Antibiotic Stewardship for the Newborn Population: Ample Opportunities for Improvement

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ILPQC Annual Conference
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Co-leader, Northwest Neonatal Improvement Priority Alliance
Disclosures

• Dr. Dukhovny served as faculty and consultant for Vermont Oxford Network

• Most antibiotics are not FDA approved for neonates
Objectives

• To define what antibiotic stewardship means in the NICU

• To assess your NICU/hospital current practices with respect to antibiotic stewardship

• To identify and apply key resources available to build/enhance antibiotic stewardship programs
Clinical research notebook of Sir Alexander Fleming, recording experiments on 11 December 1928 on 'inhibition by moulds', British Library, Additional MS 56162, f. 26

the thoughtless person playing with penicillin treatment is responsible for the death of the man who eventually succumbs to infection with the penicillin-resistant organism. I hope this evil can be averted (Alexander Fleming, 1945)
PENICILLIN
BLENDED SCOTCH, HONEY, GINGER, LEMON, ARDBEG

Clinical research notebook of Sir Alexander Fleming, recording experiments on 11 December 1928

the death of the man who eventually succumbs to infection with the penicillin-resistant organism. I hope this evil can be averted (Alexander Fleming, 1945)
Variation in antibiotic use in NICU

Figure 1 from Schulman et al. *Pediatrics* 2015.
Antibiotic Stewardship

• "coordinated interventions designed to improve and measure the appropriate use of [antibiotic] agents by promoting the selection of the optimal [antibiotic] drug regimen, including dosing, duration of therapy, and route of administration” (PIDS, SHEA, IDSA)

• Many components to an Antibiotic Stewardship Program (ASP):
  • Right antibiotic
  • Right dose
  • Right duration
  • Right patient

• Some (many) patients are getting unnecessary exposure to antibiotics in the NICU
  • But…“Babies are sick and vulnerable to infection”
Antibiotic Exposure in Well Appearing Newborns

- 14.7% of well appearing infants
- 12.7% of total live births

Figure 2 from Mukhopadhyay et al. J. Perinatology 2013
Introduction of Early Onset Sepsis Risk Calculator (Kaiser) – Blood Cultures

Figure 1 from Kuzniewicz et al. JAMA Pediatrics. 2017
Introduction of Early Onset Sepsis Risk Calculator (Kaiser) – Antibiotics

Figure 2 from Kuzniewicz et al. JAMA Pediatrics. 2017
We Are Over-treating preemies: 22-28 weeks, NRN Study

Early Onset Sepsis Incidence: 0.5% 2.5%

<table>
<thead>
<tr>
<th>Antibiotic Use in Low-Risk and Comparison Infants Surviving &gt;12 Hours</th>
<th>Low Risk of EOS, N = 584c</th>
<th>Comparison Group, N = 8422</th>
<th>Pa</th>
</tr>
</thead>
<tbody>
<tr>
<td>N (Column %) or as Shown</td>
<td>1940 (34.4)</td>
<td>4106 (48.8)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Antibiotics for ≥5 d starting within 72 h</td>
<td>1911/5611 (34.1)</td>
<td>3897/8213 (47.4)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Antibiotics in the absence of EOS</td>
<td>1890/5590 (33.8)</td>
<td>3862/8177 (47.2)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Antibiotics in the absence of positive EOS culture (cases and contaminants)b</td>
<td>1771/5334 (33.2)</td>
<td>3649/7752 (47.1)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Antibiotics in the absence of a positive blood or CSF culture result, NEC, or SIP ≤7 d c</td>
<td>66</td>
<td>19</td>
<td>&lt;.001</td>
</tr>
</tbody>
</table>

Table 5 from Puopolo et al. *Pediatrics.* 2017
Variation Persists

Low Risk Group (0.5% EOS)

High Risk Group (2.5% EOS)

Figure 1 from Puopolo et al. *Pediatrics*. 2017
What are the downsides to Antibiotics?

