Reconsidering risks of Early Onset Sepsis

Dissecting the literature that informs the CDC Guidelines

Elise C. Brown, MD, MPH
CPMG Internal Medicine & Pediatrics
January 27th, 2012
• I have no financial disclosures
Goals:

• Take a “deep dive” into the literature citations of the CDC guidelines with regard to care of infants whose mothers may have had chorioamnionitis

• Consider alternate strategies for care of these newborns
The Problem:

• the incidence of EO-GBS disease in the infant still remains 0.22-0.4 cases per thousand live births in the United States
Background: 1996

• risk-based screening for GBS & IAP of GBS+ mothers was recommended

• if a mother had a fever, she should receive IAP for prevention of Early Onset GBS in the neonate
next revision: 2002

- distinguished between mother with “chorioamnionitis” vs GBS alone
- “If a woman receives intrapartum antibiotics for treatment of suspected chorioamnionitis, her newborn should have a full diagnostic evaluation and empiric therapy pending culture”
• there became guideline that appeared to many pediatricians to be more precise: if a mother had been diagnosed with chorioamnionitis, the infant should have a workup including labs and administration of broad spectrum antibiotics, pending negative cultures
data to support this:

• retrospective review of 18,299 births over a 12-month period (1995-1996)
• 15.2% had labs ("CBC and/or blood culture")
• mothers did NOT have prenatal GBS cultures; risk-based prophylaxis was used
this means moms got antibiotics for...

- chorio (35%)
- ROM >18 hours (48%)
- fever or clinical s/s of infection (40%)
- preterm labor (22%)
- GBS carrier (known) (6%)
- reason for IAP undetermined (10%)
interestingly...

• 8% of moms with documented chorio did not get any IAP
• 9% of moms with ROM >18 hours did not get any IAP
• 10% of moms with other clinical s/s of infection, including fever, did not get any IAP
• 12% of preterm births did not get any IAP
• 3% of known GBS carriers did not get any IAP
2.2% of the infants met criteria for “proven, probable, or possible bacterial infection”

- 0.8% had a positive culture
- 1.4% had clinical s/s of sepsis/infection
kicker:

- if the mother had not been treated with antibiotics, the presence of maternal chorioamnionitis was demonstrated to be an independent risk factor for neonatal sepsis (AOR of 2.40); if the mother had been treated with intrapartum antibiotics, the diagnosis of chorioamnionitis was no longer significantly associated with neonatal infection
My conclusion:

- if a mother has chorioamnionitis, administration of intravenous antibiotics to the mother is actually a successful means of preventing early onset disease in the infant
Fastforward: 2010

- “Chorioamnionitis is an important risk factor for early-onset GBS disease in women with GBS colonization and can reflect an intrauterine onset of infection in the neonate (45, 63, 210-212).”
Yancey, et al. (1996)

- retrospective investigation of GBS disease in a group of high risk women
- authors were investigating the utility of rapid GBS testing methods at the time of delivery
moms rec’d IAP

• GBS positive (using their rapid assay), PLUS:
  • infant <37 weeks, OR
  • mom had fever
  • history of prior infant with GBS dz
infants

- all “at risk” had CBC, blood culture, +/- LP
- antibiotic administration up to the discretion of the neonatologist
their conclusions:

• infants of mothers with chorioamnionitis have a higher rates of sepsis (culture proven or not) than infants of mothers without chorioamnionitis

• less Fetal Scalp Monitoring should be used
by the way...

- they had 82 mothers with documented chorio. of these deliveries, 6 infants had “proven” sepsis, and 58 (yes, 71%) had “clinical sepsis” -- including hypotension, apnea, NEC, respiratory distress, lethargy, etc. etc.
• description of an outbreak of EO-GBS
• conclusion: they recommended antibiotic prophylaxis for mothers who were GBS+, or mothers w/ fever, who had preterm labor, or PROM. They made no recommendations for the treatment of infants
• literature review regarding risk factors for EO-GBS

• They concluded that infants of moms with chorioamnionitis should have a full workup and get antibiotics for 48 hours pending negative investigation
• conclusion: GBS positive moms should get IAP, and specifically that the antibiotics should be given prior to delivery
• conclusion: for term babies, when moms have chorioamnionitis: giving maternal antibiotics prior to cord-clamping prevented more neonatal disease compared to withholding antibiotics
back to the CDC...

