td>
<td></td>
</tr>
<tr>
<td><strong>E</strong> Klebsiella or Ecoli</td>
<td>$39,403</td>
</tr>
<tr>
<td>resistant to quinolones or 3GC</td>
<td></td>
</tr>
</tbody>
</table>

Why have Antimicrobial Stewardship?

Antibiotics are unlike any other drugs in that use of the antibiotic in one patient can compromise its efficacy in another.

Anyone can prescribe antibiotics despite a lack of specialized training.

Unlike an antihypertensive agent, which benefits only the patient for whom it is prescribed, antimicrobials can impact countless others.

Resistant microorganisms can be spread to patients who have never received an antibiotic.

You can’t “catch cancer” from the patient next to you.

You CAN catch drug-resistant microorganisms!
The Goal of Antimicrobial Stewardship Programs

• To promote the appropriate use of antimicrobials\(^2,3\)
  – The right selection, duration, dose, timing and route of administration

• To improve clinical outcomes\(^2\)
  – By reducing the emergence of resistance
  – By limiting drug-related adverse events
  – By minimizing the risk of unintentional consequences
    • eg, *Clostridium difficile* infection

The combination of effective antimicrobial stewardship with a comprehensive infection control program has been shown to limit the emergence and transmission of antimicrobial-resistant bacteria.\(^1\)

Antimicrobial Stewardship Team

Ideal versus Reality

Optimal Team Members (A-III)¹

Core Team Members (A-III)¹

OSU Antimicrobial Stewardship Program

ASP is a corporate commitment!
Tools to Get Started

- **Practice Guidelines**
  IDSA & Society for Healthcare Epidemiology of America publication
  Pagani L. *Clin Infect Dis* 2009:48;626-32

- Meet the other “team members” in your hospital
  Learn what they do and how they do it

Step 1: Develop an interdisciplinary team and define the roles and responsibilities of team members

Step 2: Select strategies by which to execute an antimicrobial stewardship program (ASP)

Step 3: Present results of ASP projects to the medical staff
Insights from ID Pharmacists on ASP guidelines

**Patient safety** in both medical literature and newspapers antibiotics are the 2\textsuperscript{nd} most common class of drugs to cause reactions

Reducing antibiotic purchases alone encourages the perception it’s purely “cost-savings” rather than *quality improvement*

**Size of ASP** should meet hospital requirements

Before intervention, the *scope of authority* should be approved by administration

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Components of Antimicrobial Stewardship

• “Front End”—provided at the point of prescribing
  – Formulary Restriction and Preauthorization
  – Interactive decision support
  – Guidelines, order sets
  – Requires additional personnel (e.g. pharmacists)

• “Back End”—after the antimicrobial has been prescribed
  – Prospective Feedback Audit
  – Streamlining or de-escalation
  – Dose optimization
  – Parenteral to oral conversion
  – Requires additional personnel support (e.g. pharmacists)
How does an antimicrobial stewardship team actually work together?
The Epidemiologist and Infection Control

- Implement infection control measures³

- Gather data and monitor:¹
  - Process measures (eg, compliance with hand hygiene guidelines or timing of perioperative antibiotics)
  - Patient outcomes (eg, rates of specific health care-associated infections)

- Use process and outcome measures to determine the impact of stewardship on antimicrobial use and resistance patterns²

- Investigate of local outbreaks of infection²

Soap-sniffing Technology Encourages Hand Washing To Reduce Hospital-acquired Infections, Save Money

ScienceDaily (June 5, 2009) — Call it a Breathalyzer for the hands. Using sensors capable of detecting drugs in breath, new technology developed at University of Florida monitors health-care workers' hand hygiene by detecting sanitizer or soap fumes given off from their hands.

Here's how it works.
1. The hospital workers squirt sanitizer gel before passing their hands under a wall-mounted sensor.
2. A wireless signal from a badge the worker is wearing activates a green light on the handwashing sensor.
3. When the worker approaches the patient's bedside, a monitor detects the status of the badge. Clean hands get a green light.
4. If the person has not washed, the badge will vibrate as a reminder to wash their hands again.
The Role of the Microbiologist

- Provides surveillance data on antimicrobial resistance\(^1\) gathered through antibiograms\(^4\)
  - Assesses regional susceptibility
  - Monitors trends over time
  - Can be unit-specific or hospital-wide\(^2\)

- Develops combination antibiograms\(^3\)
  - Used when there is a risk of resistant bacteria (eg, \textit{P. aeruginosa})
  - Combination therapy against primary pathogen and resistant bacteria

- Provides diagnostic testing to help make better antimicrobial choices\(^1\)
  - Rapid MRSA/SA testing (1 hours)
  - Hodge test to detect carbapenemases