• Increasing resistant organisms - can be helped by modified use of antibiotics Marston et al. *JAMA* 2016

• NICU Problems:
  • NEC from prolonged empiric antibiotics Cotten et al. *Pediatrics* 2009
## Antibiotics and NEC in ELBWs

### Table 5: Multivariate Logistic Regression Analysis of Antibiotic Duration and NEC or Death

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Duration of Initial Empirical Antibiotic Treatment (Odds per Day)</th>
<th>P</th>
<th>Prolonged Initial Empirical Antibiotic Treatment</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>NEC or death (total, N = 3883; with outcome, n = 884)</td>
<td>1.04 (1.02–1.06)</td>
<td>&lt;.01</td>
<td>1.30 (1.10–1.54)</td>
<td>&lt;.01</td>
</tr>
<tr>
<td>NEC (total, N = 3899; with outcome, n = 427)</td>
<td>1.07 (1.04–1.10)</td>
<td>&lt;.001</td>
<td>1.21 (0.98–1.51)</td>
<td>.08</td>
</tr>
<tr>
<td>Death (total, N = 3882; with outcome, n = 631)</td>
<td>1.16 (1.08–1.24)</td>
<td>&lt;.001</td>
<td>1.46 (1.19–1.78)</td>
<td>&lt;.001</td>
</tr>
</tbody>
</table>

ORs were adjusted for study center, gestational age, small-for-gestational age status, gender, black race, 5-minute Apgar score of <5, rupture of membranes for > 24 hours, outborn, prenatal steroid treatment, intrapartum antibiotic treatment, maternal hypertension, maternal hemorrhage, and multiple birth. The total numbers of infants shown represent the numbers of infants with nonmissing outcome and covariate data who were included in each model.
Microbiome and Neurodevelopment

CONCLUSIONS AND RELEVANCE  Gut microbiota of very preterm newborns at week 4 is associated with NICU practices and 2-year outcomes. Microbiota could be a noninvasive biomarker of immaturity.

Figure 3 from Roze et al JAMA OPEN Network 3 (9); 2020
What’s the downside to Antibiotics?

- Increasing resistant organisms - can be helped by modified use of antibiotics. Marston et al. *JAMA* 2016

- NICU Problems:
  - NEC from prolonged empiric antibiotics. Cotten et al. *Pediatrics* 2009
  - Change individual AND NICU flora (resistance)
  - Long term effects?
  - COSTS!!!
### Characteristics of bacterial infections in the study sample with and without antibiotic resistance

<table>
<thead>
<tr>
<th></th>
<th>Infections without antibiotic resistance (n = 12,766,374), mean</th>
<th>Infections with antibiotic resistance (n = 1,232,541), mean</th>
<th>p value*</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td><strong>Office-based</strong></td>
<td><strong>Emergency department</strong></td>
<td><strong>Prescription drugs</strong></td>
</tr>
<tr>
<td></td>
<td>372</td>
<td>132</td>
<td>96</td>
</tr>
<tr>
<td></td>
<td>572</td>
<td>250</td>
<td>305</td>
</tr>
<tr>
<td></td>
<td>3.50</td>
<td>0.001</td>
<td>0.017</td>
</tr>
<tr>
<td></td>
<td>77</td>
<td>114</td>
<td>181</td>
</tr>
<tr>
<td></td>
<td>0.288</td>
<td>0.068</td>
<td>0.068</td>
</tr>
<tr>
<td></td>
<td><strong>Home health</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>68</td>
<td>181</td>
<td></td>
</tr>
<tr>
<td></td>
<td>0.068</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Year</th>
<th>Office-based</th>
<th>Emergency department</th>
<th>Prescription drugs</th>
<th>Outpatient</th>
<th>Home health</th>
</tr>
</thead>
<tbody>
<tr>
<td>2011</td>
<td>14,583,893</td>
<td>1,201,543</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>2012</td>
<td>11,786,935</td>
<td>1,229,999</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>2013</td>
<td>12,881,578</td>
<td>1,225,623</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>2014</td>
<td>14,290,029</td>
<td>1,568,221</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yearly average, 2002–14</td>
<td>13,998,915</td>
<td>1,232,541</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

*Thorpe et al. Health Affairs 2018*

**$2.2 Billion Dollars (2014) attribute to infections with antibiotic resistance**
NATIONAL ACTION PLAN FOR COMBATING ANTIBIOTIC-RESISTANT BACTERIA

2020-2025
October 2020

From the Federal Task Force on Combating Antibiotic-Resistant Bacteria
What’s the downside to Antibiotics?