• "Intrapartum fever, one sign of chorioamnionitis in parturient women, has been associated with failure of intrapartum antibiotics to prevent GBS disease in the newborn (68, 213)."

- case-control study of intrapartum antibiotics for the prevention of EO-GBS
- conclusion: antibiotics should be administered to the mother >2 hours prior to delivery for maximum effectiveness
• They advocated for a strategy of early antibiotic administration to a mother with chorioamnionitis, because, “once infection has been established, the preventive effect of chemoprophylaxis is diminished.”
Ascher, et al. (1993) investigated specific cases of neonatal sepsis in which mom had received intrapartum antibiotics, and trying to figure out the etiology of the IAP-failure.
• They identified 96 infants in a 3-year period who had GBS-proven disease.
• 18 of them had actually received antibiotics.
• 16 of those 18 were EO-GBS
• 13 of the 16 mothers who had received antibiotics had been given antibiotics for a diagnosis of chorioamnionitis, and yet the babies went on to become sick.
back to the CDC...

- "Intrapartum treatment of chorioamnionitis can prevent neonatal sepsis (214, 215)."
• OB GYN literature
• conclude that infants do better if a mom has had chorioamnionitis and received antibiotics
back to the CDC...

• "The diagnosis of chorioamnionitis usually is made clinically on the basis of signs and symptoms such as fever (which might be low-grade), uterine tenderness, fetal tachycardia, maternal tachycardia, and foulsmelling or purulent amniotic fluid. In an effort to avert neonatal infections, maternal fever alone in labor may be used as a sign of chorioamnionitis and hence indication for antibiotic treatment, particularly among women with a significant risk factor for chorioamnionitis (e.g., prolonged labor or prolonged rupture of membranes)."
Because an association has been observed between epidural labor analgesia and fever, chorioamnionitis might be overdiagnosed in women with epidurals, which could lead to unnecessary diagnostic evaluations and unnecessary exposure to empirical antibiotics in neonates (216).

- describes the association of maternal temps and epidural use, so points out that not all maternal fevers are infectious.
back to the CDC...

• "However, multistate surveillance data suggest that although epidural use is common (in 67% of births), intrapartum temperature of >=100.4°F [>=38.0°C] (3.3% of births) and physician diagnoses of chorioamnionitis (3.1% of births) remain relatively rare (102) (CDC, unpublished data, 2009)."
102: VanDyke, et al. (2009)

- NEJM article about implementation of universal screening guidelines & adherence to GBS prophylaxis; it does not discuss maternal fever or chorioamnionitis.
CDC concludes:

• “Consultation with obstetric providers to determine whether chorioamnionitis is suspected is important for guiding neonatal management.”
CPMG & Exempla experience

• since 2002 (when we were no longer in compliance with the CDC guidelines) through September, 2011: 60,721 live births
• We have never routinely given antibiotics to all infants whose mothers have been diagnosed with chorioamnionitis
• during that time, we routinely cultured (and got CBCs) from all babies of febrile mothers -- whether they had a diagnosis of chorioamnionitis or not
excluding immediately symptomatic infants:

- We’ve had 62 “positive” cultures -- 37 of which (59%) were coag neg staph

- Of the other 25 “positive” cultures -- 10 of which were probably real (also excluding things like corynebacterium, micrococcus and strep salivarius)
“real positive” cultures

- 6 Group B Strep
- 2 E. coli
- 1 Staph aureus
- 1 acinetobacter (which turned out to be contaminant!)
• this is a “real” positive rate of 0.165 per thousand live births overall, and
• 0.098 per thousand lives births for GBS
• no deaths clinically?
• of the 6 GBS+ cultures
  • one was symptomatic at birth, one symptomatic at 8 hrs of life, and the other 4 were asymptomatic
  • 3 moms were GBS negative, one mom had a Tm=100.7 but no chorio
  • 3 moms known GBS positive. 2 didn’t get prophylaxis due to precipitous deliveries, but had no fever/chorio, the other didn’t have precipitous delivery documented, but also had no
of the 4 non-GBS+

- 2 E. coli: one mom had fever/chorio, the other was GBS positive but no fever/chorio; both f/u cultures NEGATIVE

- one S. aureus: mom did not have fever/chorio; she was GBS positive; f/u culture NEGATIVE

- one Acinetobacter: was ultimately determined to be contaminant (f/u culture neg)