ENTEROCOCCI

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Evansville, IN
OBJECTIVES

- Discuss basic antimicrobial susceptibility principles and resistance mechanisms for *Enterococcus*
- Describe issues surrounding AST of enterococci
  - Vancomycin
  - Aminoglycosides and synergy testing
- Discuss antimicrobial susceptibility testing and reporting strategies
Enterococci are intrinsically resistant to a number of agents and are extremely adept at acquiring antimicrobial resistance.

Infections typically present in immunocompromised individuals further hindering treatment strategies.

Persist in the hospital environment allowing for opportunities for transmission.

Common colonizers of the GI tract.

In the U.S., approximately 30% of enterococcal isolates are resistant to vancomycin.
46-year old male inpatient becomes febrile while receiving vancomycin for MRSA bacteremia. The Gram stain of the positive blood culture broth reveals GPC and a Verigene BC-GP test was performed. The test indicated the presence of *E. faecium*, but no resistance determinants were detected (i.e. negative for *vanA* and *vanB*). The patient remained on vancomycin and Gram negative coverage was added while awaiting culture results. Two days later, the isolate is identified as confirmed as *E. faecium* and phenotypic susceptibility testing reveals the isolate is resistant to vancomycin (MIC >64). What happened?
### VANCOMYCIN RESISTANCE GENES

<table>
<thead>
<tr>
<th></th>
<th>VanA</th>
<th>VanB</th>
<th>VanM</th>
<th>VanD</th>
<th>VanE</th>
<th>VanC</th>
</tr>
</thead>
<tbody>
<tr>
<td>Vancomycin</td>
<td>≥64</td>
<td>≥4</td>
<td>&gt;256</td>
<td>64-128</td>
<td>8-32</td>
<td>2-32</td>
</tr>
<tr>
<td>Teicoplanin</td>
<td>R</td>
<td>S</td>
<td>S-R</td>
<td>S-R</td>
<td>S</td>
<td>S</td>
</tr>
<tr>
<td>Transferable</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>No</td>
<td>No</td>
<td>No</td>
</tr>
<tr>
<td>Notable</td>
<td>VRE</td>
<td>VRE</td>
<td>VRE</td>
<td>E. gallinarum</td>
<td>E. casseliflavus</td>
<td></td>
</tr>
</tbody>
</table>

Others: VanD, VanG, VanL, VanN; table adapted from O’Driscoll and Crank

- **Determination of specific resistance gene (often) unnecessary**
- **Vancomycin and teicoplanin MICs can be helpful in differentiating VRE from enterococci that are vancomycin-resistant**

O’Driscoll T & Crank CW, Infect & Drug Resist, 2015
Numerous platforms available with that primarily target vanA and vanB

Performance of direct from positive blood assays is well established as highly sensitive (~95%)
Achilles heel of a molecular assay is the target
- Commercial assays are designed to detect known, characterized resistance markers and typically only the most common resistance determinants are included

Real or perceived “misses” (i.e. true false negative vs mechanism other than one targeted) by molecular platforms when genotypically tests negative but phenotypically positive

Discordant results must be evaluated

Possible sources:

- Missed \textit{vanA} or \textit{vanB} by molecular platform
  - Martinez et. al. described less than desirable performance for detection of \textit{vanA} (sources: false negative possibly due to inhibitory substance and \textit{vanA} gene detected by Verigene (and confirmed with other molecular assay) with phenotypic susceptibility. Others have reported more favorable performance characteristics.

- Incorrect vancomycin resistance by phenotypic analysis
- Mechanism other than \textit{vanA} or \textit{vanB}

Martinez RM et. al., JCM, 2014
THE OTHER VANS

- Case: phenotypic susceptibility confirmed, ran isolate on another molecular platform and remained vanA negative. This case scenario would fit for van gene other than vanA or vanB
  - VanM – extremely rare, reported in Singapore and China
- Lack of routine monitoring of the van genes in circulation
  - Not all laboratories routinely test teicoplanin
  - Not all laboratories utilize molecular assays that target vanA and vanB
- As molecular detection continues to expand, so will recognition of these other van genes

Teo JWP et. al., JCM, 2011
Unlike blood culture assays, VRE surveillance by PCR has struggled.

