Effective Antibiotic Use in 2015

Rafael Ponce, MD
Infectious Diseases
Mercer University School of Medicine
What is Effective?

effective
əˈfektɪv/
• successful in producing a desired or intended result
Antibiotics intended result

- Eliminate infecting organism
- Decrease mortality
- Decrease morbidity
Empiric Therapy

Organism specific Therapy
Impact of inappropriate empiric therapy

• 40-bed ICU hospital
• 87 ICU patients with inadequate empiric antibiotics (exposed) matched with controls: adequate empiric regimen (unexposed).
• Exposed: 67% mortality, Unexposed: 28% mortality.
• Excess in-hospital mortality: 31%

Author’s conclusion: Inadequate antimicrobial therapy at admission to the ICU with sepsis is associated with excess mortality and increases LOS.

Why did they give the wrong regimen?
Inadequate antimicrobial therapy at admission to the ICU with sepsis is associated with excess mortality

Solution:
1. stop giving wrong empiric antibiotics.
UTI = Ciprofloxacin
Pneumonia = Ceftriaxone
Cellulitis = Bactrim
For everything else = VancZosyn
Bactrim
- **β-lactams**
  - Penicillins
  - Oxacillin/Nafcillin
  - β-lac/β-inh
    - Amp/sulbactam
    - Pip/tazobactam
- **Cephalosporins**
  - Cefazolin
  - Ceftriaxone
  - Ceftazidime
  - Cefepime
  - Ceftaroline
- **Monobactam**
- **Carbapenems**
  - Ertapenem
  - Imipenem
  - Meropenem
- **Glycopeptide**
  - Vancomycin
- **Daptomycin**
- **DNA Gyrase**
  - **Quinolones**: Cipro, Levo, Moxi.
- **Protein synthesis inhibitors**
  - Macrolides
    - Clindamycin
    - Linezolid
  - Aminoglycosides
  - Tetracyclines
  - Tigecycline
- **Folate synthesis**
  - Bactrim
"Atypicals"

Cell Wall
- **β-lactams**
  - Penicillins
  - Oxacillin/Nafillin
- **β-lac/β-inh**
  - Amp/sulbactam
  - Pip/tazobactam
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  - Meropenem

**Glycopeptide**
- Vancomycin

Cell Membrane
- **Daptomycin**

DNA Gyrase
- **Quinolones**: Cipro, Levo, Moxi.

Protein synthesis inhibitors
- Macrolides
  - Clindamycin
  - Linezolid
- **Aminoglycosides**
- **Tetracyclines**
- **Tigecycline**

Folate synthesis inhibitors
- Bactrim

DNA
RNA
50S
30S
Gram positives

- **Cell Wall**
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    - Penicillins
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  - Linezolid
$eta$-lactam resistance

1. Penicillin binding protein

2. Beta lactamase

3. Penicillin binding protein

4. Beta lactamase breaks a bond in the beta-lactam ring of penicillin to disable the molecule. Bacteria with this enzyme can resist the effects of penicillin and other beta-lactam antibiotics.

5. Penicillin binding protein
**S. aureus (MSSA)**

- **Cell Wall**
  - β-lactams
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    - Oxacillin/Nafcillin
    - β-lac/β-inh
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- **Folate synthesis: Bactrim**
  - Aminoglycosides
  - Tetracyclines
  - Tigecycline
MRSA
Methicillin Resistant *S. aureus*

- MecA: PBP2a
S. aureus (MRSA)

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**Cell Wall**

**Cell Membrane**

**DNA Gyrase**

- **Quinolones**: Cipro, Levo, Moxi.

**Protein synthesis inhibitors**

- **Macrolides**: Clindamycin
  - Linezolid
- **Aminoglycosides**
- **Tetracyclines**
- **Tigecycline**

**Folate synthesis**

- **Bactrim**

- **30S**
- **50S**

- **RNA**
- **DNA**
**Gram negatives**

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  - Cipro,
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Cell Membrane

DNA Gyrase
- • Quinolones: Cipro, Levo, Moxi.

