

When Two Major Health Initiatives Collide: Preventing Pregnancy and Protecting Milk Supply in NICU Mothers

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California Dreamin': Communities Moving Beyond the Horizon
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Ifeyinwa Asiodu, PhD, RN, IBCLC* and Beverly Rossman, PhD, RN**

*UCSF School of Nursing, San Francisco, CA

**Rush University Medical Center College Of Nursing, Chicago, IL

Benefits of Human Milk for Very Low Birth Weight Infants

- Reduces risk of prematurity associated complications
 - Necrotizing enterocolitis (NEC)
 - Chronic lung disease (CLD)
 - Late onset sepsis (sepsis)
 - Rehospitalization
 - Neurodevelopmental problems (infancy, childhood)
- Reduces associated costs for families, health care, educational systems, and society at large

Background & Significance Hormonal Birth Control

- Active ingredient = synthetic form of progesterone.
- Decrease in progesterone is necessary to make milk.
- Mothers of premature infants experience a less coordinated transition to making milk.
- Hormonal birth control given too early may interfere with breastfeeding or milk production.

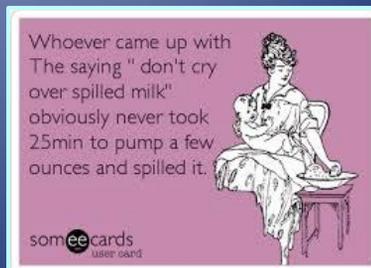
Early HM Supply & Coming to Volume

- Prenatal colostrum production (lactogenesis I) transitions to copious milk production during lactogenesis II
 - Typically within 72 hours after delivery, **independent of breastfeeding**
 - Delayed lactogenesis II in term mothers associated with lower rates of continued exclusive and overall HM provision
- Coming to volume (CTV): critical window between initiation and maintenance of lactation during which breastfeeding mothers establish a threshold HM volume
 - ~500mLs/day within 5 days of delivery
 - Regulated by the healthy **breastfeeding** infant's sucking and milk removal stimuli

Neville 2001; Chapman,D.J. 1999; Brownell,E. 2012; Neville 1988 Parker, L.A. 2012

Premature Delivery and Lactation

- Premature delivery may delay lactogenesis
 - Direct physiologic factors
 - Relative immaturity of pregnancy-induced breast development
 - Lack of early direct breastfeeding/infant-led lactation stimulation
 - Breast pump dependent for weeks to months
 - Obesity and hypertension
 - Cesarean section
- Sociodemographic factors
 - SES



Parker, L.A. 2012; Hill,P.D. 2001; Hill,P.D. 2005; Henderson 2008
 Russo 2004 Nommsen-Rivers,L.A. 2012; Nommsen-Rivers 2010;
 Chapman,D.J. 1999; Dewey,K.G. 2003; Turcksin 2012 Brownell,E. 2012

Coming To Volume in Mothers who Deliver Early

- Early pumped HM volumes appear to influence the probability of long term HM provision in preterm infants
 - In mothers of preterm infants, Hill et al found pumped HM output on day 6-7 of life predicted HM supply at 6 weeks of age
 - Wilson et al: higher volumes at day 7 associated with higher rates of exclusive HM feedings at 36 weeks corrected GA

Parker, L.A. 2012; Hill,P.D. 2005 Wilson 2015



Coming to Volume Study

- Analyzed daily pumping records of >200 mothers of VLBW infants
 - Most women of color and low SES
- Only 22% and 39% of mothers CTV (350-500 mL/day) in weeks 1 and 2, respectively
- CTV predicted any HM feeding at discharge
 - 76% if successful CTV week 2 vs. 36% if unsuccessful, $p < 0.01$

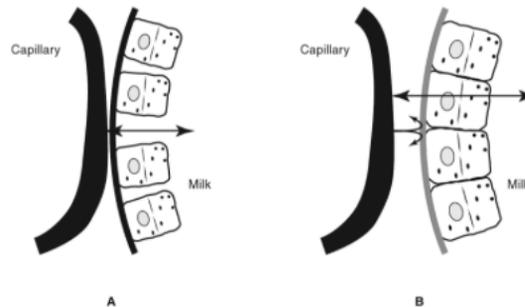
Hoban et al. ISRHML poster 2016

New Directions

- Need to study what happens before CTV: initiation of lactation
 - Lactogenesis II: "milk coming in"
 - Triggered by rapid decline in progesterone following delivery of the placenta
 - Once progesterone-inhibition of prolactin is removed, prolactin catalyzes closure of tight junctions (TJ) in the mammary epithelium

TJ closure prevents lactose from exiting the gland via open paracellular pathways

Figure 3-8 (A) FIRST 4 DAYS POSTPARTUM. GAPS BETWEEN ALVEOLAR CELLS BEFORE LACTOGENESIS. (B) AFTER 14 DAYS POSTPARTUM. INTRACELLULAR GAPS CLOSE TIGHTLY TO ONE ANOTHER FOLLOWING LACTOGENESIS.