Poor positive predictive value associated with *vanB* results.

- Numerous reports of *vanB* in non-enterococci (e.g. *Clostridium, Eggerthella, Ruminococcus*, others)
- Leads to high number of false positives

Use of PCR has allowed for detection of previously unrecognized phenotypes.

Mak A et. al., JCM, 2009
Bourdon N et. al., Diagn Microbiol Infect Dis, 2010
Genotypic resistance detected but phenotypically susceptible

Termed Vancomycin Variable Enterococci (VVE) harbor “silent” resistance which may result in VSE to VRE transition while on therapy

Ontario outbreak (2012) with >95 patients in 13 hospitals positive for vanA-carrying vancomycin-susceptible isolates

- WHAT ABOUT THE REVERSE PROBLEM?

<table>
<thead>
<tr>
<th>PCR (vanA)</th>
<th>Agar (6ug/ml vanc)</th>
<th>Broth microdilution</th>
</tr>
</thead>
<tbody>
<tr>
<td>Result</td>
<td>Pos</td>
<td>Growth/No Growth</td>
</tr>
</tbody>
</table>

VVE strains pose a significant challenge for diagnostic tests used for VRE detection
VANCOMYCIN-DEPENDENT ENTEROCOCCI

- Will not grow *in vitro* in the absence of vancomycin
- Detected during surveillance or by molecular methods

Tambyah PA et. al., Emerg Infect Dis, 2004
Disk diffusion or Etest plates should be held for a full 24 hours and zones examined using transmitted light

- Enhancement of growth that allows for better detection of intermediate resistance at 24 hrs compared to 18 hrs
- Growth may be hazy in which transmitted light aids in recognition of inner growth

Commercial systems vs Etest

- Vancomycin MIC determination is somewhat method dependent; however, categorical agreement typically high
- Etests generally produce vancomycin MICs that are $1 \log_2$ concentration higher than the commercial systems
Correct reporting of VRE for infection control purposes

- Primarily interested in isolates carrying *vanA* or *vanB*

- Be aware of discrepancies between molecular and phenotypic methods (may be surveillance and infection isolates) and attempt to resolve
AMINOGYLCOCIDES VERSUS ENTEROCOCCUS
Enterococci are intrinsically resistant or exhibit inherent reduced susceptibility to a number of GP agents.

For serious enterococcal infections, such as those stemming from an endovascular source (e.g. heart valve) require a bactericidal regimen for optimal outcomes.

Although ampicillin is the preferred therapy for ampicillin-susceptible enterococcal infections, MICs against enterococci are typically elevated.

Furthermore, enterococci are resistant to clinically achievable concentrations of aminoglycosides (monotherapy).

Combination of a cell wall agent (e.g. ampicillin) plus aminoglycoside results in bactericidal synergism.
Beta-lactams (ampicillin) are structurally similar to the building blocks of the cell wall (pentapeptides).

Aminoglycosides inhibit protein synthesis, so they must enter the cell in order to work.

Cell wall agent (e.g. beta-lactam or glycopeptide) allows penetration of the aminoglycoside into the cell → synergy.

In the lab, a disk containing high levels of the aminoglycoside are used to test for synergy of the agent when used in combination with a cell wall drug.
Screening test for high level aminoglycoside resistance (HLAR) can be performed by disk diffusion, broth microdilution, or agar dilution.

Both gentamicin and streptomycin should be considered independently as one cannot predict the other.

Other aminoglycosides are considered inferior and should not be tested.

<table>
<thead>
<tr>
<th>Agent</th>
<th>Standard disk content*</th>
<th>HLAR disk content</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gentamicin</td>
<td>10 μg</td>
<td>120 μg</td>
</tr>
<tr>
<td>Streptomycin</td>
<td>10 μg</td>
<td>300 μg</td>
</tr>
</tbody>
</table>

*Do not use standard disk content for testing enterococci.
CONSIDERATIONS

- Unnecessary to test and/or report HLAR on isolates other than those from blood cultures or specimens submitted for evaluation of endocarditis

- Other select cases: CSF – enterococcal meningitis
  - No reported mortality benefit with combination therapy
For enterococci, aminoglycoside results should NEVER be reported as susceptible or resistant.