Protein synthesis inhibitors
- Macrolides
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- • Aminoglycosides
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DNA Gyrase
- RNA
- 50S
- 30

Chromosome

DNA

Cell Wall

Folate synthesis:
- Bactrim

Why did they give the wrong empiric regimen?

Author’s conclusion: Inadequate antimicrobial therapy at admission to the ICU with sepsis is associated with excess mortality
Solution:
1. stop giving wrong empiric antibiotics.

What if they got a wrong empiric regimen because of resistance?
Table 2. Pathogens isolated in blood and the source of sepsis in exposed and unexposed patients (number of isolations in blood cultures is shown in parentheses)

<table>
<thead>
<tr>
<th>Pathogen</th>
<th>Exposed</th>
<th>Unexposed</th>
</tr>
</thead>
<tbody>
<tr>
<td><em>Acinetobacter</em> spp.</td>
<td>9 (6)</td>
<td>1 (1)</td>
</tr>
<tr>
<td><em>Aeromonas hydrophila</em></td>
<td>3 (3)</td>
<td>1 (1)</td>
</tr>
<tr>
<td><em>Aspergillus</em> spp.</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td><em>Bacteroides</em> <em>fragilis</em></td>
<td>0</td>
<td>1 (1)</td>
</tr>
<tr>
<td><em>Brucella</em> <em>melitensis</em></td>
<td>1 (1)</td>
<td>0</td>
</tr>
<tr>
<td><em>Candida</em> spp.</td>
<td>15 (10)</td>
<td>3 (3)</td>
</tr>
<tr>
<td><em>Clostridium</em> spp.</td>
<td>0</td>
<td>2 (2)</td>
</tr>
<tr>
<td><em>Escherichia coli</em></td>
<td>24 (17)</td>
<td>26 (17)</td>
</tr>
<tr>
<td><em>Enterobacter</em> spp.</td>
<td>1</td>
<td>8 (3)</td>
</tr>
<tr>
<td><em>Enterococcus</em> spp.</td>
<td>4 (2)</td>
<td>6 (6)</td>
</tr>
<tr>
<td><em>Hemophilus</em> spp.</td>
<td>0</td>
<td>1 (1)</td>
</tr>
<tr>
<td><em>Klebsiella</em> spp.</td>
<td>2 (2)</td>
<td>17 (8)</td>
</tr>
<tr>
<td><em>Nocardia</em> spp.</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td><em>Morganella</em> spp.</td>
<td>1</td>
<td>1 (1)</td>
</tr>
<tr>
<td><em>Pneumocystis</em> <em>jiroveci</em></td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td><em>Prevotella</em> spp.</td>
<td>1 (1)</td>
<td>0</td>
</tr>
<tr>
<td><em>Proteus</em> spp.</td>
<td>5</td>
<td>2 (1)</td>
</tr>
<tr>
<td><em>Pseudomonas</em> <em>aeruginosa</em></td>
<td>12 (4)</td>
<td>4 (2)</td>
</tr>
<tr>
<td><em>Serratia</em> spp.</td>
<td>0</td>
<td>2 (2)</td>
</tr>
<tr>
<td><em>Staphylococcus</em> <em>aureus</em></td>
<td>5 (4)</td>
<td>2 (1)</td>
</tr>
<tr>
<td><em>Staphylococcus</em> <em>epidermidis</em></td>
<td>2 (2)</td>
<td>1 (1)</td>
</tr>
<tr>
<td><em>Stenotrophomonas</em> <em>maltophilia</em></td>
<td>2</td>
<td>0</td>
</tr>
<tr>
<td><em>Streptococcus</em> <em>pneumoniae</em></td>
<td>3 (1)</td>
<td>10 (4)</td>
</tr>
<tr>
<td><em>Streptococcus</em> spp.</td>
<td>0</td>
<td>5 (3)</td>
</tr>
</tbody>
</table>

In exposed, only pathogens treated inadequately are shown in this table. In addition, the following pathogens were also isolated in these patients and treated adequately with the *empirical* therapy: *Enterococcus* spp. (3), *E. coli* (3), *Streptococcus* spp. (3), *Proteus* sp. (1), *Pseudomonas* sp. (1) and *B. fragilis* (1). Bacteraemia was polymicrobial in two exposed subjects.