Source: Used with permission from Hale TW. Medications and mother's milk. 9th ed. Amarillo, TX: Pharmasoftware; 2000:6.

Failure of closure = interrupted HM synthesis at a critical lactation stage
Difficult or impossible to remedy after the fact!

Carraway K et al. Glycoprotein contributions to mammary gland and mammary tumor structure and function: Roles of adherens junctions, ErbBs and membrane MUCs. J Cellular Biochem 2005

Risk in Premature Delivery

- Are mothers who deliver very prematurely more at risk of failure or delay of TJ closure?
 - No studies in literature in mothers of VLBWs
 - One small study of Late Preterm mothers (31-35 weeks) = 82% delayed closure*

*Cregan M.D. et al. Initiation of lactation in women after preterm delivery. Acta Obstet Gynecol Scand. Sept 2002.

Public Health Relevancy



- Early LARC in this population
 - Progesterone-only, long-acting reversible contraceptives (LARC)
 - Prolong the inter-pregnancy interval (IPI)
 - IPI; period between delivery and conception of the next pregnancy
 - <18 months; increases risk for preterm birth and low birth weight infants
 - Reduce risk of repeat preterm birth
 - TJ closure and initiation of lactation is triggered by rapid decline in endogenous progesterone
 - This population:
 - Already at risk of lactation delay or failure
 - Inconclusive data regarding effect on lactation with early LARC

Public Health Relevancy

- In VLBW population, low income mothers significantly less likely to maintain HM provision through to NICU discharge
- Our data suggest these mothers are more often offered LARCs immediately post-birth due to concerns about follow up and risk of short IPI



The American College of
Obstetricians and Gynecologists
WOMEN'S HEALTH CARE PHYSICIANS

COMMITTEE OPINION

Number 670, August 2016

Immediate Postpartum Long-Acting Reversible Contraception

Table 1. Centers for Disease Control and Prevention's 2010 Medical Eligibility Criteria* Classifications for Postpartum Long-Acting Reversible Contraception[†]

Condition	Implant	LNG-IUD	Cu-IUD
Less than 10 minutes after delivery of placenta	–	2	1
10 minutes after delivery of placenta to less than 4 weeks after delivery	1	2	2
More than 4 weeks after delivery	1	1	1
Less than 1 month postpartum [‡]	2	2	1
More than 1 month postpartum [‡]	1	1	1

Abbreviations: LNG=levonorgestrel; Cu=copper; IUD=intrauterine device.

*This section includes guidance based on the 2010 *U.S. Medical Eligibility Criteria for Contraceptive Use* from the Centers for Disease Control and Prevention. Updates to these recommendations are available on the Centers for Disease Control and Prevention web site (<http://www.cdc.gov/reproductivehealth/UnintendedPregnancy/USMEC.htm>).

[†]Categories: 1=A condition for which there is no restriction for the use of the contraceptive method; 2=A condition for which the advantages of using the method generally outweigh the theoretical or proven risks; 3=A condition for which the theoretical or proven risks usually outweigh the advantages of using the method; 4=A condition that represents an unacceptable health risk if the contraceptive method is used.

[‡]Recommendations among breastfeeding women.

Data from the *U.S. Medical Eligibility Criteria for Contraceptive Use*, 2010. CDC. U.S. medical eligibility criteria for contraceptive use, 2010; adapted from the World Health Organization medical eligibility criteria for contraceptive use, 4th edition. *MMWR* 2010;59 (No. RR-4).

