Deconstruction Junction: How to Separate the Good Evidence From the Bad (From the Ugly)

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ABSTRACT

In this column, the author reprises recent selections from the Lamaze International research blog, *Science & Sensibility*. Each selection discusses a new study that demonstrates the need to look closely at research articles to avoid being misled. Examples include new research on the effectiveness of intrapartum antibiotics for preventing early onset Group B streptococcal disease in newborns, a recent study on the incidence of infection after cesarean surgery and vaginal birth, and a new study demonstrating long-term benefits of skin-to-skin contact between the mother and infant after birth.

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When I began reviewing research for Lamaze International, as the author of the quarterly newsletter, *Research Summaries for Normal Birth*, I believed, somewhat naively, that if we could just get the word out about the evidence for natural birth, we would begin to see the gap between evidence and practice narrow. For four years, I scoured the literature for new studies and summarized them for *Research Summaries* subscribers. The more time I spent looking at peer-reviewed research articles, however, the more clear it became that studies are often flawed, limited, or even biased. More troubling than that: Major shifts in policy and practice often resulted from flawed research. Simply summing up and reporting on new studies would not give readers the skills to communicate effectively about research,

promote healthy birth practices, and combat the use of harmful and ineffective practices.

Advocating for evidence-based practice unfortunately involves far more than just knowing what new studies have been published. We must know how to make sense of a new study—to look closely and determine for ourselves if the methods and assumptions are valid, the results reliable, and the conclusions applicable. Lamaze International's new research blog, *Science & Sensibility*, is intended to help childbirth educators and other birth professionals gain the skills necessary to deconstruct the evidence. For this column, I have chosen three recent *Science & Sensibility* posts that demonstrate different shortcomings in the research that make our job more complicated—but not impossible.

Lamaze International's new research blog, *Science & Sensibility*, is intended to help childbirth educators and other birth professionals gain the skills necessary to deconstruct the evidence related to current birth practices. Visit the *Science & Sensibility* Web site (www.scienceandsensibility.org) to stay up to date and comment on the latest evidence that supports natural, safe, and healthy birth practices.

Amy Romano, host of the Science & Sensibility research blog, invites readers to respond to the posts reprinted in this article. Log on to the URLs presented in the corresponding footnote for each section's main heading.

By deconstructing a new Cochrane systematic review, we see how bias and flaws in individual trials can undermine the rigorous process of systematic review and produce unreliable results. By deconstructing two studies on the association between cesarean surgery and postpartum infection, we see how the populations studied and the methods of measuring outcomes can obscure the true consequences of cesarean surgery. Finally, in deconstructing several studies of newborn transitional care, we discover that many elements of the care environment can counteract the benefits of skin-to-skin contact, making it difficult to observe the benefits of keeping mothers and babies together after birth.

Lamaze members have free access to the Cochrane Library, including the full text of systematic reviews. Log on as a member at the Lamaze Web site (www.lamaze.org) to access this member benefit.

THE NEW GROUP B STREPTOCOCCAL COCHRANE REVIEW: A HOT MESS!¹

Advocates for evidence-based care feel our ears perk up when we hear about a new Cochrane systematic review. Cochrane Review = Evidence! Right? Indeed, systematic reviews are near the top of the “evidence pyramid,” and Cochrane systematic reviews are the gold standard for their rigor and transparency. A Cochrane review can even conclusively settle important clinical controversies. But sometimes Cochrane reviews leave us with more questions than answers.

The Cochrane Library recently released a systematic review evaluating the effectiveness of intrapartum antibiotics for known maternal Group B streptococcal (GBS) colonization (Ohlsson & Shah, 2009). And it's a hot mess.

The four included trials that compared intravenous antibiotics with no treatment in labor collectively had only 500 participants, which we automatically know is far too small to find statistically significant differences in a condition that affects 1 in 2,000 newborns, and results in death or long-term complications even less frequently. But small sample sizes were the least of the problems here. The reviewers noted several other problems with the trials:

- In one study, researchers tracked their findings and halted the trial as soon as a significant difference was found (favoring treatment with antibiotics). This is a blatant form of bias—it is like flipping a penny until you got heads 5% more often than you got tails. If you keep flipping long enough (or stop flipping soon enough) you'll be able to find that 5% difference simply by chance.