What can we do to reduce antibiotic resistance?
Improve Patient “Handoff”

After abdominal exam

After alcohol foam
Data of resistance pre and post admission

- Inpatients nasal and peri rectal swabs on days 0, 2, 4, 7, 15, and 30.
- Swabs culture for MRSA, VRE, and Cipro resistant *Pseudomonas sp.*
- Baseline colonization: MRSA 3%, VRE 1%, *Pseudomonas sp.* 0.5%
- Acquisition: MRSA 3%, VRE 2%, *Pseudomonas sp* 1%

Nosocomial transmission of resistant organisms without contact isolation

• 93 patients with ESBL+ Enterobacteriaceae were hospitalized.
• 133 contact patients (shared the same room prior to contact isolation) had rectal swabs on admission and at discharge.
• Only 2 (1.5%) contact patients were found with same organism by molecular typing.

If not in the hospital, then where?

- 100 healthy volunteers traveling outside Northern Europe.
- Rectal swabs before and after travel.
- Upon return, 24% had ESBL+ E. coli
- 5 of 21 (23%) persisted after 6 months.

TABLE 4. Descriptive statistics on 100 Swedish travelers with negative pretravel rectal swabs for ESBL-producing Enterobacteriaceae

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Value for group</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>ESBL negative</td>
</tr>
<tr>
<td></td>
<td>(n = 76)</td>
</tr>
<tr>
<td>No. (% of male travelers)</td>
<td>35 (46)</td>
</tr>
<tr>
<td>Median age (yr)</td>
<td>42</td>
</tr>
<tr>
<td>No. (% of vegetarians)</td>
<td>2 (3)</td>
</tr>
<tr>
<td>Median length of stay (wk) (%)</td>
<td>2.0</td>
</tr>
<tr>
<td>No. (% of travelers on vacation)</td>
<td>67 (88)</td>
</tr>
<tr>
<td>No. (% of business travelers)</td>
<td>10 (13)</td>
</tr>
<tr>
<td>No. (% of travelers visiting friends or relatives</td>
<td>10 (13)</td>
</tr>
<tr>
<td>No. (% of travelers staying at a hotel)</td>
<td>61 (80)</td>
</tr>
<tr>
<td>No. (% of backpacking travelers)</td>
<td>6 (8)</td>
</tr>
<tr>
<td>No. (% of travelers staying with friends or relatives)</td>
<td>9 (12)</td>
</tr>
<tr>
<td>No. (% of travelers with gastroenteritis)</td>
<td>17 (22)</td>
</tr>
<tr>
<td>No. (% of travelers on antibiotic treatment)</td>
<td>7 (9)</td>
</tr>
</tbody>
</table>

* Seventy-six travelers were negative for ESBL-producing strains after their trip, whereas 24 carried ESBL-producing Escherichia coli. The only statistically significant difference between the groups was gastroenteritis during travel (P = 0.003).

Major Rivers Systems Salvador-Brazil

- World Cup Stadium
- Dique de Tororo
- Dique do Cabrito
- Pau da Lima
- Pituaçu
Dique do Cabrito – Salvador, Brazil

- Water samples: *E. coli*
  - 50% were ESBL+ (resistant to all cephalosporins)
  - 71% quinolone resistant (Ciprofloxacin)
  - 66% Bactrim resistant
Antibiotic resistance problem
Selection pressure: Antibiotic use

Image Description:
- The image depicts a pie chart titled "Estimated Annual Antibiotic Use in the United States".
- The chart shows the following data:
  - Livestock: 13,540,000 kg
  - Humans: 3,290,000 kg
  - Aquaculture: 150,000 kg
  - Crops: 150,000 kg
  - Pets: 70,000 kg
- The chart is color-coded: Livestock is blue, Humans is red, Aquaculture is green, Crops is yellow, and Pets is purple.
Antibiotic restriction policy?

Antibiotics don’t select for resistance, people using antibiotics select for resistance.

