



# The OASCN Collaborative

(Optimizing Antibiotic Stewardship in California NICUs)

## Learning Session #: 8

## Antibacterial Drugs for EOS

June 10, 2021

# Antibiotics are Popular

Rank	2005 <sup>a</sup>	2010 <sup>b</sup>	2018 <sup>c</sup>
1	<b>Ampicillin</b>	<b>Ampicillin</b>	<b>Ampicillin</b>
2	<b>Gentamicin</b>	<b>Gentamicin</b>	<b>Gentamicin</b>
3	Ferrous sulfate	Caffeine	Caffeine
4	Poly-Vi-Sol	Surfactant	Surfactant
5	<b>Cefotaxime</b>	<b>Vancomycin</b>	Morphine
6	Caffeine	Furosemide	<b>Vancomycin</b>
7	Furosemide	Fentanyl	Furosemide
8	<b>Vancomycin</b>	Dopamine	Fentanyl
9	Surfactant	Midazolam	Midazolam
10	Metoclopramide	Metoclopramide	Acetaminophen

- a. Clark RH, et al. Pediatrics 2006
- b. Hsieh EH, et al. Am J Perinatol 2014
- c. Greenberg RG, et al. Hot Topics 2020

***“The combination of ampicillin and gentamicin is the appropriate empirical antibiotic regimen for most infants who are at risk for EOS.”***

**AAP COFN, COID Pediatrics 2018**

# Early Onset Sepsis

## GRAM POSITIVE COVERAGE (GBS, LM, VGS, EC, SA)

Drug	Critique
Ampicillin	+GBS, LM, VGS, EC, some anaerobes, -SA, ↑ E coli resistance <sup>1</sup>
Pen G	Same as ampicillin, lower GBS MIC, -SA, limited GNB
Amoxicillin <sup>2</sup>	PO step down tx, Amox-clav for broader spectrum <sup>3</sup>
Clindamycin	+GBS, +SA, bacteriostatic, - LM, +Mycoplasma hominis
Linezolid	+GBS, LM, VGS, EC,+MRSA, +VRE, bacteriostatic/cidal
Cefepime	+GBS, +VGS, +MSSA, - LM - EC, +GNB