ACOG Committee Opinion, October, 2015

Box 2. Best Practices for Long-Acting Reversible Contraception Insertion*

- Provide long-acting reversible contraception (LARC) methods the same day as requested, whenever possible, if pregnancy can reasonably be excluded.
- Offer LARC methods at the time of delivery, abortion, or dilation and curettage for miscarriage. (without regard to breastfeeding status)
- Screen for sexually transmitted infections at the time of intrauterine device (IUD) insertion; if the screening test result is positive, treat the infection without removal of the IUD.
- Offer the copper IUD as the most effective method of emergency contraception.

*For more information, see U.S. selected practice recommendations for contraceptive use, 2013; adapted from the World Health Organization selected practice recommendations for contraceptive use, 2nd edition. Division of Reproductive Health, National Center for Chronic Disease Prevention and Health Promotion, Centers for Disease Control and Prevention. *MMWR* November 19, 2013;62(1-5):1-59.

“Given available evidence, women considering immediate postpartum hormonal LARC **should be counseled about the theoretical risk** of reduced duration of breastfeeding, but that the preponderance of the evidence has not shown a negative effect on actual breastfeeding outcomes.”

Immediate Postpartum Long-Acting Reversible Contraception
ACOG Committee Opinion 670, August 2016

Public Health Relevancy

- No national guidelines about the administration of Depo Provera® and other hormonal contraceptives for NICU mothers
- Thus, early administration of LARC may be a potentially modifiable barrier to the initiation and maintenance of lactation in this disadvantaged population

When Two Major Health Initiatives Collide: Preventing Pregnancy and Protecting Milk Supply in NICU Mothers

Purpose and Methodology

- Determine mothers knowledge about the effect of hormonal contraception on breastfeeding and priorities for breastfeeding and contraception
- Qualitative, descriptive study
 - Twenty-five mothers of very low birth weight infants (<1500 gms)
 - Semi-structured interviews and a contraceptive knowledge survey
 - Within first two weeks after birth
 - Conventional content analysis

Methodology

- Inclusion Criteria:
 - Mothers of a preterm infant (<34 weeks) hospitalized in the RUMC NICU
 - 14 days post-admission
 - 18 years of age and older
 - English Speaking

Participant Demographics

Sample: $n=25$ mothers

- Race/Ethnicity
 - Black - 12
 - White - 5
 - Latina - 7
 - Asian - 1
- Marital Status
 - Married - 13
 - Not Married - 3
 - Not Married, but living with FOB - 9
- Age Range
 - 18-37 years old
 - 26.8 years Median age
- WIC Status
 - Eligible - 10
 - Not Eligible – 13
- Insurance
 - Private - 10
 - Medicaid - 14

Study Results

Results

- Providing milk more important than using contraception
 - Best for baby
 - Majority of mothers viewed providing milk as their job, but a job they were happy to do
- Mothers stated no interest in having sexual intercourse or were not currently having sex
 - “I do not even want to hear the word sex!”



Results

- 100% unaware of possible effect
- Most mothers counseled by Breastfeeding Peer Counselors and Nurses
- Some conflict with resident providers, low-hormonal contraception use
 - 3 Mothers received hormonal birth control immediately after birth (Depo, IUD, POP)

Results

- **Impact of Contraception on Lactation**
 - 12% (3/25) began using contraception immediately after birth
 - Depo Provera - 2 days after birth
 - IUD - Immediately after delivery of placenta
 - Progesterone Only Pills- 2 days after birth
 - Mothers using IUD and POP never came to volume
 - Mother using Depo Provera did not experience an impact to milk supply

Results

- **Interpregnancy Interval**
 - Risk factor for preterm birth
 - 20% (5/25) knew about short IPI
 - 8% (2/25) mothers conducted their own research
 - Breastfeeding Peer Counselors educated mothers about IPI

Contraception

Priorities for Contraceptive Choices

- Convenience of use
- Avoidance of side effects
- Ease of access/No visit to healthcare provider

Where women get their contraceptive information

- *Healthcare provider
- Friends
- Family
- Social media

Who is responsible for use of and choice of contraception?

- Self ($n=22$)
 - "I am. Guys are just 'do whatever'. So if you ain't makin' sure yourself, it's like you just spoke into the air."
- Self and Partner ($n=3$)

Awareness of efficacy of different methods?

- One-third discussed efficacy
 - 5 of those 8 got pregnant using condoms

Contraceptive Discussions

- Mothers asked about contraceptive use prior to discharge from the postpartum unit (1-3 days)
 - Advised to get any type of contraception, specifically Depo Provera® and low-hormonal birth control methods
 - Providers asked if mothers were providing milk
BUT
 - Providers counseled that low-hormonal birth control would not impact milk supply

"She started me on the pill the day after my surgery. I told her I was breastfeeding and was it ok. She said this pill would allow me to produce milk but still be on the pill."