Doctor: “you have a virus, you don’t need antibiotics”
Patient: “I want a second opinion”
US Outpatient Antibiotics in 2011

- Outpatient antibiotic use, 60% of total.
- 265.2 million courses
- 842 prescriptions per 1000 persons (average)
- Infants, children 3-9, adults >65: rate >1000 per 1000 persons.

Table 2. Antibiotic Courses Prescribed and Prescriptions Per Provider in 2011, by Provider Specialty

<table>
<thead>
<tr>
<th>Provider Specialty</th>
<th>Prescriptions, No. in Millions (%)</th>
<th>Providers, No.</th>
<th>Prescriptions per Provider, Rate</th>
</tr>
</thead>
<tbody>
<tr>
<td>All Providers</td>
<td>262.5</td>
<td>911 814</td>
<td>289</td>
</tr>
<tr>
<td>Persons &lt;20 y</td>
<td>73.8 (29)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Persons ≥20 y</td>
<td>182.8 (71)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Family practice</td>
<td>64.1 (24)</td>
<td>96 073</td>
<td>667</td>
</tr>
<tr>
<td>Persons &lt;20 y</td>
<td>12.9 (21)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Persons ≥20 y</td>
<td>49.7 (79)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Dermatology</td>
<td>8.2 (3)</td>
<td>11 329</td>
<td>724</td>
</tr>
<tr>
<td>Pediatrics</td>
<td>32.4 (12)</td>
<td>54 228</td>
<td>598</td>
</tr>
<tr>
<td>Otolaryngology</td>
<td>4.1 (2)</td>
<td>9536</td>
<td>430</td>
</tr>
<tr>
<td>Emergency medicine</td>
<td>13.8 (5)</td>
<td>32 346</td>
<td>427</td>
</tr>
<tr>
<td>Internal medicine/pediatrics</td>
<td>1.4 (1)</td>
<td>3329</td>
<td>421</td>
</tr>
<tr>
<td>Internal medicine</td>
<td>32.1 (12)</td>
<td>83 841</td>
<td>383</td>
</tr>
<tr>
<td>Physician assistants</td>
<td>17.5 (7)</td>
<td>63 467</td>
<td>276</td>
</tr>
<tr>
<td>Infectious diseases</td>
<td>1.3 (1)</td>
<td>6166</td>
<td>211</td>
</tr>
<tr>
<td>Dentistry</td>
<td>25.6 (10)</td>
<td>122 706</td>
<td>208</td>
</tr>
<tr>
<td>Obstetrics/gynecology</td>
<td>6.7 (3)</td>
<td>37 590</td>
<td>178</td>
</tr>
<tr>
<td>Nurse practitioners</td>
<td>19.5 (7)</td>
<td>109 741</td>
<td>178</td>
</tr>
<tr>
<td>Surgery (general)</td>
<td>6.9 (3)</td>
<td>69 536</td>
<td>99</td>
</tr>
<tr>
<td>Pediatric subspecialty</td>
<td>0.8 (&lt;1)</td>
<td>8273</td>
<td>97</td>
</tr>
<tr>
<td>Medical subspecialty</td>
<td>6.9 (3)</td>
<td>74 424</td>
<td>93</td>
</tr>
<tr>
<td>Other</td>
<td>8.2 (3)</td>
<td>113 783</td>
<td>72</td>
</tr>
<tr>
<td>Urology</td>
<td>6.0 (2)</td>
<td>10 131</td>
<td>59</td>
</tr>
</tbody>
</table>
Outpatient antibiotic courses per 1000 persons age >65

Effective Antibiotic Use 2015

Rafael Ponce, MD
Infectious Diseases
Mercer University School of Medicine
UTI
1. Positive urine culture ≠ UTI
Asymptomatic bacteriuria

• 673 asymptomatic women with bacteriuria.
• Not treated 312, treated 362.
• At 6 months, symptomatic recurrence seen in 23 (7.6%) of untreated and in 98 (29.7%) of treated.