Rather indicate “Synergy” or “No Synergy”:

- SYN vs SYN-R in UpToDate

Use of comments:

- Synergy is achievable with gentamicin and susceptible cell wall agent.
- Gentamicin is synergistic with a cell wall agent that is also susceptible.
**WHAT IF RESISTANT TO ALL CELL WALL AGENTS TESTED?**

*E. faecium*

<table>
<thead>
<tr>
<th>Agent</th>
<th>Interp</th>
</tr>
</thead>
<tbody>
<tr>
<td>Penicillin</td>
<td>R</td>
</tr>
<tr>
<td>Ampicillin</td>
<td>R</td>
</tr>
<tr>
<td>Vancomycin</td>
<td>R</td>
</tr>
<tr>
<td>Daptomycin</td>
<td>R</td>
</tr>
<tr>
<td>HL Gentamicin</td>
<td>SYN</td>
</tr>
<tr>
<td>HL Streptomycin</td>
<td>SYN</td>
</tr>
</tbody>
</table>

- Gentamicin is synergistic with a cell wall agent that is also susceptible
REPORTING WHEN RESISTANT TO CELL WALL AGENTS

- Confirm susceptibility
- Knowing the MICs for cell wall agents will be helpful
  - Strains of *E. faecium* with ampicillin MICs of ≤64 ug/ml may respond to high-dose ampicillin therapy in combination with gentamicin
  - Combination therapy with two cell wall agents is gaining in popularity
- Report aminoglycoside synergy even if the cell wall agents are reported as resistant

Murray BE, NEJM, 2000
Principle: Two main mechanisms that contribute to high-level beta-lactam resistance in enterococci

- Production of beta-lactamase
- **Overproduction of PBP5 – low affinity for many beta-lactams**

Combination of cell wall agents

- Ampicillin plus daptomycin
- Ampicillin plus ceftriaxone
- Ampicillin plus ceftaroline
- Many others

Synergy testing can be difficult to interpret and not recommended as routine testing
S. PNEUMONIAE
Discuss basic antimicrobial susceptibility principles and resistance mechanisms for *S. pneumoniae* versus penicillin and ceftriaxone.

Discuss antimicrobial susceptibility testing and reporting strategies.
Common inhabitants of the upper respiratory tract and can be isolated from the nasopharynx of 5-90% of the population.

Most infections occur by direct extension (e.g. pneumonia) or by hematogenous spread (e.g. meningitis, peritonitis, bacteremia).

Meningitis and non-meningitis breakpoints exist for the common beta-lactams used to treat pneumococci (penicillin, cefepime, cefotaxime, ceftriaxone).
Generally speaking, breakpoints are established based upon physiologically achievable concentrations

- Somewhat biased toward blood concentrations
- Penicillin breakpoints historically based on CSF concentrations

Penicillin penetrates poorly into the CNS; higher concentrations are achieved in fluids other than CSF

CLSI incorporated meningitis and non-meningitis breakpoints in 2008 allowing penicillin to remain in the arsenal for treatment of community acquired pneumonia

Weinstein MP et. al., CID, 2009
### BETA-LACTAM BREAKPOINTS

<table>
<thead>
<tr>
<th>Agent</th>
<th>Non-Meningitis (MIC)</th>
<th>Meningitis (MIC)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>S</td>
<td>I</td>
</tr>
<tr>
<td>Penicillin</td>
<td>≤2</td>
<td>4</td>
</tr>
<tr>
<td>Cefotaxime</td>
<td>≤1</td>
<td>2</td>
</tr>
<tr>
<td>Ceftriaxone</td>
<td>≤1</td>
<td>2</td>
</tr>
<tr>
<td>Cefepime</td>
<td>≤1</td>
<td>2</td>
</tr>
</tbody>
</table>

- Reliable disk diffusion breakpoints do not yet exist. In vitro activity is best determined by a MIC-based method.
Amoxicillin, ampicillin, cefepime, cefotaxime, ceftriaxone, cefuroxime, ertapenem, imipenem, and meropenem may be used to treat pneumococcal infections; however, reliable disk diffusion susceptibility tests for these agents do not yet exist.

