Antibiotic Stewardship
Successes and Opportunities in the NICU

Jennifer Goldman MD, MS
Associate Professor Pediatrics
Medical Director, Antimicrobial Stewardship
September 1, 2020

Objectives
• Understand the importance of antimicrobial stewardship in health care
• Consider unique factors that impact antimicrobial stewardship in the NICU
• Identify opportunities for antimicrobial stewardship in the NICU
Antimicrobial Stewardship

“Optimal selection, dosage, and duration of antimicrobial treatment that results in the best clinical outcome for the treatment or prevention of infection with minimal toxicity to the patient and minimal impact on subsequent resistance”

Why antimicrobial stewardship?

Antimicrobial Stewardship Milestones
Why AS: Antimicrobial Resistance

ANTIBIOTIC RESISTANCE THREATS IN THE UNITED STATES

2019

The Threat of Antibiotic Resistance in the United States

Antibiotic resistance—when germs develop the ability to defeat the antibiotics designed to kill them—is one of the greatest global health challenges of modern time.

New National Estimate

Each year, antibiotic-resistant bacteria and fungi cause at least an estimated:

- 2,868,700 infections
- 35,900 deaths
- 223,900 cases
- 12,800 deaths
Antimicrobial resistance—a threat to neonate survival

Why AS: Inappropriate Prescribing

In U.S. 2010 – 2011:
- 13% all outpatient visits result in antibiotic prescriptions
- 154 million antibiotic prescriptions in ambulatory care settings
- 30% deemed unnecessary

Fleming-Dutra KE et al. JAMA. 2016;315(17):1864-1873
Inpatient Pediatric Antibiotic Use 2016-2017

Across 32 children’s hospitals, approximately 1 in 3 hospitalized children are receiving 1 or more antibiotics at any given time.

Tribble A et al. CID 2020. ahead of print

AS in the NICU

• Antibiotics are the most commonly prescribed medications in the NICU
• Estimated that 20-50% of antibiotics prescribed in the NICU are inappropriate
• Common reasons for inappropriate use included failure to narrow antibiotic coverage after microbiologic results were known and prolonged surgical prophylaxis


Why AS: Lack of New Antibiotics in Pediatrics
The number of new antibiotics developed and approved has steadily decreased in the past three decades, leaving fewer options to treat resistant bacteria.

![Graph showing number of new antibiotics approved vs. year intervals.](https://www.cdc.gov/drugresistance/pdf/11-2013-508.pdf)

<table>
<thead>
<tr>
<th>Year Approved</th>
<th>Drug</th>
<th>Indication</th>
<th>Approval in Pediatrics</th>
</tr>
</thead>
<tbody>
<tr>
<td>2019</td>
<td>Recarbrio (imipenem, cilastatin, and relebactam)</td>
<td>complicated intra-abdominal and urinary tract infections</td>
<td>≥ 3 months of age</td>
</tr>
<tr>
<td>2018</td>
<td>Nuzyra (omadacycline)</td>
<td>community-acquired bacterial pneumonia and acute bacterial skin and skin structure infections</td>
<td></td>
</tr>
<tr>
<td>2018</td>
<td>Xerava (eravacycline)</td>
<td>complicated intra-abdominal infections</td>
<td></td>
</tr>
<tr>
<td>2018</td>
<td>Zemdri (plazomicin)</td>
<td>complicated urinary tract infections</td>
<td></td>
</tr>
<tr>
<td>2017</td>
<td>Baxdela (delafloxacin)</td>
<td>acute bacterial skin and skin structure infections</td>
<td></td>
</tr>
<tr>
<td>2017</td>
<td>Vabomere (meropenem and vaborbactam)</td>
<td>complicated urinary tract infections</td>
<td></td>
</tr>
<tr>
<td>2016</td>
<td>Avycaz (ceftazidime-avibactam)</td>
<td>complicated intra-abdominal and urinary tract infections</td>
<td>≥ 3 months of age</td>
</tr>
<tr>
<td>2015</td>
<td>Dalvance (dalbavancin)</td>
<td>acute bacterial skin and skin structure infections</td>
<td>≥ 3 months of age</td>
</tr>
<tr>
<td>2014</td>
<td>Orbactiv (oritavancin)</td>
<td>acute bacterial skin and skin structure infections</td>
<td></td>
</tr>
<tr>
<td>2014</td>
<td>Sivextro (tedizolid phosphate)</td>
<td>acute bacterial skin and skin structure infections</td>
<td></td>
</tr>
<tr>
<td>2014</td>
<td>Zerbaxa (ceftolozane+tazobactam)</td>
<td>complicated intra-abdominal and urinary tract infections and bacterial pneumonia</td>
<td></td>
</tr>
</tbody>
</table>