- Increasing resistant organisms - can be helped by modified use of antibiotics  Marston et al. *JAMA* 2016

- NICU Problems:
  - NEC from prolonged empiric antibiotics  Cotten et al. *Pediatrics* 2009
  - Change individual AND NICU flora (resistance)
  - Long term effects?
  - COSTS!!!

- Asthma risk with exposure in the 1\textsuperscript{st} year of life  Mara et al. *Pediatrics* 2009

- Mitigate benefits of breastfeeding  Korpela et al *JAMA Peds* 2016

- 90% of adult patients with cancer receive antibiotics in last week of life  Juthani-Mehta et al *JAMA* (viewpoint) 2016
Reducing Unnecessary Antibiotic Exposure Works!

- Vancomycin reduction strategy in the NICU Chiu et al. *PIDJ* 2011
- Inpatient pediatrics ASP programs Smith et al. *JPIDS* 2015
  - Reduce antibiotic utilization
  - Decrease costs
  - Reduce prescribing errors
  - Education
  - Restriction on prescribing antibiotics
  - Audits
  - Clinical practice guidelines
- No increased safety concerns noted
CDC Core Elements for ASP

- Leadership support
- Accountability
- Drug expertise (i.e. pharmacy/physician leaders)
- Policies to support optimal antibiotic use (i.e. clinical consensus)
- Tracking
- Reporting/Sharing
- Education

- Family Engagement
- Equity
VON Initiative: Choosing Antibiotics Wisely

- Avoid routine continuation of antibiotic therapy beyond 48 hours for initially asymptomatic infants without evidence of bacterial infection.
  - Avoid routine screening term-equivalent or discharge brain MRIs in preterm infants.
  - Avoid routine daily chest radiographs without an indication for intubated infants.
  - Avoid routine use of pneumograms for pre-discharge assessment of ongoing and/or prolonged apnea of prematurity.
  - Avoid routine use of anti-reflux medications for treatment of symptomatic gastroesophageal reflux disease (GERD) or for treatment of apnea and desaturation in preterm infants.

Figure 1 from Schulman et al. Pediatrics 2015

Ho et al. Pediatrics 2015
Over 1300 members

A Worldwide Community of Practice

343 International Participants from 32+ Countries
iNICQ Choosing Antibiotics Wisely 2016, 2017, 2018

• Webinars (6-9/year)
  – Topic content
  – QI content
  – Coaching
• Antibiotic Stewardship Toolkit
  – Potentially better practices
• Day audits of policies/stewardship/practice (2/year)
• On the ground team work
• Network of learning
  – Web based
  – Discussion list-serve
Goals of being part of iNICQ

• Different for every center
• Follow the Institute for Health Care Improvement (IHI) Model for Improvement to do on the ground, multi-disciplinary work
• Participating centers have a range of expertise doing QI work
VON iNICQ Key Driver Diagram

Aim

Eliminate overuse and misuse of antibiotics in the NICU*

*NICUs of all levels from community NICU to quaternary NICU

1° Drivers

- Organizational commitment and culture
- Policies and protocols for specific neonatal conditions
- Pharmacy driven interventions to assure appropriate antibiotic treatment
- Regular reporting on antibiotic use and resistance to doctors, nurses and relevant staff