Local antibiograms should help ASP direct the empiric use of antibacterials
Do MD’s Use Hospital Antibiotics?
Online survey of 545 residents at a University Teaching Hospital

- How data is communicated to the medical staff is critical

# Hospital-wide Antibiogram

% susceptibility to antimicrobials

<table>
<thead>
<tr>
<th></th>
<th>Pip/tazo</th>
<th>Cefepime</th>
<th>Imipenem</th>
<th>Cipro</th>
<th>Tobramycin</th>
</tr>
</thead>
<tbody>
<tr>
<td><em>K. pneumoniae</em> (954)</td>
<td>91</td>
<td>95</td>
<td>99</td>
<td>88</td>
<td>92</td>
</tr>
<tr>
<td><em>E. cloacae</em> (287)</td>
<td>79</td>
<td>95</td>
<td>95</td>
<td>92</td>
<td>91</td>
</tr>
<tr>
<td><em>E. coli</em> (1971)</td>
<td>96</td>
<td>99</td>
<td>99</td>
<td>98</td>
<td>98</td>
</tr>
<tr>
<td><em>P. aeruginosa</em> (1039)</td>
<td>87</td>
<td>70</td>
<td>81</td>
<td>70</td>
<td>89</td>
</tr>
<tr>
<td><em>A. baumannii</em> (121)</td>
<td>91</td>
<td>80</td>
<td>100</td>
<td>70</td>
<td>85</td>
</tr>
</tbody>
</table>
ICU Antibiogram
First isolates only 1999

<table>
<thead>
<tr>
<th></th>
<th>Pip/tazo</th>
<th>Cefepime</th>
<th>Imipenem</th>
<th>Cipro</th>
<th>Tobramycin</th>
</tr>
</thead>
<tbody>
<tr>
<td><em>K. pneumoniae</em></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>(32)</td>
<td>66</td>
<td>71</td>
<td><strong>100</strong></td>
<td>63</td>
<td>63</td>
</tr>
<tr>
<td><em>E. cloacae</em></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>(13)</td>
<td>77</td>
<td>77</td>
<td>92</td>
<td>77</td>
<td>69</td>
</tr>
<tr>
<td><em>E. coli</em></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>(16)</td>
<td>94</td>
<td>94</td>
<td>94</td>
<td>100</td>
<td>94</td>
</tr>
<tr>
<td><em>P. aeruginosa</em></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>(37)</td>
<td>81</td>
<td>59</td>
<td>70</td>
<td>78</td>
<td>95</td>
</tr>
<tr>
<td><em>A. baumannii</em></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>(21)</td>
<td>86</td>
<td>14</td>
<td>86</td>
<td>52</td>
<td>19</td>
</tr>
</tbody>
</table>
ASP Management of complicated intra-abdominal infections

- *E. coli* is the most frequently cultured organism in cIAI
- Reviewed the antibiogram
  Ertapenem was selected for surgical patients with community-acquired cIAI

<table>
<thead>
<tr>
<th>MIC breakpoints (µg/ml)</th>
<th>Ampicillin/ Sulbactam</th>
<th>Piperacillin/ Tazobactam</th>
<th>Cefazolin</th>
<th>Cefepime</th>
<th>Imipenem (a)</th>
</tr>
</thead>
<tbody>
<tr>
<td># isolates</td>
<td>≤8/4</td>
<td>≤16/4</td>
<td>≤8</td>
<td>≤8</td>
<td>≤4</td>
</tr>
<tr>
<td>Escherichia coli</td>
<td>1600</td>
<td>45</td>
<td>95</td>
<td>86</td>
<td>100</td>
</tr>
<tr>
<td>Escherichia coli-ESBL</td>
<td>36 (a)</td>
<td></td>
<td></td>
<td></td>
<td>100</td>
</tr>
</tbody>
</table>
Evidence-Based Surgical Use of Ertapenem

• Ertapenem is FDA-approved for:
  – Complicated intra-abdominal infections (cIAI)
    Ertapenem 1 g daily vs. piperacillin/tazobactam 3.375 g every 6 hr

  665 patients with perforated/abscessed appendicitis, colonic, small intestine, or biliary infections, and generalized peritonitis

  Success rates: ertapenem 83.6% vs. 80.4% pip/tazo

Targeted Empiric Coverage

- Ertapenem
- Ampicillin/sulbactam
- Piperacillin/tazobactam
- Imipenem

Anaerobes
Resistant ESBL’s
Pseudomonas aeruginosa
Non-Pseudomonas gram-negatives
Gram-positives

