PROPHYLACTIC ANTIBIOTICS ON LABOR & DELIVERY

Irina Cassimatis MD, MSc
No disclosures
ANNUAL U.S BIRTHS

National Center for Health Statistics 2018
UNIVERSITY OF UTAH DELIVERIES (2017)

- Cesarean delivery: 27%
- Vaginal Delivery: 73%

3361 deliveries
ANTIBIOTIC PROPHYLAXIS

• Goal is to have therapeutic tissue levels at time of microbial contamination

• Agent of choice should be long acting, narrowly focused on the likely bacteria, inexpensive, and have a low incidence of adverse effects
## GENITOURINARY TRACT MICROBIOLOGY

<table>
<thead>
<tr>
<th>Gram positive aerobic</th>
<th>Gram negative aerobic</th>
<th>Anaerobic</th>
<th>Mycoplasma</th>
<th>Other</th>
</tr>
</thead>
<tbody>
<tr>
<td>GBS</td>
<td>E. coli</td>
<td>Peptostreptococcus</td>
<td>Mycoplasma</td>
<td>Chlamydia</td>
</tr>
<tr>
<td>S. aeurus</td>
<td>Klebsiella</td>
<td>Peptococcus</td>
<td>Ureaplasma</td>
<td></td>
</tr>
<tr>
<td>Enterococcus</td>
<td>Proteus</td>
<td>Bacteroides</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Pseudomonas</td>
<td>Gardnerella</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Enterobacter</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

ANTIBIOTIC MISUSE

- Allergic reactions
- GI disturbance
- Unknown fetal effects
- Potential healthcare costs
- Antibiotic resistance

Ledger. BJOG 2013
Stiemsma. Pediatrics 2018
Burden of *Clostridium difficile* Infection in the United States

C. DIFF AMONG PERIPARTUM WOMEN

Kuntz et al. Infect Control Hosp Epidemiol 2010
OBJECTIVES

• Post-op antibiotics following cesarean in BMI > 30
• Cesarean complicated by Triple-I
• Manual placental removal
• Obstetric anal sphincter injury
Surgical site infection (SSI) following cesarean section:
– reported rates of 3–20 %

OBESITY IN PREGNANCY

2016
Percent of adults aged 18 years and older who have obesity†
View by: Total

CDC. National Center for Chronic Disease Prevention and Health Promotion, 2018
CEFAZOLIN DOSING FOR BMI > 30

• **Standard dose recommendation:** 2g cefazolin within 60 minutes of incision

Bratzler et al. Am J Health Syst Pharm 2013
Post-cesarean extended oral prophylaxis in BMI > 30
Effect of Post-Cesarean Delivery Oral Cephalexin and Metronidazole on Surgical Site Infection Among Obese Women: A Randomized Clinical Trial

Amy M. Valent, DO1; Chris DeArmond, RN2; Judy M. Houston, RPh3; et al

### Table 2. Study Outcomes

<table>
<thead>
<tr>
<th>Outcomes</th>
<th>Cephalexin-Metronidazole (n = 202)</th>
<th>Placebo (n = 201)</th>
<th>Mean Between-Group Difference, % (95% CI)</th>
<th>Relative Risk (95% CI)</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Primary outcome</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Surgical site infection&lt;sup&gt;a&lt;/sup&gt;</td>
<td>13 (6.4) [3.0 to 9.8]</td>
<td>31 (15.4) [10.4-20.4]</td>
<td>9.0 (2.9 to 15.0)</td>
<td>0.41 (0.22-0.77)</td>
<td>.01</td>
</tr>
<tr>
<td><strong>Secondary outcomes</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Incisional morbidity&lt;sup&gt;b&lt;/sup&gt;</td>
<td>20 (9.9) [5.8 to 14.1]</td>
<td>32 (15.9) [10.8-21.0]</td>
<td>6.0 (-0.5 to 13.0)</td>
<td>0.61 (0.37-1.04)</td>
<td>.18</td>
</tr>
<tr>
<td>Fever of unknown etiology</td>
<td>9 (4.5) [1.6 to 7.3]</td>
<td>10 (5.0) [2.0-8.0]</td>
<td>0.5 (-3.6 to 4.6)</td>
<td>0.89 (0.37-2.14)</td>
<td>.94</td>
</tr>
<tr>
<td>Wound separation</td>
<td>16 (7.9) [4.2 to 11.7]</td>
<td>22 (10.9) [6.6-15.3]</td>
<td>3.0 (-2.7 to 8.8)</td>
<td>0.72 (0.39-1.33)</td>
<td>.56</td>
</tr>
<tr>
<td>Cellulitis</td>
<td>12 (5.9) [2.7 to 9.2]</td>
<td>27 (13.4) [8.9-18.2]</td>
<td>7.5 (1.7 to 13.0)</td>
<td>0.44 (0.23-0.84)</td>
<td>.04</td>
</tr>
<tr>
<td>Endometritis</td>
<td>2 (1.0) [-0.4 to 2.4]</td>
<td>8 (4.0) [1.3-6.7]</td>
<td>3.0 (-0.05 to 6.0)</td>
<td>0.24 (0.53-1.16)</td>
<td>.05</td>
</tr>
</tbody>
</table>