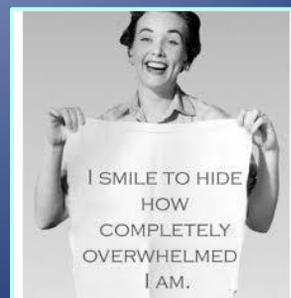
G1 P1 with history of PCOS . Started on POP 2 days after birth

Contraception and Providing Milk

Conversations about postpartum contraception occur during period of emotional vulnerability



Most mothers want time to think before making a decision



What do Informed Mothers Choose?

100% of Mothers



0% of Mothers



Contraceptive Issues

- Desire for more children
 - Partner desires not in line with mother's
- Fertility issues
 - Questionable desire to use contraception
- Long-term options
- Lack of knowledge of Inter Pregnancy Interval (IPI)

Conclusion

- Providing milk was important for mothers
- Future interventions:
 - Communication
 - Timing
 - Informed decisions
 - IPI Education

Lessons Learned

- Institutional Review Board (IRB)
- 2nd Interviews – Not feasible for some mothers
- Loss of mothers
- Follow-up by phone



**When Two Public Health Priorities
Collide: Early Hormonal Contraception
and Lactation Initiation in Mothers of
Very Preterm Infants:
Human Milk Biomarker Study**

Rebecca Hoban, MD, PI

Goal

To determine when LARCs can be safely administered so they do not interfere with the initiation of lactation in the vulnerable population of mothers who delivery very prematurely

Human Milk Biomarker Study

- Virtually nothing known about TJ closure biomarkers in mothers who:
 - Deliver very preterm infants
 - Use a breast pump rather than breastfeed to initiate lactation
- Measure validated biomarkers in HM that accurately measure TJ closure
 - Na, lactose, citrate, and protein

Biomarker Study

- **Aim:** For breast pump dependent mothers of VLBW infants, determine the number of hours post birth that four biomarkers of TJ closure (Na, lactose, citrate and protein) reach established historical norms for healthy mothers of full term, exclusively breastfeeding infants
- **Hypothesis:** Mothers of VLBW infants will experience delay in achieving normal values for all biomarkers, singly and in combination

Biomarker Study

- **Aim:** For breast pump dependent mothers of very preterm infants, determine the relationship between timing of TJ closure and clinical indices of "the milk coming in", including perceptions of breast fullness and measured pumped HM volume
- **Hypothesis:** Biomarkers will be modestly correlated with clinical indices, with pumped HM volume being more predictive than perceptions of breast fullness

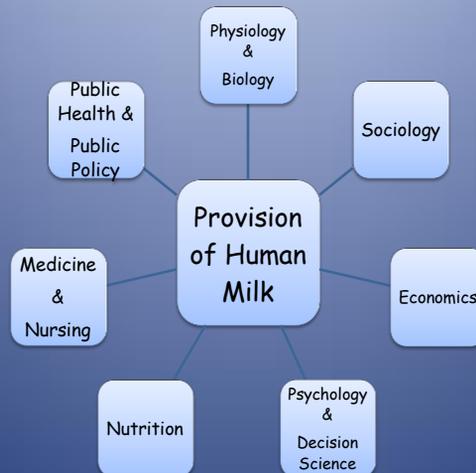
Method

- Mothers of VLBW infants will keep pumping logs x 2 weeks
- Milk samples of 2mL (or less if low volumes) collected q12 hours for first 2 weeks of life and frozen
 - Will label when milk "comes in"

Overall goal of our recent HM research

- Precise determination of when milk will come in based on biomarkers and risk factors
 - Affect timing of when to use donor HM, hormonal contraceptives
- To determine most important risk factors for delayed lactation in VLBW population
 - Modify risk factors as able
 - Targeted intense lactation support to moms w/unmodifiable characteristics
 - When to target
 - What to target

The Human Milk Ecosystem



Questions, Concerns

- Obligations to mothers re: risk/benefit ratio in light of inconclusive data
- Postpartum challenges to informed decision making
- Ensuring equity in counseling
- Helping mothers evaluate priorities and preferences

Steube, Bryant, Lyerly; 2016