- In the same study, researchers changed to a different statistical test that allowed them to achieve statistical significance with their data, when the originally planned (and more appropriate) test would have produced a nonsignificant finding.
- None of the studies used placebos, so women, care providers, and hospital staff knew which women received antibiotics and which did not. This may have altered treatment of the women or the babies, possibly in ways that would make no antibiotics appear safer (for instance, avoiding or delaying membrane rupture in a woman who is GBS positive but not getting antibiotics).
- One study excluded women who developed fevers in labor. GBS colonization can cause maternal fever and newborn sepsis, so excluding these cases makes no sense.
- Some women included in the studies were likely GBS negative because methods used to determine GBS status were inadequate.
- Outcomes were poorly defined.
- Data on a substantial proportion of women and babies were missing.
- Groups were mysteriously differently sized.
- Need I go on?

The Cochrane reviewers, in my opinion, did a respectable job with what they had, but what they had was garbage and, as the saying goes, “Garbage in, garbage out.” You can't make reliable conclusions out of a bunch of bad research, even if you're a Cochrane reviewer.

So what were the findings? Three trials, which were around 20 years old, compared ampicillin or penicillin to no treatment and found no clear differences in newborn deaths, although the occurrence of early GBS infection in the newborn was reduced with antibiotics.

More, better research is needed, but the Cochrane reviewers are not optimistic:

Ideally the effectiveness of intrapartum antibiotics to GBS colonized women to reduce neonatal GBS infections should be studied in adequately sized double blind controlled trials. The opportunities to conduct such trials have likely been lost as practice guidelines have been introduced in many jurisdictions. (Ohlsson & Shah, 2009, p. 11)

In the meantime, women should be aware that other evidence, albeit not from randomized controlled trials, suggests that antibiotic treatment reduces deaths from early onset GBS disease in

¹Posted July 30, 2009, at <http://www.scienceandsensibility.org/?p=358>

newborns. According to the Centers for Disease Control and Prevention, a steady decline in GBS disease has been seen in individual institutions, in the whole U.S. population, and in other countries as antibiotic use has risen. But these population-level data cannot tell us whether antibiotics or some other factor caused the decline.

What other advice can we share with women?

1. Be aware that antibiotics are not harmless. Severe allergic reactions are possible, and antibiotic use in labor can result in thrush (candida infection), which causes painful breastfeeding and sometimes early weaning. We do not know about other possible harmful effects because they have never been studied adequately or at all.
2. No study confirms the effect of labor practices on GBS infection in newborns, but here we can use our common sense. Care providers should avoid or minimize sweeping/stripping membranes before labor, breaking the bag of waters, vaginal exams, and other internal procedures, especially those that break the baby's skin and can be a route for infection. These include internal fetal scalp electrodes for fetal heart rate monitoring and fetal blood sampling.
3. Keep mothers and babies skin-to-skin after birth. This exposes the baby to beneficial bacteria on the mother's skin, facilitates early breastfeeding, and lowers the likelihood that the baby will exhibit signs or symptoms that mimic infection, such as low temperature or low blood sugar, which could cause the need for blood tests or spinal taps to rule out infection.

NO DIFFERENCE? THE CASE OF CESAREAN SURGERY AND POSTPARTUM INFECTION²

When a study compares one practice with another and reports "no difference" in outcomes, is that the end of the story? Not necessarily. "No significant difference" can mean any of these:

- There really is no difference.
- The study was too small to find the difference *that really is there* (it lacked "statistical power").
- The outcome was measured or reported in a way that obscured a difference *that really is there*.
- The statistical test yielded a "false negative result," failing to find a difference *that really is there* (this

How do we know when "no difference" means "no difference" and when "no difference" means "keep looking"?

type of error occurs in up to 1 out of 20 statistical results).

So in 3 out of our 4 possibilities, the difference really is there, we just can't see it. How do we know when "no difference" means "no difference" and when "no difference" means "keep looking"? To understand this problem, and how to best get around it, let's have a look at postpartum maternal morbidity after cesarean surgery versus vaginal birth.