Empiric coverage
Study of Susceptibility of Gram-negative Pathogens After 4 Years with Ertapenem on Formulary

- **Design**
  - In vitro surveillance study
- **Setting**
  - Ohio State University Medical Center, Columbus, Ohio
- **Methods**
  - In vitro susceptibilities of gram-negative aerobes determined by Etest (ertapenem), or microdilution MICs for imipenem, piperacillin/tazobactam, cefepime, and tobramycin
- **Primary endpoint**
  - Effect of ertapenem on imipenem susceptibility to *P. aeruginosa*

Ertapenem: No Effect on aerobic Gram-Negative susceptibilities to imipenem

Example: ASP Team Approach to Complicated Intra-abdominal Infections

- Presents recommended change to empiric antibiotics for cIAI to surgical division
- Monitors hand hygiene compliance in SICU
- Presents surgical infection data from surgeon at infection control meeting
- Presents declining E. coli susceptibilities to antibiotic subcommittee
- Publishes the antibiogram
- Compiles data necessary for surveillance
# Study of Susceptibility of Aerobic Gram-negative Rods After 3 Years on Formulary

<table>
<thead>
<tr>
<th>Design</th>
<th>Retrospective analysis of hospital susceptibility data from June 2002 to December</th>
</tr>
</thead>
<tbody>
<tr>
<td>Setting</td>
<td>344-bed community teaching hospital in Santa Monica, California, US</td>
</tr>
<tr>
<td>Methods</td>
<td>In vitro susceptibilities of gram-negative rods to formulary antibiotics determined</td>
</tr>
<tr>
<td>Primary endpoint</td>
<td>Susceptibility of gram-negative rods to imipenem, ertapenem, levofloxacin, cefepime, gentamicin, and piperacillin/tazobactam</td>
</tr>
</tbody>
</table>

Results

<table>
<thead>
<tr>
<th>Month</th>
<th>Min</th>
<th>Max</th>
<th>Mean</th>
<th>Median</th>
<th>Standard Error</th>
</tr>
</thead>
<tbody>
<tr>
<td>Before Ertapenem added</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>0-9</td>
<td>60.00</td>
<td>81.00</td>
<td>70.00</td>
<td>69.0</td>
<td>2.69</td>
</tr>
<tr>
<td>After Ertapenem was added,</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Before the substitution</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>10-20</td>
<td>63.00</td>
<td>91.00</td>
<td>77.00</td>
<td>77.0</td>
<td>2.90</td>
</tr>
<tr>
<td>After the substitution</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>21-48</td>
<td>67.00</td>
<td>100.00</td>
<td>87.86</td>
<td>89.0</td>
<td>1.62</td>
</tr>
</tbody>
</table>

Absence of Association between use of Ertapenem and Change in Antipseudomonal Carbapenem Susceptibility rates in 25 Hospitals

Ref Eagye K., Nicolau D. Infect Control Hosp Epidemiol 2010;31(5);485-90
New diagnostic tests should be incorporated in ASP planning
Clinical and Economic Impact of rapid PCR blood culture test for detection of SA/MRSA in patients with SAB

- **Objective**: Evaluate the clinical & economic impact of the rapid PCR MRSA/SA blood culture test with interventions by ID pharmacists

- **Method**: A comparative study of hospitalized patients with SAB before and after PCR blood culture test implementation.

Evaluate the difference in time from blood culture draw to optimal anti-staphylococcal therapy (OAT) for SAB, hospital length of stay (LOS), mortality, cost of care pre and post introduction of rapid PCR MRSA/SA BC

Ref: Bauer K, Goff DA Clin Inf Dis 2010; 51(9):1074–1080
Findings

The rapid PCR MRSA/SA BC test decreased the time to OAT after time of blood culture draw in MSSA bacteremia (p=0.002) by **1.6 days**.

The rapid differentiation of MSSA and MRSA in blood cultures enables faster switch to OAT

- Mean hospital costs were reduced by $21,287 in the post-PCR test group (p=0.02)
- ICU cost were $9,930 less in the post-PCR test group (p=0.03)

Communication by the microbiology tech of the PCR MRSA/SA BC test result to the ID PharmD resulted in earlier OAT that was associated with a decreased LOS and costs.
Measuring Success

- Reduced:
  - Antimicrobial resistance
  - Hospital cost
  - Use of nontargeted antimicrobials

- Improved clinical outcomes
  - Decreased length of hospital stay
  - Reduced adverse events
  - Decreased length of antibiotic treatment

Conclusion

- ASP can make a difference in patient care
- Each team member provides unique talents
- Escalating rates of antimicrobial resistance and lack of new antimicrobials, creates an urgent need for ASP in hospitals