2° Drivers

- Create a charter with senior leadership that dedicates necessary human, financial and information technology resources to NICU stewardship programs
- Appoint a single leader responsible for program outcomes in the NICU
- Engage a multidisciplinary NICU stewardship team
- Educate clinicians about resistance and optimal prescribing for newborn infants
- Establish transparency in reporting of antibiotic use
- Engage parents as team members and partners in improvement

- Test, implement and continually refine policies and protocols that support optimal antibiotic use for specific neonatal conditions including suspected early and late onset sepsis, NEC and surgical conditions
- For each condition address criteria for diagnosis, indications for treatment, antibiotic choice, dose, duration and stopping
- Implement 48 hour “time out” for suspected sepsis

- Appoint a single pharmacist leader responsible for improving antibiotic use in the NICU
- Require pre-approval for certain antibiotics
- Include a pharmacist on daily rounds
- Use predefined antibiotic order sets and alerts
- Create forcing functions for 48 hour “time out”

- Monitor antibiotic prescribing in the NICU with process and outcome measures
- Use prospective audit and feedback of antibiotic use
- Generate automated reports of AUR and other key measures of antibiotic prescribing and use
- Build decision support and reminders into the EHR
Starting Point

**FIGURE 1**
Percent compliance with the CDC’s Core Elements of Hospital ASPs among 143 NICUs.

Ho et al. *Pediatrics* 142 (6) Dec 2018
# iNICQ Collaborative Progress

## Table 2: CDC Core Elements of ASPs Among Participating NICUs Across the 4 Audits

<table>
<thead>
<tr>
<th></th>
<th>February 2016 (N = 143)</th>
<th>November 2016 (N = 137)</th>
<th>February 2017 (N = 146)</th>
<th>November 2017 (N = 141)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Leadership commitment</td>
<td>15.4%</td>
<td>51.1%</td>
<td>60.3%</td>
<td>68.8%</td>
<td>&lt;.0001</td>
</tr>
<tr>
<td>Accountability</td>
<td>54.5%</td>
<td>89.1%</td>
<td>89.7%</td>
<td>95.0%</td>
<td>&lt;.0001</td>
</tr>
<tr>
<td>Drug expertise</td>
<td>61.5%</td>
<td>85.4%</td>
<td>83.6%</td>
<td>85.1%</td>
<td>&lt;.0001</td>
</tr>
<tr>
<td>Time out</td>
<td>21.7%</td>
<td>56.9%</td>
<td>61.6%</td>
<td>72.3%</td>
<td>&lt;.0001</td>
</tr>
<tr>
<td>Tracking</td>
<td>14.7%</td>
<td>68.6%</td>
<td>63.7%</td>
<td>78.0%</td>
<td>&lt;.0001</td>
</tr>
<tr>
<td>NHSN reporting</td>
<td>6.3%</td>
<td>13.1%</td>
<td>14.4%</td>
<td>17.7%</td>
<td>.0046</td>
</tr>
<tr>
<td>Ongoing education</td>
<td>32.9%</td>
<td>73.0%</td>
<td>75.3%</td>
<td>87.2%</td>
<td>&lt;.0001</td>
</tr>
<tr>
<td>All of the above</td>
<td>0%</td>
<td>5.8%</td>
<td>5.5%</td>
<td>9.9%</td>
<td>.0005</td>
</tr>
</tbody>
</table>

The table shows the percent of NICUs that participated in 1 or more of the VON Day Audits that met each of the core CDC elements of antibiotic stewardship. N refers to the number of individual NICUs that participated in each audit.
VON Day Audit

**FIGURE 1**

NICU AUR among participating NICUs across the 4 audits. The box and whiskers plot represents the median (solid line), interquartile range (box) and lowest to highest values for each of the four audits. The p-value represents the Cochrane-Armitage test for trend.