Asymptomatic bacteriuria during short-term urinary catheter

Factors Predisposing to Bacteriuria during Indwelling Urethral Catheterization
Richard A. Garibaldi, M.D., John P. Burke, M.D., Marion L. Dickman, Ph.D., and Charles B. Smith, M.D. N Engl J Med 1974
2. Pyuria ≠ UTI
Pyuria with asymptomatic bacteriuria

- 32% of young women
- 70% of diabetic women
- 90% of elderly institutionalized patients
- 90% of hemodialysis patients
- 30–75% of patients with short-term catheters
- 50–100% of patients with long-term indwelling catheters in place

3. Smelly urine ≠ UTI
Acute bronchitis
Antibiotics for acute bronchitis

- 17 trials with 5099 participants.
- were less likely to have an abnormal lung exam (RR 0.54, 95% CI 0.41 to 0.70; NNTB 6)
- Reduction in **days feeling ill** (-0.64 days, 95% CI -1.16 to -0.13)
- Reduction in days with **limited activity** (-0.49 days, 95% CI -0.94 to -0.04).
- The differences in proportions with activity limitations at follow-up did not reach statistical significance.
- Trend towards an increase in adverse effects in the antibiotic group (RR 1.20, 95% CI 1.05 to 1.36; NNT for an additional adverse effect 24).

Useful Tools

Sanford Guide: Antimicrobial Rx

Antimicrobial Therapy, Inc.  Medical

Everyone

Offers in-app purchases

This app is compatible with all of your devices.
SANFORD GUIDE

Antimicrobial Therapy

Search

Syndromes

Pathogens

Anti- infectives

Prevention

Tools

News
**Bronchitis, Acute, Age > 5 years**

**Bronchitis**: older children, adolescents, adults

**Clinical Setting**

- Acute bronchitis in adolescents and adults is defined as self-limited inflammation of the upper airways due to infection or irritants.
- It should be differentiated from small airway disease by the presence of airway obstruction.
- Pertussis should be considered in all patients with prolonged cough.
- Purulent sputum alone is not an indication for antibiotic therapy.
- Patients should be counseled that cough may persist for 2-3 weeks.
- If fever/rigets, get chest x-ray. See also, Mycoplasma pneumonia.

**Etiologies**

- Viral (usually)
- M. pneumoniae (5%)
- C. pneumoniae (5%)
- Bordetella pertussis

**Primary Regimens**

- Antibiotics are not effective and are not indicated
- Pertussis is the exception
- Antitussive (limited evidence) ± inhaled bronchodilators
- Inhaled corticosteroids are sometimes used but efficacy has not been systematically evaluated

**Alternative Regimens**

- None

**Comments**

Tick Gallery

Ticks, Images

- For geographic distribution of American ticks, see http://www.cdc.gov/ticks/geographic_distribution.html

Lone Star Tick
IDSA Practice Guidelines

Clinical Practice Guidelines by Category

Antimicrobial Agent Use
Infections by Organ System
Infections by Organism
Other Guidelines
Translations of IDSA Practice Guidelines
Mobile Practice Guidelines
Pocketcards
Practice Guidelines Discussion Forum

Guideline Methodology and Other Resources

Translations of IDSA Practice Guidelines
IDSA is broadening its international reach by expanding knowledge and improving patient care by making several of its clinical practice guidelines available in languages other than English. Volunteer members of the IDSA Translation Bureau review all translations to ensure the accuracy and quality of the translation.
To effectively use antibiotics

Know when not to use.

Know what use.
Thank you
Please take < 90 seconds to evaluate this session. Time permitting, speaker will take questions following evaluation. Responses are not displayed and are important in maintaining high quality education.
The overall performance of the speaker:

1. Poor
2. Fair
3. Average
4. Good
5. Excellent
How well were the learning objectives met?

1. Poor
2. Fair
3. Average
4. Good
5. Excellent

[Bar chart showing percentages for each level: Poor (0%), Fair (3%), Average (6%), Good (37%), Excellent (55%)]
Did speaker present a balanced view of therapeutic options?

1. Yes
2. No
3. N/A

- Yes: 95%
- No: 2%
- N/A: 3%
How useful will this session be in your practice?

1. Poor
2. Fair
3. Average
4. Good
5. Excellent
As a result of this program, do you intend to change your patient care?

1. Yes
2. No

81%
19%
Thank you!