Perhaps you've heard that there's "no difference" in health outcomes between cesarean surgery and vaginal birth. This is what women have been told ever since a so-called "State-of-the-Science Conference" report was issued by the National Institutes of Health (NIH) in 2006 (Visco et al., 2006). After evaluating the body of literature comparing planned vaginal birth and planned cesarean surgery in healthy women, the NIH reported, among other findings, that the evidence that infection is more likely with planned cesarean is "weak." The report said that, although observational studies find a link between cesarean and infection, the only randomized controlled trial of planned cesarean versus planned vaginal birth showed "no significant difference" in infection rates.

In contrast, a new population-based study from Denmark, involving over 32,000 women giving birth between 2001 and 2005, reported that women who gave birth by cesarean were nearly 5 times more likely than women who gave birth vaginally to experience a wound infection, urinary tract infection, or blood stream infection (Leth, Møller, Thomsen, Uldbjerg, & Nørgaard, 2009). Most of the difference was attributed to wound infection, which occurred in 5.6% of women having unscheduled cesareans in labor, 3.9% of women having scheduled cesareans, and only 0.08% of women giving birth vaginally. In the United States, where up to 500,000 cesareans may be safely preventable each year, these data suggest that more than 20,000 postpartum wound infections could be avoided annually, along with the excess cesareans.

So what is the disconnect between the "state of the science," which tells us evidence is "weak," and this new study, which paints a very different picture?

First, the NIH conference, and the Agency for Healthcare and Research Quality (AHRQ)-sponsored systematic review underpinning the

²Posted August 7, 2009, at <http://www.scienceandsensibility.org/?p=405>

Read about the evidence for the six healthy birth practices at the Lamaze Web site (www.lamaze.org).

conference, compared *planned* routes of delivery, while the Danish study compared *actual* routes of delivery. The reviewers acknowledge that studies comparing planned vaginal birth and planned elective cesarean surgery in women with no pregnancy complications are scarce, and randomized controlled trials are absent. Rather than conduct a systematic review without any randomized controlled trials, the reviewers included the Term Breech Trial (Hannah et al., 2000), even though the results of the review would affect recommendations made to women carrying head-down babies. But the Term Breech Trial's results are not applicable to women carrying head-down babies, especially when infection is the outcome of interest. Why? Because 57% of women randomized to give birth vaginally actually had cesareans, and most of these presumably underwent the cesareans in labor, which increases infection risk (along with risks of hemorrhage and other complications). What's more, breech vaginal births are much more likely than vertex vaginal births to involve episiotomies, instrumental delivery, or both, which increase the likelihood of infection. So in the Term Breech Trial, the vaginal birth group included far more women with cesareans, episiotomies, and instrumental deliveries than we would expect to see in a similar group of women planning vaginal birth of head-down babies. Despite these limitations that make the trial useless for evaluating the true risks of infection associated with each birth route, the AHRQ reviewers rated the Term Breech Trial as the *highest quality evidence* comparing planned vaginal with planned cesarean birth, trumping observational studies. In the process, the message to women—and clinicians for that matter—transformed from, “Planning a cesarean is risky because you expose yourself to excess infection risk” to something more like, “There could be an excess risk of infection with cesarean, but it's probably small and, hey, for all we know there may be no real difference after all.”

Another reason behind the disconnect is that the Term Breech Trial (again, the “highest quality” evidence in the AHRQ review underpinning the NIH conference) only measured infections occurring *prior to hospital discharge*, a very common cutoff in both randomized controlled trials and in observational studies. The new Danish study provides striking evidence that this way of measuring infection is grossly inadequate—more than three quarters (77%) of infections occurred after hospital discharge (Leth et al., 2009). In other words, they

would have been missed if the researchers had stopped counting the number of infections as soon as the woman left the hospital. The researchers were able to capture these infections because Denmark has a national database of all births, which is linked to a national database of all clinical laboratory results of infectious diseases, a national database of all antibiotics prescribed, and a national database of all hospital readmissions. (The United States, by the way, has none of these, rendering this type of study literally impossible to conduct here.) In randomized controlled trials, following participants beyond the initial hospital stay is logistically difficult and very costly. Even when follow-up is intended, substantial numbers of new mothers may not respond to surveys or return (to the same provider/facility or at all) for postpartum care. As a result, properly constructed national databases provide an important source—sometimes the only source—of evidence on long-term outcomes.