- Cefepime – non-FDA-approved indication
- Meropenem > imipenem (seizure risk)

For *S. pneumoniae* isolated from the CSF penicillin and cefotaxime, ceftriaxone, or meropenem should be tested by a reliable MIC method and reported routinely. Such isolates can also be tested against vancomycin using the MIC or disk method.
### DECIPHERING THE M100

#### Table 2G. (Continued)

<table>
<thead>
<tr>
<th>Test/Report Group</th>
<th>Antimicrobial Agent</th>
<th>Disk Content</th>
<th>Zone Diameter Interpretive Criteria (nearest whole mm)</th>
<th>MIC Interpretive Criteria (µg/mL)</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td>S</td>
<td>I</td>
<td>R</td>
</tr>
<tr>
<td><strong>PENICILLINS</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>(4) For nonmeningitis isolates, a penicillin MIC of ≤0.06 µg/mL (or oxacillin zone ≥20 mm) can predict susceptibility to the following β-lactams: ampicillin (oral or parenteral), amoxicillin-sulbactam, amoxicillin, amoxicillin-clavulanate, cefaclor, cefdinir, cefditoren, cefepime, cefotaxime, cepodoxime, cefprozil, ceftaroline, ceftizoxime, ceftriaxone, cefuroxime, doripenem, ertapenem, imipenem, loracarbef, meropenem, and penicillin (oral or parenteral).</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>See comment (3).</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

#### A

| Penicillin | 1 µg oxacillin | ≥20 | – | – | – | – | – | – |                  |
|------------|----------------|-----|---|---|---|---|---|---|                  |

#### A

| Penicillin parenteral (nonmeningitis) | – | – | – | – | – | ≤2 | 4 | ≥8 |                  |
|--------------------------------------|---|---|---|---|---|----|---|---|                  |

(5) Isolates of pneumococci with oxacillin zone sizes of ≥20 mm are susceptible (MIC ≤ 0.06 µg/mL) to penicillin. Penicillin and cefotaxime, ceftriaxone, or meropenem MICs should be determined for those isolates with oxacillin zone diameters of ≥19 mm, because zones of ≤19 mm occur with penicillin-resistant, intermediate, or certain susceptible strains. For isolates with oxacillin zones ≤19 mm, do not report penicillin as resistant without performing a penicillin MIC test.

#### A

| Penicillin parenteral (meningitis) | – | – | – | – | – | ≤0.08 | – | ≥0.12 |                  |
|------------------------------------|---|---|---|---|---|--------|---|-------|                  |

(8) Rx: Doses of intravenous penicillin of at least 2 million units every four hours in adults with normal renal function (12 million units per day) can be used to treat nonmeningeal pneumococcal infections due to strains with penicillin MICs ≤2 µg/mL. Strains with an intermediate MIC of 4 µg/mL may require penicillin doses of 18 to 24 million units per day.

(7) For all isolates other than those from CSF, report interpretations for both meningoitis and nonmeningitis.

#### A

| Penicillin (oral penicillin V) | – | – | – | – | – | ≤0.06 | 0.12–1 | ≥2 |                  |
|-------------------------------|---|---|---|---|---|--------|--------|---|                  |

(10) Interpretations for oral penicillin may be reported for isolates other than those from CSF.
Automated instruments use these breakpoints for interpretation

Provide dosing information if possible

<table>
<thead>
<tr>
<th></th>
<th>≤2</th>
<th>4</th>
<th>≥8</th>
<th>≤0.08</th>
<th>–</th>
<th>≥0.12</th>
</tr>
</thead>
<tbody>
<tr>
<td>Penicillin parenteral</td>
<td>–</td>
<td>–</td>
<td>–</td>
<td>–</td>
<td>–</td>
<td>–</td>
</tr>
<tr>
<td>(nonmeningitis)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Penicillin parenteral</td>
<td>–</td>
<td>–</td>
<td>–</td>
<td>–</td>
<td>–</td>
<td>–</td>
</tr>
<tr>
<td>(meningitis)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