<sup>a</sup> Defined as any superficial incisional, deep incisional, or organ/space infection.

<sup>b</sup> Defined as any defect in the incisional integrity with or without the presence of an infection, including cellulitis, endometritis, and wound separation.
## INTACT VS RUPTURED MEMBRANES

### Table 3. Post Hoc Study Outcomes Stratified by Membrane Status

<table>
<thead>
<tr>
<th>Outcomes</th>
<th>No. (%) [95% CI] With Outcome</th>
<th>Mean Between-Group Difference, % (95% CI)</th>
<th>Relative Risk (95% CI)</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Ruptured Membranes (n = 126)</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Primary outcome (n = 63)</td>
<td>(n = 63)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Surgical site infection</td>
<td>6 (9.5) [2.1 to 16.9]</td>
<td>19 (30.2) [18.6 to 41.7]</td>
<td>20.6 (6.9 to 34.3)</td>
<td>0.31 (0.13-0.71)</td>
</tr>
<tr>
<td>Secondary outcomes</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Incisional morbidity</td>
<td>10 (15.9) [6.7 to 25.1]</td>
<td>19 (30.2) [18.6 to 41.7]</td>
<td>14.3 (0.5 to 29.0)</td>
<td>0.51 (0.26-0.99)</td>
</tr>
<tr>
<td>Fever of unknown etiology</td>
<td>4 (6.3) [0.2 to 12.5]</td>
<td>7 (11.1) [3.2 to 19.0]</td>
<td>4.8 (−5.2 to 14.8)</td>
<td>0.55 (0.17-1.79)</td>
</tr>
<tr>
<td>Wound separation</td>
<td>8 (12.7) [4.3 to 21.1]</td>
<td>11 (17.5) [7.9 to 27.0]</td>
<td>4.8 (−7.9 to 17.5)</td>
<td>0.70 (0.30-1.62)</td>
</tr>
<tr>
<td>Cellulitis</td>
<td>5 (7.9) [1.1 to 14.7]</td>
<td>15 (23.8) [13.1 to 34.5]</td>
<td>15.9 (3.2 to 28.6)</td>
<td>0.32 (0.13-0.83)</td>
</tr>
<tr>
<td>Endometritis</td>
<td>2 (3.2) [−1.2 to 7.6]</td>
<td>8 (12.7) [4.3 to 21.1]</td>
<td>9.5 (0.06 to 19.0)</td>
<td>0.25 (0.06-1.13)</td>
</tr>
</tbody>
</table>

| Intact Membranes (n = 277)  |                                |                                          |                        |         |
| Primary outcome (n = 138)   | (n = 139)                      |                                          |                        |         |
| Surgical site infection     | 7 (5.0) [1.4 to 8.7]           | 12 (8.7) [4.0 to 13.4]                   | 3.7 (−2.3 to 9.6)      | 0.58 (0.24-1.44) | .47     |
| Secondary outcomes          |                                |                                          |                        |         |
| Incisional morbidity        | 10 (7.2) [(2.9 to 11.5)        | 13 (9.4) [4.5 to 14.3]                   | 2.2 (−4.3 to 8.8)      | 0.77 (0.35-1.69) | .78     |
| Fever of unknown etiology   | 5 (3.6) [0.5 to 6.7]           | 3 (2.2) [−0.3 to 4.6]                    | −1.4 (−5.4 to 2.5)     | 1.67 (0.41-6.83) | .75     |
| Wound separation            | 8 (5.8) [1.9 to 9.7]           | 11 (8.0) [3.4 to 12.5]                   | 2.2 (−3.8 to 8.2)      | 0.73 (0.30-1.75) | .75     |
| Cellulitis                  | 7 (5.0) [1.4 to 8.7]           | 12 (8.7) [4.0 to 13.4]                   | 3.7 (−2.3 to 9.6)      | 0.58 (0.24-1.44) | .47     |
| Endometritis                | 0                               | 0                                         |                        |         |