So which “evidence” do we tell women? The “state of the science” or our less rigid but almost certainly more reliable assessment of the observational studies and our common sense? Of course cesarean can lead to infection—it's surgery after all. And yes, even with optimal care, some women who plan vaginal births will need to have cesareans, and some of those women will get infections. If we're serious about helping women avoid serious complications like infections, we must

- tell women who intend to give birth vaginally how they can safely achieve that, starting with the six Lamaze Healthy Birth Practices; and
- help women having vaginal births avoid practices that increase the risk of perineal trauma and, thus, the risk of perineal infection, such as episiotomy, instrumental delivery, and fundal pressure.

Women experience many physical and mental health problems in the postpartum period, some of which may be safely prevented with a different approach to care given in pregnancy, labor, and birth, or better education provided prenatally. We do not know the factors contributing to postpartum health problems because they are shamefully understudied. But one treasure trove of postpartum data in the United States provides a powerful foundation for addressing and researching postpartum health outcomes. Childbirth Connection's 2008 report, *New Mothers Speak Out* (Declercq, Sakala, Corry, & Applebaum, 2008), compiles the postpartum data and new mother testimonials from both the 2006

Listening to Mothers II survey and a follow-up survey conducted with participants 6 months later. All women's health professionals and advocates should spend time with this report so we can begin to give postpartum concerns their due attention.

ACTIVE MANAGEMENT OF NEWBORN TRANSITION: AN INVISIBLE AND UNTESTED PACKAGE OF CARE³

There's a new study out in the current issue of *Birth* (Bystrova et al., 2009) that bolsters the already remarkable body of evidence favoring skin-to-skin care (rather than placing the baby on a warmer or swaddling) right after birth. Russian researchers exposed mothers and their babies to some skin-to-skin time in the first 2 hours, and compared their behavior 12 months later to other women and their children who had been clothed or swaddled and held.

At 1 year, children who had been clothed or swaddled or who hadn't nursed in the first hour were more likely to exhibit symptoms of dysregulation (irritable, emotionally labile, aggressive, impulsive, or unable to self-regulate). In addition, when researchers observed them at play and performing a structured task, the mothers in this group were more likely to have a flat/constricted affect, lack enthusiasm, or simply seem out of sync with their infants.

Those of us who advocate for skin-to-skin contact after birth cite studies like this one when we say that letting mothers and babies interact the way nature intended is healthy and safe, and disrupting the normal transition should be done only when absolutely crucial and with dignity and efficiency. But it turns out that in the majority of studies that evaluate early skin-to-skin contact, the mothers and babies are separated and manipulated—sometimes for an extended period of time—before the “dose” of skin-to-skin time occurs. Consider this description of the “compulsory” routines to which all mothers and infants in the trial (even those in the skin-to-skin group) were subjected:

According to the Russian tradition at the time of the study, all mothers were lying on their backs during the first 2 hours after birth, and all mothers received intravenous administration of methylergometrine in connection with birth of the babies' head. The umbilical cord was clamped 10 to 15 seconds after birth, and all babies were immediately

put on an examination table with a radiant heater above. The infants were carefully dried, wrapped in a dry sheet, and left on the examination table while the attending midwife took care of the mother. The infants were then washed under warm (skin-temperature) tap water, dried, and cared for by a midwife according to hospital routines, including weighing, taking anthropometric measurements, and dripping 30 percent sulfacyl natrium into the babies' conjunctivas for prophylaxis of gonococcal ophthalmia. To prevent cord infection, Xeroform powder or 1 percent iodine solution was applied to the umbilical cord stump and on the baby's skin folds. Before the infants were brought to the maternity ward, a pediatrician examined them. Provided no bleeding was present, the suturing of vaginal ruptures, episiotomies, or both was postponed until 2 hours after delivery. (Bystrova et al., 2009, p. 101)

When I first began putting my nose in the medical literature about newborn transitional care, I was astonished to see researchers randomizing women and babies to skin-to-skin care only to bombard them with a battery of procedures and disruptions before initiating that care. That's to say nothing of the fact that once the “dose” of skin-to-skin care was administered, routine care including prolonged separation, swaddling, and who-knows-what-else ensued. Studies commonly cut off or limited the supply of skin-to-skin contact for the remainder of the hospital stay.