(6) Rx: Doses of intravenous penicillin of at least 2 million units every four hours in adults with normal renal function (12 million units per day) can be used to treat nonmeningeal pneumococcal infections due to strains with penicillin MICs ≤ 2 µg/mL. Strains with an intermediate MIC of 4 µg/mL may require penicillin doses of 18 to 24 million units per day.

(7) For all isolates other than those from CSF, report interpretations for both meningitis and nonmeningitis.

(8) Rx: Use of penicillin in meningitis requires therapy with maximum doses of intravenous penicillin (eg, at least 3 million units every four hours in adults with normal renal function).

(9) For CSF isolates, report only meningitis interpretations.
Why include interpretations for the oral formulation of penicillin?

- Penicillin V is the treatment of choice for pneumococcal pneumonia

Be aware of what antibiotics practitioners preferentially prescribe (formulary agents, local practices)
REPORTING PENICILLIN MIC RESULTS – MENINGITIS (CSF, CNS)

- Only report meningitis interpretations
- Consider options for providing dosing information

<table>
<thead>
<tr>
<th>Agent</th>
<th>MIC</th>
<th>Interp</th>
</tr>
</thead>
<tbody>
<tr>
<td>Penicillin (parenteral - meningitis)</td>
<td>1</td>
<td>R</td>
</tr>
</tbody>
</table>
For use with nonmeningitis isolates only

(5) Isolates of pneumococci with oxacillin zone sizes of ≥ 20 mm are susceptible (MIC ≤ 0.08 μg/mL) to penicillin. Penicillin and cefotaxime, ceftriaxone, or meropenem MICs should be determined for those isolates with oxacillin zone diameters of ≤ 19 mm, because zones of ≤ 19 mm occur with penicillin-resistant, intermediate, or certain susceptible strains. For isolates with oxacillin zones ≤ 19 mm, do not report penicillin as resistant without performing a penicillin MIC test.
For nonmeningitis isolates, a zone of ≤19 mm may correspond to susceptible, intermediate, or resistant MICs.

- Blood isolate
- Oxacillin zone = 19 mm
- What next?

- Perform a penicillin MIC
- Do not report penicillin as resistant without performing a MIC test
For nonmeningitis isolates, oxacillin zone ≥ 20 mm is susceptible and corresponds to a penicillin MIC 0.06 μg/ml (which would be susceptible using both meningitis and nonmeningitis breakpoints).
Per comment (4), one can report as susceptible to penicillin and can be used to predict susceptibility for several agents (e.g. cefotaxime, ceftriaxone, meropenem) for NONMENINGITIS isolates.

What about comment (7) “For all isolates other than CSF, report interpretations for both meningitis and nonmeningitis”?

<table>
<thead>
<tr>
<th>Agent</th>
<th>Result (interpretation)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Penicillin (parenteral - meningitis)</td>
<td>S</td>
</tr>
<tr>
<td>Penicillin (parenteral - nonmeningitis)</td>
<td>S</td>
</tr>
<tr>
<td>Penicillin (oral)</td>
<td>S</td>
</tr>
<tr>
<td>Ceftriaxone (meningitis)</td>
<td>S</td>
</tr>
<tr>
<td>Ceftriaxone (nonmeningitis)</td>
<td>S</td>
</tr>
</tbody>
</table>
OXACILLIN DISK FOR PREDICTING PENICILLIN SUSCEPTIBILITY

N = 1,116
No isolate with oxacillin zone of ≥20 mm had penicillin MIC >0.06 (meningitis breakpoints)

Jette LP and Sinave C, JCM, 1999
N = 695
No isolate with oxacillin zone of ≥20 mm had ceftriaxone MIC >0.5 (meningitis breakpoints)