Why AS: Regulatory Requirements

CDC Core Elements

- Leadership Commitment
- Accountability
- Pharmacy Expertise
- Action
- Tracking
- Reporting
- Education

US News and World Report

New Antimicrobial Stewardship Standard

- Infection prevention plans
- Performance improvement plans
- Using the electronic health record to collect antimicrobial prescribing data
- The hospital employs an antimicrobial stewardship program with an antimicrobial access and antimicrobial stewardship policies, guidelines, and formulary-based antimicrobial prescribing plans
- The hospital employs an antimicrobial stewardship program with an antimicrobial access and antimicrobial stewardship policies, guidelines, and formulary-based antimicrobial prescribing plans
- The hospital employs an antimicrobial stewardship program with an antimicrobial access and antimicrobial stewardship policies, guidelines, and formulary-based antimicrobial prescribing plans
Unique factors that impact antimicrobial stewardship in the NICU

AS in the NICU

Prolonged use of broad-spectrum antimicrobials in NICUs
- Candida colonization and invasive infection
- Necrotizing enterocolitis
- Late onset neonatal sepsis
- Death
- Microbiome
- Development of chronic conditions
Identify opportunities for AS in the NICU


Table 1: Clinical characteristics of high-risk NICU neonates

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>High-Risk</th>
<th>Low-Risk</th>
</tr>
</thead>
<tbody>
<tr>
<td>Birth weight (kg)</td>
<td>2.5</td>
<td>3.0</td>
</tr>
<tr>
<td>Gestational age (wks)</td>
<td>32</td>
<td>38</td>
</tr>
<tr>
<td>Maternal age (yrs)</td>
<td>25</td>
<td>30</td>
</tr>
<tr>
<td>Antenatal corticosteroids</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>


Legend: Number below indicates number of ASP episodes.
Where’s the data?

- Need to know utilization data at your institution
- By diagnosis, medication, age group, risk stratification
- Benchmarking

Sources for utilization data
- Electronic medical record
- Data warehouses
- CDC’s National Healthcare Safety Network

Electronic medical record data
Benchmarking data

Vancomycin
Cefazolin

DOT in NICU per 1,000 NICU Patient Days

Standardized Antimicrobial Administration Ratio (SAAR)

SAAR = Observed (O) Antimicrobial Use
Predicted (P) Antimicrobial Use

Purpose: To provide a standardized, risk-adjusted benchmark of antibiotic use

All Antibiotics
Aminoglycosides

Examples of AS in the NICU

Courtesy of Alex Oschman PharmD, BCPPS and Children’s Mercy Kansas City

CMH – Incidence of Ventilator Associated Tracheitis (VAT)

- 2008-2014 = 121 reviews by the antimicrobial stewardship program for VAT
  - Mean/median mCPIS score = 4
  - 35% met a definition of VAT
  - 65% were “overtreated”
  - Duration of antibiotics = Median 6 days (5-11)
- Dramatic increase in VAT the past 2 years
Quality Improvement Project

Results

- Primary aim: 85% adherence (34/40)
- Number of patients treated/year
  - Decrease from mean = 17/year to 8/year (↓ 47%)
- Diagnosis of VAT or retreatment within 30 days of 1st evaluation
  - Monitored to look at algorithm/score failure
    - 2 patients within 30 days
  - Improved discussion prior to starting antibiotics
Empiric Therapy for R/O Sepsis

Preliminary Results

- Data from 11/1 through 12/31:
  - 23 instances (46%) were started on vancomycin
    - Vancomycin use by 54%
  - Of the 46% of patients started on vancomycin:
    - 48% met the algorithm recommendations for vancomycin use
    - 52% of patients could have been started on oxacillin rather than vancomycin
Conclusions

• Antimicrobial stewardship is an important part of NICU medical care
• Use data to identify AS opportunities in the NICU
• Algorithms can help influence prescribing practices

Thank You
Jennifer Goldman
jlgoldman@cmh.edu