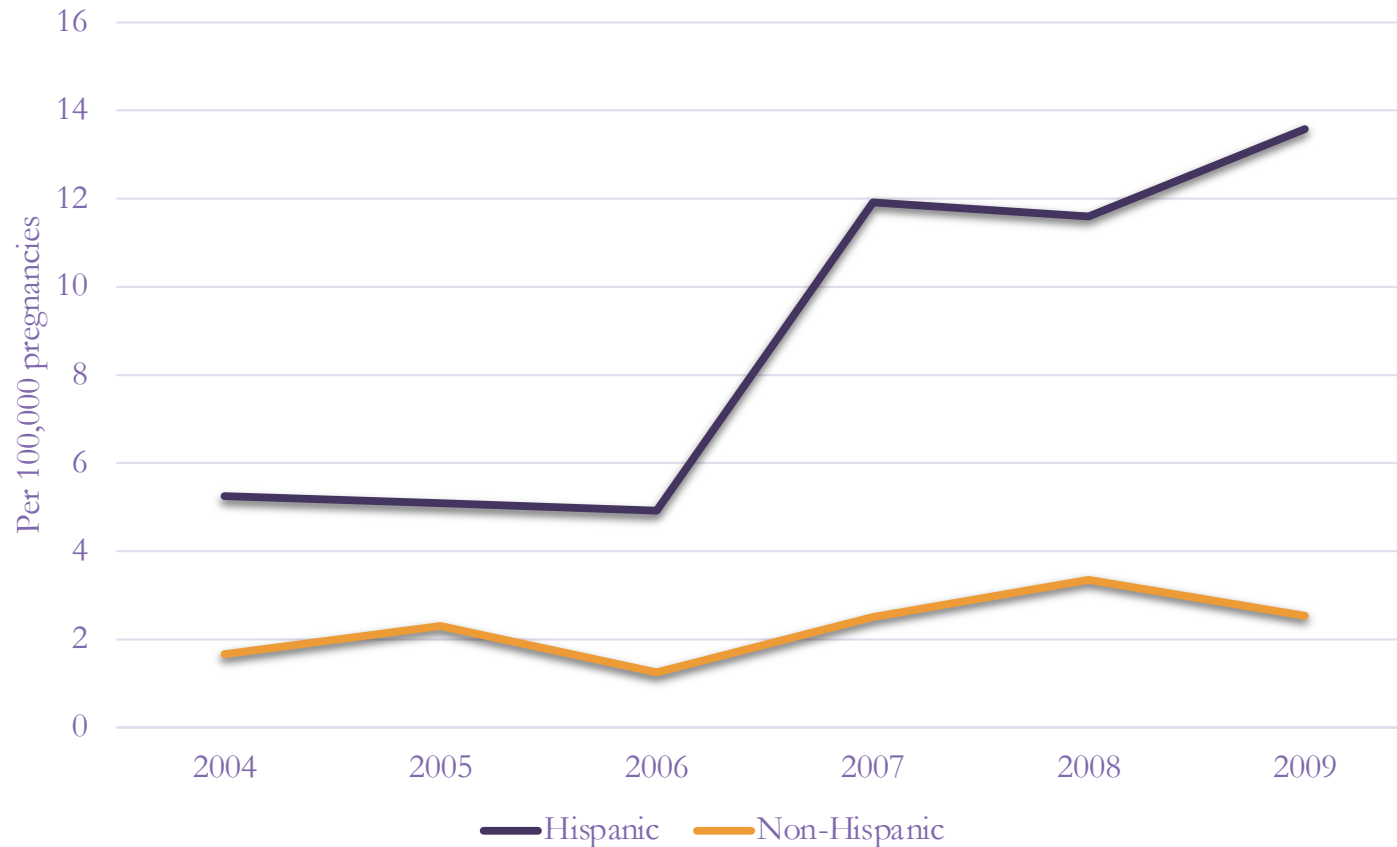
### Stewardship ideas

- Ampicillin → Penicillin
- IV → PO?
- Cefepime mono tx?

1. Stoll BJ, NRN. Pediatrics 2020
2. AFRINEST Tshetu A, et al. Lancet 2015
3. RAIN Study. Keij FM. BMJ Open 2019.

# Invasive Listeriosis U.S.

## Pregnancy-Associated Cases



Silk BJ, et al. Clin Infect Dis 2012

Antibacterial Drugs in the NICU

# Neonatal-Infant Listeria BSI

Study	Population	# Subjects	# Listeria
Kuzniewicz 2020	US NICUs EOS 10 yr	491,462*	0
Stoll 2020	NICHD EOS 2 yr	217,480*	2
Lefebvre 2017	Montreal ED 5 yr	3,559 <sup>§</sup>	0
Biondi 2014	US PRIS ED 4 yr	2,103 <sup>¶</sup>	0

\* Live births

§ blood cultures

¶ positive blood cultures

Antibacterial Drugs in the NICU

# Early Onset Sepsis

## AMPICILLIN

### Recent Activity

- **2014 PTN pop PK/simulation study<sup>1</sup> target  $t > MIC = 8$**

GA $\leq$ 34 wk		GA > 34 wk
PNA 0-7 days	PNA 8-28 days	PNA 0-28 days
50 mg/kg q12h	75 mg/kg q12h	50 mg/kg q8h