Dukhovny et al. *Pediatrics* 144 (6) Dec 2019
### TABLE 3 Percent of NICUs With Policies, Protocols, or Guidelines To Standardize the Diagnosis and Antibiotic Treatment of Common Neonatal Conditions

<table>
<thead>
<tr>
<th>Condition</th>
<th>February 2016 (N = 143)</th>
<th>November 2017 (N = 141)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Maternal risk factors,</td>
<td>53.1%</td>
<td>71.6%</td>
</tr>
<tr>
<td>Suspected or proven</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Early-onset sepsis or meningitis</td>
<td>44.8%</td>
<td>73.8%</td>
</tr>
<tr>
<td>Late-onset sepsis or meningitis</td>
<td>32.9%</td>
<td>50.4%</td>
</tr>
<tr>
<td>Ventilator-associated pneumonia</td>
<td>13.3%</td>
<td>27.7%</td>
</tr>
<tr>
<td>Central venous line infection</td>
<td>30.8%</td>
<td>48.9%</td>
</tr>
<tr>
<td>Urinary tract infection</td>
<td>14.0%</td>
<td>34.0%</td>
</tr>
<tr>
<td>Necrotizing enterocolitis</td>
<td>31.5%</td>
<td>44.7%</td>
</tr>
<tr>
<td>Surgical site infection</td>
<td>9.8%</td>
<td>19.1%</td>
</tr>
<tr>
<td>Prophylaxis for urinary tract infection</td>
<td>19.6%</td>
<td>30.5%</td>
</tr>
<tr>
<td>Prophylaxis for surgery</td>
<td>25.2%</td>
<td>27.7%</td>
</tr>
<tr>
<td>Prophylaxis for fungal sepsis</td>
<td>35.0%</td>
<td>40.4%</td>
</tr>
<tr>
<td>MRSA colonization</td>
<td>43.4%</td>
<td>51.1%</td>
</tr>
</tbody>
</table>

The table shows the percent of NICUs that participated in 1 or more of the VON Day Audits that had a policy, protocol, and/or guideline for 1 of the listed common neonatal conditions. N refers to the number of NICUs that participated in the respected audit.

Dukhovny et al. *Pediatrics* 144 (6) Dec 2019
Northwest Improvement Priority: Antibiotic Stewardship (NW IPAs)

Washington
- Kaiser Sunnyside Portland, OR
- Legacy Randall Children’s Hospital Portland, OR
- Legacy Salmon Creek Salmon Creek, WA
- Oregon Health & Science University Portland, OR
- Peace Health Southwest Vancouver, WA
- Peace Health Sacred Heart Eugene, OR
- Providence Portland Portland, OR
- Providence St. Vincent Portland, OR
- Asante Rogue Regional Medical Center Medford, OR
- Salem Hospital Salem, OR
- St. Charles Bend, OR

Oregon
- Salem Hospital Salem, OR
- St. Charles Bend, OR
Who are the NW IPAs?

• ALL 11 NICUs in Oregon and Southwest Washington
  – the remaining hospitals/birthing centers in the region provide care to well newborns, as well as triage and stabilize newborns with issues
• ~50,000 live births/year regionally
• All hospitals are members of VON
Overall Aims

• Build an ongoing regional collaboration among the 11 NICUs in the region in order to help reduce morbidity and mortality in our patient population

• Develop a partnership with the Oregon Health Authority (OHA), March of Dimes, Oregon Perinatal Collaborative (OPC) and other local/regional organizations to help optimize neonatal care and outcomes
Antibiotic Stewardship
SMART AIM

• Decrease the number of antibiotic doses per newborn per NICU per month by 10% (from baseline) by December 2016
Key Drivers

SMART AIM:
To decrease the median antibiotic utilization rate (antibiotics/newborn/participating hospital/month) by 10% (from baseline year of 2016) in 2017

Collaboration
- Continue to work together and share ideas as 11 NICUs
- Set up a venue for communication
- Set up additional teleconferences focused on regional antibiotic stewardship work

Stewardship
- Enroll in iNICQ 2016 as a region
- Begin on the ground antibiotic stewardship work at each individual center
- Determine AND share AUR