Jette LP and Sinave C, JCM, 1999
### DECIPHERING THE M100

<table>
<thead>
<tr>
<th></th>
<th>Cefepime (meningitis)</th>
<th>Cefepime (nonmeningitis)</th>
<th>Cefotaxime (meningitis)</th>
<th>Ceftriaxone (meningitis)</th>
<th>Cefotaxime (nonmeningitis)</th>
<th>Ceftriaxone (nonmeningitis)</th>
<th>Ceftaroline (nonmeningitis)</th>
<th>Cefuroxime (parenteral)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Amoxicillin</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>(nonmeningitis)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Amoxicillin-clavulanate</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>(nonmeningitis)</td>
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<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>≤2/2</td>
<td>≤2/1</td>
<td>≤0.5</td>
<td>≤0.5</td>
<td>≤1</td>
<td>≤1</td>
<td>≤0.5</td>
<td>≤0.5</td>
</tr>
<tr>
<td></td>
<td>4/2</td>
<td>4</td>
<td>1</td>
<td>1</td>
<td>2</td>
<td>2</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td></td>
<td>≥8/4</td>
<td>≥8/4</td>
<td>≥2</td>
<td>≥2</td>
<td>≥4</td>
<td>≥4</td>
<td>≥4</td>
<td>≥4</td>
</tr>
</tbody>
</table>

**RENTERAL (Including cephalosporins I, II, III, and IV. Please refer to Glossary I.)**

11. In the United States, for CSF isolates, report only nonmeningitis interpretations. There is not an FDA-approved indication for the use of cefepime for meningitis in the United States.

12. In the United States, only report interpretations for nonmeningitis and include the nonmeningitis notation on the report.

13. For CSF isolates, report only meningitis interpretations.

14. Rx: Use of cefotaxime or ceftriaxone in meningitis requires therapy with maximum doses. See comment (3).

15. For all isolates other than those from CSF, report interpretations for both meningitis and nonmeningitis.

16. Interpretable criteria are based on a dosage regimen of 800 mg every 12 h.

- **Cefepime only nonmeningitis interpretations in U.S.**
- **Cefotaxime and/or ceftriaxone meningitis and nonmeningitis interpretations should be reported**
### REPORTING CEPHALOSPORIN RESULTS - NONMENINGITIS (NON-CSF, NON-CNS)

<table>
<thead>
<tr>
<th>Agent</th>
<th>MIC</th>
<th>Interp</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cefotaxime (parenteral - meningitis)</td>
<td>1</td>
<td>I</td>
</tr>
<tr>
<td>Cefotaxime (parenteral - nonmeningitis)</td>
<td>1</td>
<td>S</td>
</tr>
<tr>
<td>Ceftriaxone (parenteral - meningitis)</td>
<td>1</td>
<td>I</td>
</tr>
<tr>
<td>Ceftriaxone (parenteral - nonmeningitis)</td>
<td>1</td>
<td>S</td>
</tr>
</tbody>
</table>

- May not be necessary to report both cefotaxime and ceftriaxone
May not be necessary to report both cefotaxime and ceftriaxone

May consider comment providing recommended dosing (CLSI indicates “maximum doses,” confer with pharmacy about recommendation)

May consider reporting of other agents with or without interpretations (e.g. cefepime, ceftaroline)

### REPORTING CEPHALOSPORIN RESULTS - MENINGITIS (CSF, CNS)

<table>
<thead>
<tr>
<th>Agent</th>
<th>MIC</th>
<th>Interp</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cefotaxime (parenteral - meningitis)</td>
<td>1</td>
<td>I</td>
</tr>
<tr>
<td>Ceftriaxone (parenteral - meningitis)</td>
<td>1</td>
<td>I</td>
</tr>
</tbody>
</table>
Small case series (4 patients) indicated that ceftaroline may be a viable treatment option for *S. pneumoniae* meningitis

- 3 out of 4 patients were successfully treated
- Potential agent for penicillin-resistant isolates

Thus far, very limited number of clinical descriptions of ceftaroline for meningitis

- Case by case basis with pharmacy/ID involvement

Sakoulas G et. al., AAC, 2015