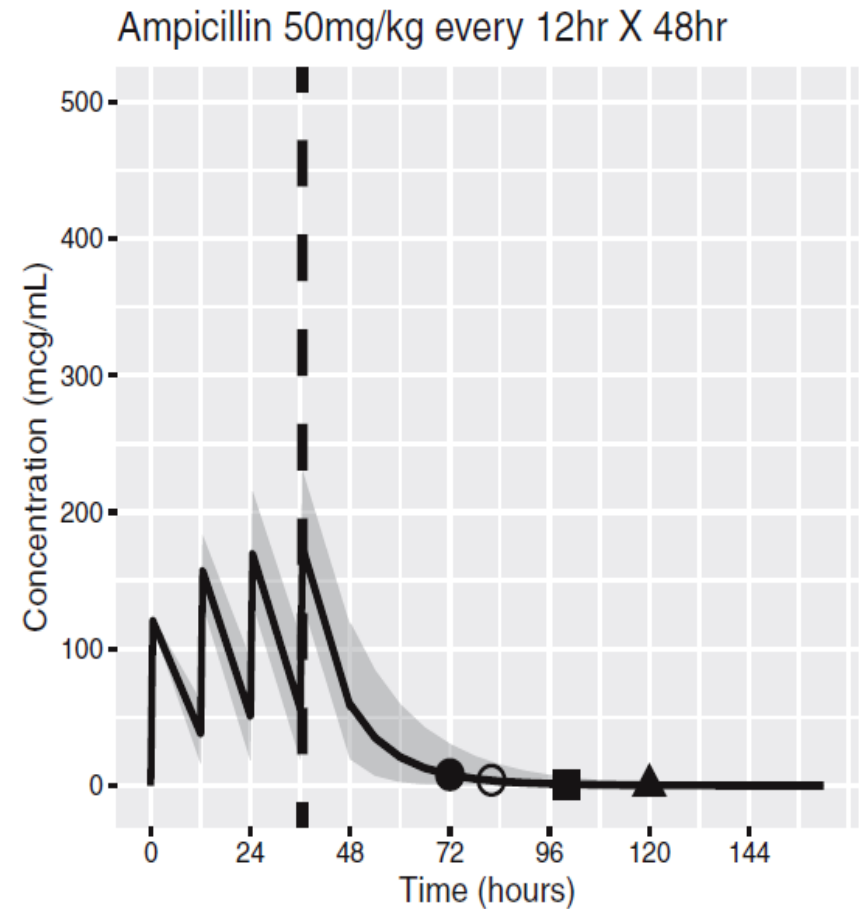
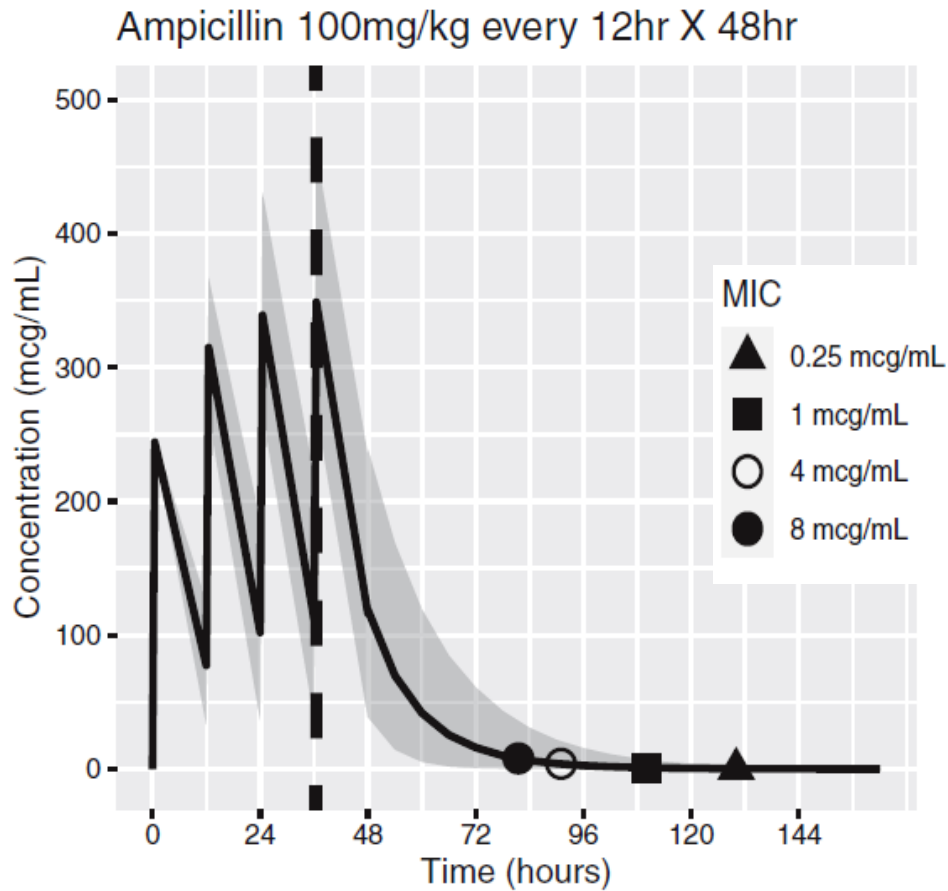
- **2018 FDA labeling change**
- **No signal of exposure associated harm from traditional 100 mg/kg dosing<sup>2</sup>**
- **Prolonged therapeutic concentrations after administration<sup>3</sup>**