Partnership
- Partner with other state and regional organization involved in perinatal health and antibiotic stewardship
  - Oregon Health Authority (OHA)
  - March of Dimes
  - Oregon Perinatal Collaborative (OPC)
  - Oregon Pediatric Improvement Partnership (OPIP)
Practically Speaking…

• Every NICU in the NW IPAs were tasked with:
  • Joining the VON Collaborative
  • Putting together a local multi-disciplinary antibiotic stewardship team
  • Developing a SMART Aim
  • Starting PDSA cycles to decrease their unnecessary antibiotic utilization
  • Participate in NW IPAs activities
  • Determine/share their Antibiotic Utilization Rate (AUR)* with NW IPAs

• NW IPA Leadership:
  • Organization and structure for collaborative QI
  • Coaching to the teams

*CDC definition of antibiotic days per 1,000 patient days
Results
Individual AURs for NW IPA Centers: Jan 2015 – May 2017

- **Y-axis (left)** – AUR
- **Y-axis (right)** – total patient days for NW IPAs
- **X-axis** – month/year
- **Thick dark blue line** - combined AUR of participating centers in NW IPAs
- **Individual lines** – NW IPAs individual centers monthly AUR
Combined AUR for NW IPAs: Jan 2015 – May 2017

- Y-axis (left) – AUR
- Y-axis (right) – total patient days for NW IPAs
- X-axis – month/year
- Thick dark blue line – combined AUR for NW IPAs

~25% reduction from baseline in antibiotic utilization
VON Day Audit

Box plots showing the percentage of infants on antibiotics for NW IPA and All VON for different months:
- NW IPA: Feb 2016, Nov 2016, Mar 2017
- All VON: Nov 2016, Mar 2017, Nov 2017
Sample Report Sent to Each Center

(Along with excel template):

NW IPAs AUR Report

Oregon Health & Science University

January 2015-December 2016
AUR of 9 out of the 11 centers in the NW IPAs from January 2015-December 2016

Notes: (a) 1 center only started data collection in August 2015; (b) only 4 centers have data through December 2016

The thick dark blue line represents the overall AUR for all the centers reporting (NW IPAs Monthly AUR)
The thick dark blue line represents the overall AUR for all the centers reporting. The other dark thick line represents the AUR for your center (OHSU).
Please note that this is not a risk adjusted graph. If your center median is above the NW IPAs, then you are utilizing more antibiotics than the other 9 centers represented. If it is below the NW IPAs, than you are averaging less.
Each center should set its own goal line (that should be realistic and attainable – 150 was set arbitrarily for purposes of demonstration)
Summary

• NW IPAs have successfully engaged all 11 NICUs in the region in collaboration and participation around antibiotic stewardship
• All 11 centers have been able to determine their AUR*
  • Labor intensive (getting better)
  • Not risk adjusted
• 2017 iNICQ participation for NW IPA centers was supported in part by the Healthcare Associated Infections Program of the Oregon Public Health Division with funding from the CDC Epidemiology and Laboratory Capacity Grant
• First collaborative QI project in region that includes all NICU participation

*CDC definition of antibiotic days per 1,000 patient days
Our Local Improvement Story: OHSU
OHSU NICU Baseline Data

OHSU NICU Baseline Antibiotic Utilization Rate (AUR): Jan '14 - Dec '15

AUR

Patient Days

Median

Month/Year

AUR (Antibiotic days per 1,000 patient days)
SMART Aim

• To decrease Antibiotic Utilization Rate (AUR) (defined as antibiotic days/1,000 patients days per CDC) from 333 antibiotic days/1,000 patient days to 283 antibiotic days/1,000 patient days (15%) by December 31, 2016
Key Drivers

**SMART AIM:** To decrease Antibiotic Utilization Rate (AUR) (defined as antibiotic days/1,000 patients days per CDC) from 333 antibiotic days/1,000 patient days to 283 antibiotic days/1,000 patient days (15%) by December 31, 2016

**Establish a culture of Antibiotic Stewardship**
- Enroll in VON Collaborative 2016
- Join regional collaborative
- Form an antibiotic stewardship team
- Determine AND share AUR