*Analyses examining subgroups according to intact or ruptured membranes are post hoc and should be considered exploratory.*

Valent et al. JAMA 2017
Cesarean section in the setting of Triple-I infection
## TRIPLE-I TREATMENT

<table>
<thead>
<tr>
<th>Antibiotic</th>
<th>Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ampicillin</td>
<td>2g q6h PLUS</td>
</tr>
<tr>
<td>Gentamicin</td>
<td>5mg/kg daily OR 1.5mg/kg q8h</td>
</tr>
<tr>
<td>Ampicillin-sulbactam</td>
<td>3g q6h</td>
</tr>
<tr>
<td>Ticarcillin-clavulanate</td>
<td>3.1g q4h</td>
</tr>
<tr>
<td>Cefoxitin</td>
<td>2g q8h</td>
</tr>
<tr>
<td>Cefotetan</td>
<td>2g q12</td>
</tr>
<tr>
<td>Pipercillin-tazobactam</td>
<td>3.375g q6h</td>
</tr>
</tbody>
</table>

Hopkins. Cochrane Database Syst Rev 2002
CEPHALOSPORINS VS AMINOPENICILLINS

• First generation Cephalosporins vs Aminopenicillins
  – 7 studies; 1487 women

  – No significant difference in maternal endometritis
    • (RR = 1.09, CI 0.69 – 1.71)

Gyte. Cochrane Database of Syst Review 2014
# UREAPLASMA COVERAGE IN TRIPLE-I

## TABLE 1 Incidence of *Ureaplasma* infection, polymicrobial infections, and chorioamnionitis in women delivering preterm, late preterm, or at term