Here are just a few of many, many examples of disruptive care in the “skin-to-skin” arm of trials included in the Cochrane Systematic Review of early skin-to-skin contact (SSC), as reported by Moore, Anderson, and Bergman (2007):

- Regarding Bystrova et al. (2003):

All infants were immediately placed under a radiant warmer, dried, washed, weighed, given eye prophylaxis and cord care during the first 20 min postbirth. 1) SSC group = babies were placed prone and SSC on mother's chest for 90 min. (Moore et al., 2007, p. 20)

- Regarding K. Mizuno, N. Mizuno, Shinohara, and Noda (2004):

SSC group = extensive SSC (M = 63.7 min) immediately postbirth with effective suckling. Then mothers and infants were separated for 24 hours and infants were fed formula. After 24 hours rooming-

³Posted July 6, 2009, at <http://www.scienceandsensibility.org/?p=305>

in with. . .breastfeedings [every three hours]. (Moore et al., 2007, p. 24)

- Regarding Moore and Anderson (2007):

SSC group = infant placed prone SSC on mother's abdomen. Baby moved to warmer after cord cut. [The duration of the separation not specified.] Then infant placed prone on mother's bare chest between breasts. Moved to cross cradle nursing position when infant displayed early hunger cues. (Moore et al., 2007, p. 24)

Much less (if anything) about the mother's care is described in these studies, but we can assume that such care often if not routinely involved vigorous "massage" of the woman's uterus, injection of artificial oxytocin and intravenous fluids, episiotomy repair, and the use of prewarmed blankets. The studies exclude women having cesarean surgery altogether, so we cannot measure its effects, which are likely to be significant and long-lasting (Swain et al., 2008). And when mothers and infants first come together—regardless of how long they've waited and what has occurred in the interim—they are almost invariably in cold, brightly-lit environments filled with strangers.

So what are the lessons here?

The first lesson is that we cannot judge a study by its abstract. The abstracts of the studies discussed above don't give a hint of the routine practices happening in the background of the "experiment," and they often leave out other important information, too. Sometimes, the full-text papers themselves don't describe routines of care, and we are left guessing. Advocating for increased open access to medical journals will help us judge for ourselves if a study is about what it says it's about, and whether its findings are reliable or applicable.

The second lesson is that we most likely don't know the extent of the harm the current package of newborn care causes because we haven't measured it. When researchers observe "normal" newborn transition and mother-infant bonding behavior in a typical hospital environment, they are in fact observing how babies and mothers adapt to and overcome disruptions that may include early clamping of the umbilical cord, suctioning, and routine separation. However brief and benign these

practices seem, they disrupt the normal adaptation that has been honed throughout evolution to ensure that our species survives. When "active management" of newborn transition is all we ever see, its effects become invisible. And when problems occur, these reinforce the dominant view that birth is intrinsically risky, when in fact these problems may arise from practices imposed on healthy women and babies right after birth—or, for that matter, in labor.

The final lesson relates to the second. Studies that measure the elements of physiologic care very often occur in contexts that are decidedly not physiologic. This context can drown out the effects of small changes we make in one element of care. Thinking back to the current study of skin-to-skin contact, if we *hadn't seen* any difference in that trial, would it have been because early maternal-infant contact doesn't "work" to produce the desired outcome? Maybe. Or maybe it would have been because the harms of "compulsory" practices dictated by tradition overwhelmed and obscured the beneficial effects of skin-to-skin care. Put another way, if we see such remarkable benefits of skin-to-skin contact in the studies we have (however flawed), just imagine what benefits we might see if the contact truly was immediate, prolonged, and undisturbed.

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