**Initiation of antibiotics**
- Identify areas for improvement
- Vancomycin reduction strategies
- Clarification/updates of clinical consensus guidelines

**Duration of antibiotics**
- Pharmacy/IT Driven Interventions

**Communication with families**
- Help engage parents in conversations around antibiotic use
## Interventions

<table>
<thead>
<tr>
<th>Interventions</th>
<th>Time</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pre-NICU ASP</td>
<td>July 2015</td>
<td>Introduction of Kaiser Sepsis Calculator</td>
</tr>
<tr>
<td>1</td>
<td>December 2015</td>
<td>NICU ASP Team Formed</td>
</tr>
<tr>
<td>2</td>
<td>March 2016</td>
<td>Clinical Consensus Guidelines Changes: -48 to 36 hour rule out - Vancomycin reduction</td>
</tr>
<tr>
<td>3</td>
<td>January 2017</td>
<td>Monthly OHSU ASP Meetings</td>
</tr>
<tr>
<td>4</td>
<td>February/March 2017</td>
<td>“Hard Stops” for rule out sepsis for early and late onset sepsis</td>
</tr>
<tr>
<td>5 – DCH Wide</td>
<td>October 2017</td>
<td>Pediatric ASP Team Rounds M-F</td>
</tr>
<tr>
<td>6</td>
<td>November 2017</td>
<td>Parent Information Cards</td>
</tr>
</tbody>
</table>
Results
In 1 year, our median AUR decreased from baseline of 333 to 214 antibiotic days per patient days (35.7% reduction)
In 2 years, our median AUR increased (May 2017) from a baseline of 188 to 253 antibiotic days per patient day (34.6% increase).

Remains 24% below the baseline data pre-intervention.
OHSU NICU AUR – Year 5

OHSU NICU Antibiotic Utilization Rate (AUR): Jan ’14 - Sept ’20

Month/Year

AUR (Antibiotic days per 1,000 patient days)

Patient Days

Median
Keys to Our Success

• We have successfully reduced unnecessary antibiotic utilization

• Keys to our success:
  • Easy topic for staff to buy into (subtracting rather than adding care)
  • Pharmacy Engagement
  • IT Support
  • Infectious Disease/Control (Adult ASP Team)
  • Just getting started
  • Collaboration - first collaborative QI project in region that includes all NICU participation
Opportunities for Improvement

- Understanding variation in AUR
  - Antibiotics by indications
  - Mapping to infections/NEC
  - Getting to the provider level/feedback
- Improving the timing of antibiotic administration on initiation
- Family engagement
- Measuring impact on disparity
- Standardization of guidelines
  - Low hanging fruit (early and late onset sepsis)
  - Culture negative sepsis, VAP, etc
- Balancing Measures
### SUPPLEMENTAL TABLE 2 Balancing Measures

<table>
<thead>
<tr>
<th>Year</th>
<th>Nosocomial Infection Rate&lt;sup&gt;a&lt;/sup&gt;</th>
<th>Total Deaths</th>
<th>Deaths Attributed to Infection&lt;sup&gt;b&lt;/sup&gt;</th>
<th>Infection-Related Mortality&lt;sup&gt;c&lt;/sup&gt;</th>
</tr>
</thead>
<tbody>
<tr>
<td>2013</td>
<td>1.19</td>
<td>21</td>
<td>4</td>
<td>0.19</td>
</tr>
<tr>
<td>2014</td>
<td>1.23</td>
<td>17</td>
<td>4</td>
<td>0.24</td>
</tr>
<tr>
<td>2015</td>
<td>0.77</td>
<td>23</td>
<td>3</td>
<td>0.13</td>
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<tr>
<td>2016</td>
<td>0.62</td>
<td>31</td>
<td>5</td>
<td>0.16</td>
</tr>
<tr>
<td>2017</td>
<td>1.06</td>
<td>25</td>
<td>4</td>
<td>0.16</td>
</tr>
<tr>
<td>2018</td>
<td>0.56</td>
<td>24</td>
<td>4</td>
<td>0.17</td>
</tr>
</tbody>
</table>

<sup>a</sup> Defined as the number of cases after 72 h of life where bacteria was isolated from blood or cerebrospinal fluid per 1000 patient-days.