<table>
<thead>
<tr>
<th>Author(s) of reference (yr)</th>
<th>Reference no.</th>
<th>GA (wk)</th>
<th>Specimen type</th>
<th>n</th>
<th>Ureaplasma infection</th>
<th>Polymicrobial infection</th>
<th>Ureaplasma spp.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Viscardi et al. (2008)</td>
<td>222</td>
<td>&lt;33</td>
<td>S/CSF</td>
<td>313</td>
<td>74/313 (23.6)</td>
<td>—&lt;sup&gt;a&lt;/sup&gt;</td>
<td>30/46 (65.0)</td>
</tr>
<tr>
<td>Hassanein et al. (2012)</td>
<td>310</td>
<td>&lt;35</td>
<td>CB</td>
<td>30</td>
<td>13/30 (43.3)</td>
<td>No polymicrobial infections</td>
<td>16/46 (35.0)</td>
</tr>
<tr>
<td>Gray et al. (1992)</td>
<td>311</td>
<td>&lt;28</td>
<td>AF</td>
<td>2,461</td>
<td>8/2,461 (0.4)</td>
<td>—&lt;sup&gt;b&lt;/sup&gt;</td>
<td>7/13 (53.8)</td>
</tr>
<tr>
<td>Yoon et al. (1998)</td>
<td>60</td>
<td>≤36</td>
<td>AF</td>
<td>120</td>
<td>25/120 (20.8)</td>
<td>11/120 (9.0)</td>
<td>0/8 (0.0)</td>
</tr>
<tr>
<td>Yoon et al. (2003)</td>
<td>312</td>
<td>≤35</td>
<td>AF</td>
<td>252</td>
<td>23/252 (9.1)</td>
<td>—&lt;sup&gt;c&lt;/sup&gt;</td>
<td>5/25 (20.0)</td>
</tr>
<tr>
<td>Park et al. (2013)</td>
<td>136</td>
<td>&lt;34</td>
<td>AF</td>
<td>56</td>
<td>35/56 (62.5)</td>
<td>7/56 (12.5)</td>
<td>26/47 (55.31)&lt;sup&gt;f&lt;/sup&gt;</td>
</tr>
<tr>
<td>Kacerovsky et al. (2014)</td>
<td>16</td>
<td>24–36</td>
<td>AF</td>
<td>124</td>
<td>26/124 (21.0)</td>
<td>5/124 (4.0)&lt;sup&gt;d&lt;/sup&gt;</td>
<td>3/6 (50.0)</td>
</tr>
<tr>
<td>Romero et al. (2015)</td>
<td>313</td>
<td>≤35</td>
<td>AF</td>
<td>59</td>
<td>6/24 (25.0)</td>
<td>10/24 (41.7)</td>
<td>2/6 (33.3)&lt;sup&gt;f&lt;/sup&gt;</td>
</tr>
<tr>
<td>Stepan et al. (2016)</td>
<td>314</td>
<td>24–34</td>
<td>AF</td>
<td>122</td>
<td>33/122 (27.0)</td>
<td>8/122 (6.6)</td>
<td>29/33 (87.9)</td>
</tr>
<tr>
<td>Musilova et al. (2015)</td>
<td>315</td>
<td>24–36</td>
<td>AF</td>
<td>166</td>
<td>40/166 (24.1)</td>
<td>19/166 (11.4)</td>
<td>4/33 (12.1)</td>
</tr>
<tr>
<td>Stepan et al. (2016)</td>
<td>316</td>
<td>24–36</td>
<td>AF</td>
<td>386</td>
<td>103/386 (26.7)</td>
<td>32/386 (8.3)</td>
<td>16/103 (15.5)&lt;sup&gt;f&lt;/sup&gt;</td>
</tr>
<tr>
<td>Berger et al. (2009)</td>
<td>317</td>
<td>≤33</td>
<td>AF/PL</td>
<td>114</td>
<td>32/114 (28.1)</td>
<td>—&lt;sup&gt;a&lt;/sup&gt;</td>
<td>11/25 (44.0)&lt;sup&gt;f&lt;/sup&gt;</td>
</tr>
<tr>
<td>Hillier et al. (1988)</td>
<td>1</td>
<td>&lt;37</td>
<td>PL</td>
<td>112</td>
<td>32/112 (28.6)</td>
<td>—&lt;sup&gt;c&lt;/sup&gt;</td>
<td>17/29 (58.6)&lt;sup&gt;f&lt;/sup&gt;</td>
</tr>
<tr>
<td>Stein et al. (1994)</td>
<td>318</td>
<td>Any GA</td>
<td>PL</td>
<td>182</td>
<td>21/182 (11.5)</td>
<td>—&lt;sup&gt;e&lt;/sup&gt;</td>
<td>11/16&lt;sup&gt;f&lt;/sup&gt;</td>
</tr>
<tr>
<td>Van Marter et al. (2002)</td>
<td>319</td>
<td>&lt;36</td>
<td>PL</td>
<td>206</td>
<td>58/155 (37.4)</td>
<td>—&lt;sup&gt;e&lt;/sup&gt;</td>
<td>51/77 (66.2)</td>
</tr>
<tr>
<td>Miralles et al. (2003)</td>
<td>320</td>
<td>&lt;33</td>
<td>PL</td>
<td>14</td>
<td>5/14 (35.7)</td>
<td>4/5 (80.0)</td>
<td>7/78 (9.0)</td>
</tr>
<tr>
<td>Egawa et al. (2007)</td>
<td>135</td>
<td>&lt;32</td>
<td>PL</td>
<td>83</td>
<td>4/83 (4.8)</td>
<td>5/83 (6.0)&lt;sup&gt;b&lt;/sup&gt;</td>
<td>1/5 (20.0)</td>
</tr>
<tr>
<td>Olomu et al. (2009)</td>
<td>321</td>
<td>≤28</td>
<td>PL</td>
<td>866</td>
<td>52/866 (6.0)</td>
<td>21/52 (40.4)</td>
<td>4/4 (100.0)</td>
</tr>
<tr>
<td>Kasper et al. (2010)</td>
<td>202</td>
<td>&lt;34</td>
<td>AF</td>
<td>118</td>
<td>32/118 (27.1)</td>
<td>—&lt;sup&gt;a&lt;/sup&gt;</td>
<td>0/2 (0.0)</td>
</tr>
<tr>
<td>Namba et al. (2010)</td>
<td>134</td>
<td>≤32</td>
<td>PL</td>
<td>151</td>
<td>63/151 (41.7)</td>
<td>13/151 (8.6)</td>
<td>9/24 (37.5)</td>
</tr>
<tr>
<td>Roberts et al. (2012)</td>
<td>4</td>
<td>&gt;37</td>
<td>PL</td>
<td>195</td>
<td>2/195 (1.0)</td>
<td>1/195 (0.5)</td>
<td>4/33 (12.1)</td>
</tr>
<tr>
<td>Gundrus et al. (1984)</td>
<td>322</td>
<td>Various</td>
<td>PL</td>
<td>801</td>
<td>156/801 (19.5)</td>
<td>18/801 (2.2)&lt;sup&gt;b&lt;/sup&gt;</td>
<td>21/53 (39.6)</td>
</tr>
<tr>
<td>Sweeney et al. (2016)</td>
<td>62</td>
<td>&gt;32</td>
<td>PL</td>
<td>535</td>
<td>42/535 (7.9)</td>
<td>4/57 (7.0)</td>
<td>12/38 (31.6)</td>
</tr>
<tr>
<td>Cox et al. (2016)</td>
<td>133</td>
<td>&lt;37</td>
<td>PL</td>
<td>57</td>
<td>13/57 (22.8)</td>
<td>—&lt;sup&gt;e&lt;/sup&gt;</td>
<td>9/24 (37.5)</td>
</tr>
</tbody>
</table>