1. Tremoulet A, et al. AAC 2014
2. Ericson JE, et al. PIDJ 2020
3. Le J, et al. JPIDS 2021

Antibacterial Drugs in the NICU

# Early Onset Sepsis

## AMPICILLIN ELGAN PDAE

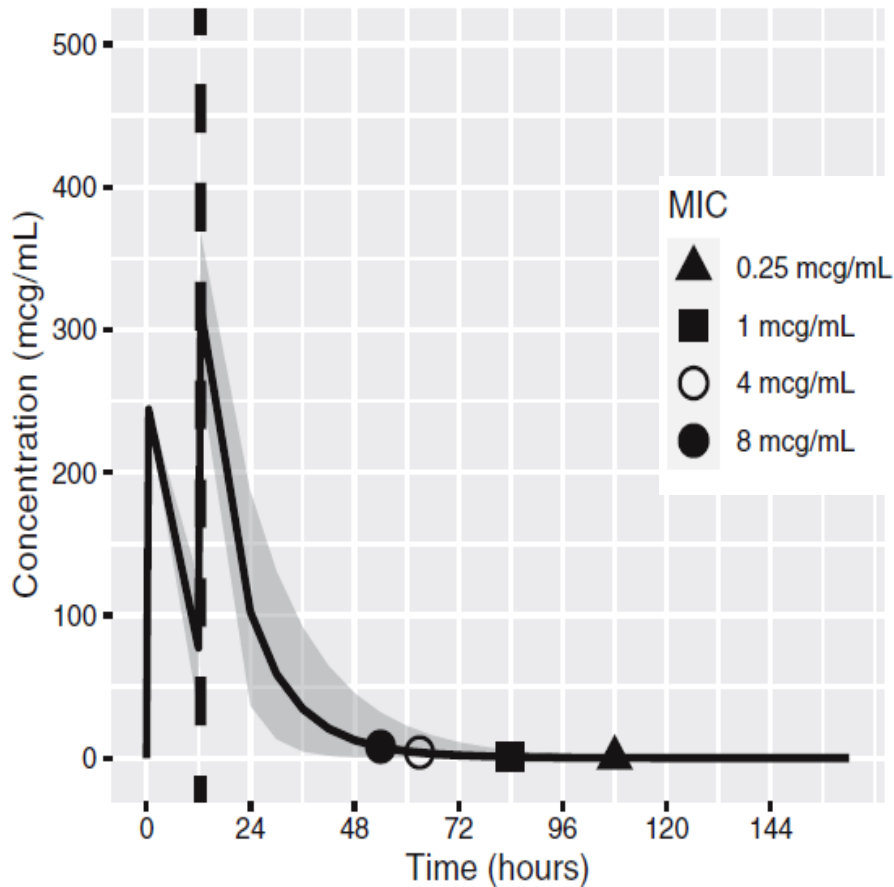




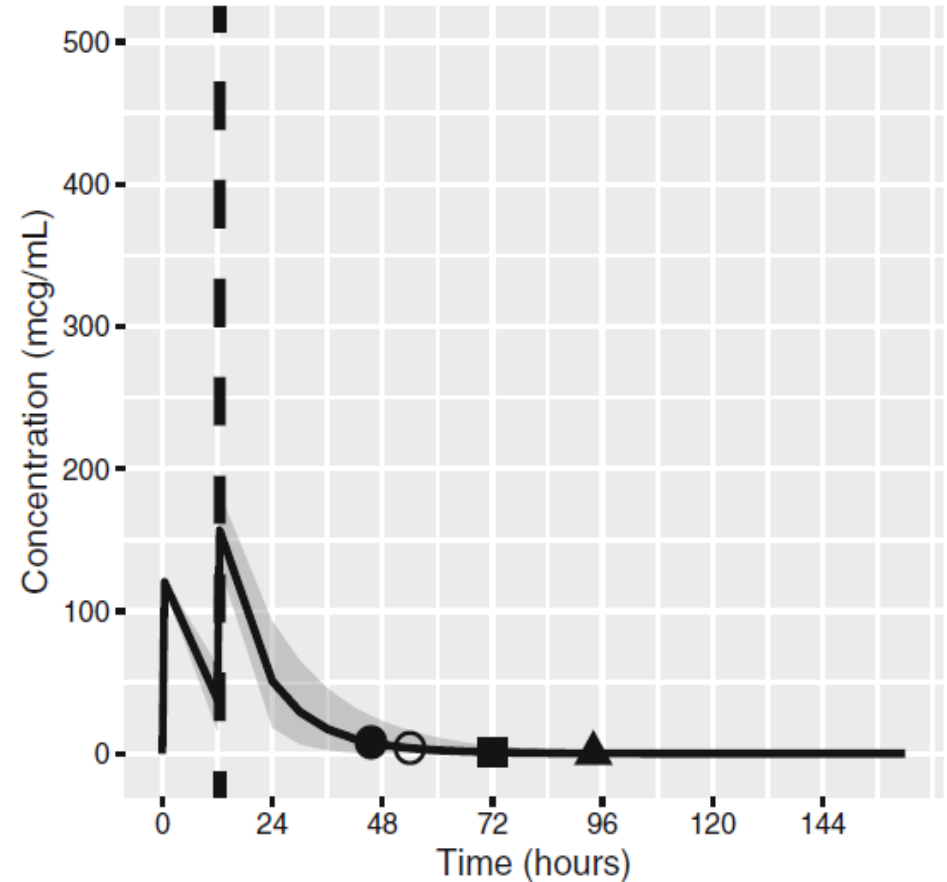
# Early Onset Sepsis

## AMPICILLIN ELGAN PDAE

Ampicillin 100mg/kg every 12hr X 24hr



Ampicillin 50mg/kg every 12hr X 24hr



# Early Onset Sepsis

## GRAM NEGATIVE COVERAGE (E coli, Klebsiella, H influenzae)

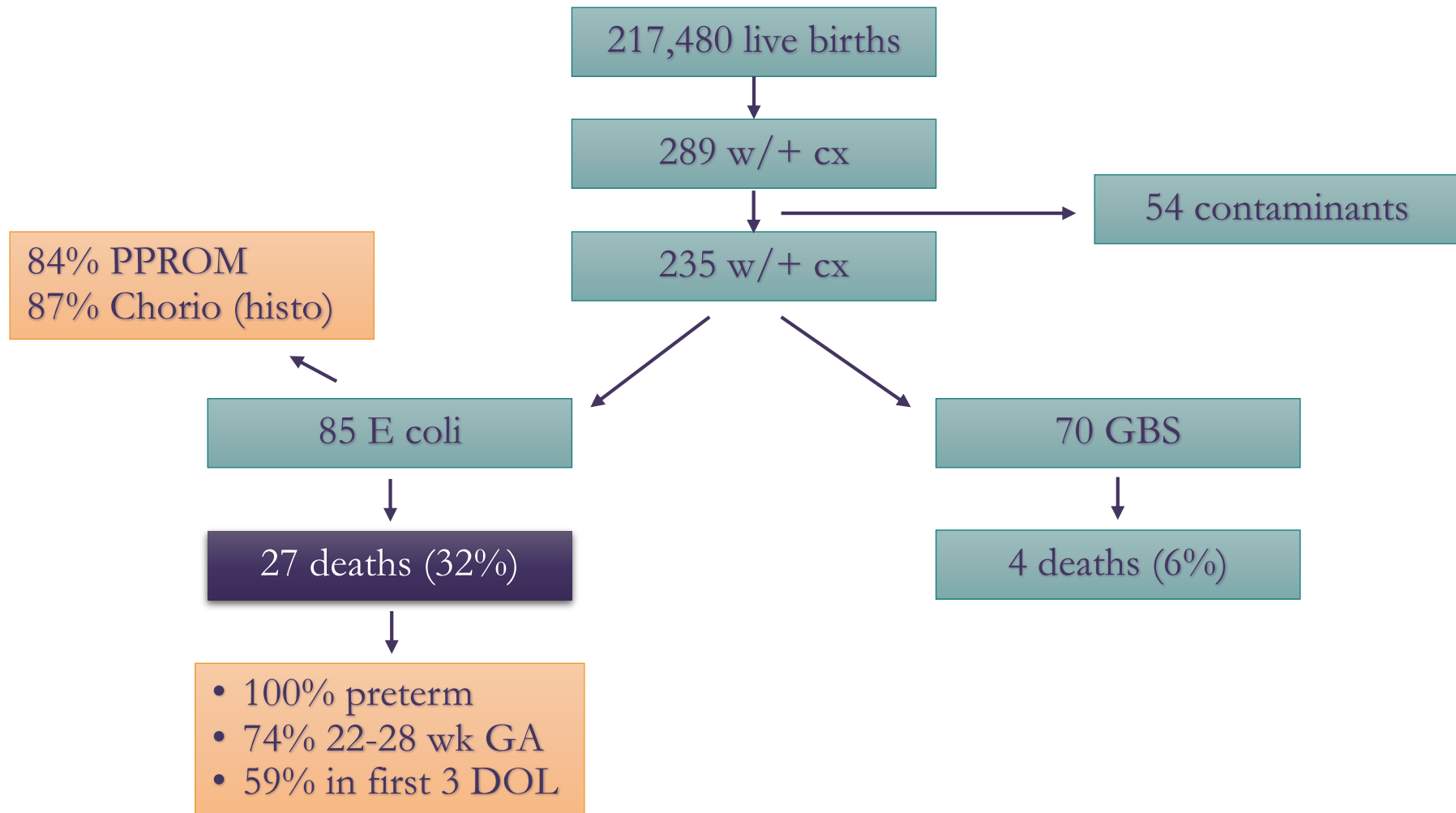
Drug	Critique
Gentamicin	GPC synergy? - anaerobes, ↑ E coli resistance, <sup>1</sup> CSF penetration?
Amikacin	High E coli susceptibility, +MDRO