<sup>b</sup> Defined as having a diagnosis of sepsis, pneumonia, or meningitis that contributed to death.

<sup>c</sup> Deaths attributed to infection divided by total deaths.
Balancing Measures

• Impact on family
• Disparity gap
• Process measures
  – Delay in initiation of antibiotics
  – Antibiotics stopped too early
• Outcomes
  – Mortality, Sepsis, NEC
  – Long term outcomes (beyond scope?)
Newborn ASP Strategies

- Implementation of Early Onset Sepsis Calculator
- Engagement of the Mother-Baby Units
- Shortening the time of rule out from 48 to 36 hours (some to 24 hours)
- IT interventions – hard stops
- Engaging the families in conversation
- Education of staff
- Multidisciplinary
  - Pharmacy
  - Microbiology lab
  - ID
What Can You Do?

• NICU/Newborn Level
  – What are your antibiotic prescribing practices?
  – How does your microbiology lab work?
  – Do you track them?

• Hospital Level
  – Is there an antibiotic stewardship program?
    • Adult vs. Pediatric
    • Data (NHSN AU/AR Modules)

• System/State
  – What are other centers doing?
  – Does your state department of public health have funding and support?
Antibiotic Stewardship

• “coordinated interventions designed to improve and measure the appropriate use of [antibiotic] agents by promoting the selection of the optimal [antibiotic] drug regimen, including dosing, duration of therapy, and route of administration” (PIDS, SHEA, IDSA)

• Many components to an Antibiotic Stewardship Program (ASP):
  • Right antibiotic
  • Right dose
  • Right duration
  • Right patient
Stewardship Opportunities

Aim

Eliminate overuse and misuse of antibiotics in the NICU*  
*NICUs of all levels from community NICU to quaternary NICU

1st Drivers

Organizational commitment and culture

Policies and protocols for specific neonatal conditions

Pharmacy driven interventions to assure appropriate antibiotic treatment

Regular reporting on antibiotic use and resistance to doctors, nurses and relevant staff

2nd Drivers

- Create a charter with senior leadership that dedicates necessary human, financial and information technology resources to NICU stewardship programs
- Appoint a single leader responsible for program outcomes in the NICU
- Engage a multidisciplinary NICU stewardship team
- Educate clinicians about resistance and optimal prescribing for newborn infants
- Establish transparency in reporting of antibiotic use
- Engage parents as team members and partners in improvement

- Test, implement and continually refine policies and protocols that support optimal antibiotic use for specific neonatal conditions including suspected early and late onset sepsis, NEC and surgical conditions
- For each condition address criteria for diagnosis, indications for treatment, antibiotic choice, dose, duration and stopping
- Implement 48 hour “time out” for suspected sepsis

- Appoint a single pharmacist leader responsible for improving antibiotic use in the NICU
- Require pre-approval for certain antibiotics
- Include a pharmacist on daily rounds
- Use predefined antibiotic order sets and alerts
- Create forcing functions for 48 hour “time out”

- Monitor antibiotic prescribing in the NICU with process and outcome measures
- Use prospective audit and feedback of antibiotic use
- Generate automated reports of AUR and other key measures of antibiotic prescribing and use
- Build decision support and reminders into the EHR
Figure 1 from American Nurses Association White Paper & CDC “Redefining the Antibiotic Stewardship Team” 2017
www.nursingworld.org
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  – Stefanie Rogers, MD (Providence St. Vincent)

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- Just the team leaders are listed here, although there are over 90 participants between the 11 sites (including physicians, nurses, nurse practitioners, pharmacists, parents, fellows and medical students)
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Thank You!
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