MACROLIDE THERAPY AT TIME OF CESAREAN

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Adjunctive Azithromycin Prophylaxis for Cesarean Delivery

Alan T.N. Tita, M.D., Ph.D., Jeff M. Szychowski, Ph.D., Kim Boggess, M.D.,
George Saade, M.D., Sherri Longo, M.D., Erin Clark, M.D., Sean Esplin, M.D.,
Kirsten Cleary, M.D., Ron Wapner, M.D., Kellett Letson, M.D., Michelle Owens, M.D.,
Adi Abramovici, M.D., Namasivayam Ambalavanan, M.D., Gary Cutter, Ph.D.,
and William Andrews, M.D., Ph.D., for the C/SOAP Trial Consortium*
Antibiotic prophylaxis in the setting of manual placental removal
## UNIVERSITY OF UTAH – MANUAL PLACENTAL REMOVAL

<table>
<thead>
<tr>
<th>Year</th>
<th>Manual removal of placenta</th>
<th>Cefazolin given</th>
</tr>
</thead>
<tbody>
<tr>
<td>2015</td>
<td>472</td>
<td>418 (89%)</td>
</tr>
<tr>
<td>2016</td>
<td>448</td>
<td>412 (92%)</td>
</tr>
<tr>
<td>2017</td>
<td>334</td>
<td>238 (71%)</td>
</tr>
</tbody>
</table>
ANTIBIOTICS AT TIME OF PLACENTAL REMOVAL

• NO RCTs to evaluate effectiveness of antibiotic prophylaxis to prevent endometritis after manual removal of placenta

Chongsomchai. Cochrane Database of Syst Reviews 2014
Observational studies: systematic review

- Three eligible cohort studies (n=567)

- **Primary outcome:** puerpural fever or endometritis

- **Results:** no difference
  - (OR = 0.84, 95% CI 0.38 to 1.85)

- **Limitations:**
  - small number of low quality non-randomized studies

Chibueze et al. BMC Pregnancy Childbirth 2015
Obstetric anal sphincter injuries (OASIS)
OASIS

• Anal sphincter injuries: up to 24% of obstetric vaginal lacerations

• Wound breakdown: 0.1–5% of obstetric vaginal lacerations

Williams. Obstet Gynecol 2006
OBSTETRIC LACERATION PROPHYLAXIS - RCT

• **Intervention:** single dose of 2\textsuperscript{nd} or 3\textsuperscript{rd} generation cephalosporin at time of repair

• **Primary outcome:** evidence of a perineal wound complication at the 2-week postpartum visit

Duggal et al. Obstet Gynecol 2008
PERINEAL WOUND COMPLICATIONS

Duggal et al. Obstet Gynecol 2008

Perineal wound complication rates (%)

- Wound disruption: 8.2% (Antibiotic), 20.7% (Placebo)
- Purulent discharge: 4.1% (Antibiotic), 7.2% (Placebo)
- Wound complication: 8.2% (Antibiotic), 24.1% (Placebo)

Duggal et al. Obstet Gynecol 2008
In Summary...
CESAREAN PROPHYLAXIS IN OBESITY

• 48 hours of Keflex and Flagyl requires additional studies
CESAREAN IN THE SETTING OF TRIPLE-I

• Add Clindamycin at time of cesarean

• Additional cephalosporin not necessary

• Azithromycin: probably beneficial, excellent research question
MANUAL PLACENTAL REMOVAL

- Antibiotics probably not necessary

- Another great research question!
OASIS

• Complications devastating

• Potential to reduce morbidity outweighs possible side effect of antibiotic administration
QUESTIONS?
REFERENCES

• Centers for Disease Control and Prevention. National Center for Chronic Disease Prevention and Health Promotion, Division of Nutrition, Physical Activity, and Obesity. Data, Trend and Maps [online]. [accessed Apr 10, 2018].
• Gyte GML, Dou L, Vazquez JC. Different classes of antibiotics given to women routinely for preventing infection at caesarean section. Cochrane Database of Systematic Reviews 2014, Issue 11.
• Hopkins L, Smaill F. Antibiotic regimens for management of intraamniotic infection. Cochrane Database Syst Rev. 2002
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