***“Additional broad-spectrum agents may be indicated in infants who are critically ill and, in preterm infants, at highest risk for GNB EOS, until appropriate culture results are known.”***

AAP COFN, COID Pediatrics 2018

Antibacterial Drugs in the NICU

# NICHD NRN EOS



Stoll BJ, NRN. Pediatrics 2020

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Antibacterial Drugs in the NICU

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Drug	Critique
Gentamicin	GPC synergy? - anaerobes, ↑ E coli resistance, <sup>1</sup> CSF penetration?
Amikacin	High E coli susceptibility, +MDRO
Aztreonam	Same narrow spectra as AMGs, + CSF, high E coli susceptibility
Ceftazidime	FDA approved neonates, +CSF, poor GP coverage, -ESBL
Cefepime	Similar to cefotaxime +PSA, + Amp-C producers, -ESBL
Pip-Tazo	Broad enough for mono tx, not great for meningitis

### Stewardship ideas

- Add cephs to AMG if at risk of overwhelming E coli sepsis: VLBW w/hx of PPRM + chorio<sup>1,2</sup>
- Gentamicin → amikacin or aztreonam
- Start with cefepime monotx (no amp or PCN)

Antibacterial Drugs in the NICU

1. Stoll BJ, NRN. Pediatrics 2020  
2. Puopolo KM, et al. Pediatrics 2018

***“The combination of penicillin and aztreonam, or cefepime single drug therapy, are appropriate empirical antibiotic regimens for infants meeting positive predictive thresholds for EOS. Amikacin should be added for those at highest risk of GNB EOS”***

AAP COFN, COID Pediatrics 20XX??