Where’s the milk? Delayed lactogenesis II

Kathleen A. Marinelli MD, IBCLC, FABM, FAAP
Chair, United States Breastfeeding Committee
Associate Professor of Pediatrics, Univ. of CT School of Medicine
CT Human Milk Research Center,
Connecticut Children’s Medical Center
Hartford, CT USA

Faculty Disclosure Information

I have nothing to disclose, except that I am a firm believer that human milk is the optimal feeding for all human babies, with very few exceptions.

Kathleen A. Marinelli MD, IBCLC, FABM, FAAP

The participant will be able to:
- clearly understand the physiology of normal lactogenesis
- discuss the pathophysiology leading to delayed lactogenesis
- list at least 3 causes of delayed lactogenesis
- discuss in detail how to clinically manage delayed lactogenesis for both mother and infant
Lactogenesis I, II, and III

- Lactogenesis I – differentiation of alveolar epithelial cells into lactocytes that secrete colostrum, with ~100mL available to infant on day one postpartum
- Lactogenesis II – onset of copious milk secretion occurring between 36 and 96 hours postpartum
- Lactogenesis III – maintenance of milk production

A thought.....

- As we look at the factors required for successful lactogenesis, keep in mind what may in fact go “wrong” resulting in delayed lactogenesis

Hormones of Lactation

- Lactogenesis I
  - ductal growth – estrogen, growth hormone
  - alveolar development – progesterone, prolactin, placental lactogen
  - mammary parenchyma – glucocorticoids
- Lactogenesis II
  - withdrawal of progesterone in the presence of high circulating levels of prolactin
Hormones of Lactation

- Metabolic hormones (coordinate metabolism)
  - Insulin – regulating nutrient fluctuation to the mammary gland by shunting nutrients away from traditional storage depositories, thereby making them more readily available for milk synthesis
  - Thyroid hormones – efficient milk production

Hormones of Lactation

- Lactogenesis III
  - Prolactin - required for milk synthesis to occur
  - Oxytocin – cause milk ejection, produces analgesic effects, reduces stress, causes uterine contractions, establishes caring and bonding behaviors (hormone of love)

Lactogenesis II - Getting the show on the road

- blood flow, oxygen, and glucose uptake increase, and citrate concentration increases sharply
- increased milk citrate and lactose are considered reliable markers for the second stage of lactogenesis
- progesterone receptors are lost in lactating mammary tissues, decreasing the inhibitory effect of circulating progesterone
- maternal secretion of insulin, growth hormone (GH), cortisol, and parathyroid hormone (PTH) facilitates the mobilization of nutrients and minerals required for lactation
Infant suckles at the breast.

Stimulation of nerve endings in mother's nipple/areola sends signal to mother's hypothalamus/pituitary.

Pituitary releases Prolactin (ant. Pit.) and oxytocin (post. Pit)

Hormones travel via bloodstream to mammary gland to stimulate milk production and milk ejection reflex (let-down).

Indicators of Lactogenesis II

- Changes in colostrum/milk composition (biomarkers)
  - Decrease in sodium and chloride
  - Increase in citrate and lactose
- These changes precede the onset of the large increase in milk volume by 24 hours
- Maternal perception of onset of lactation is a valid proxy for lactogenesis II
Maternal indicators of onset of lactation

- Breast swelling
- Milk leakage
- Physical appearance of milk
- Infant cues
- Breast fullness
- Breast heaviness, hardness

- Breast tingling
- Wide range of when this occurs 1-148 hours post birth

Mean Milk Volume of Fully Breastfeeding US Women During the First Week Postpartum

Figure 8. Mean milk volume produced by American women fully breastfeeding their infants during the first week postpartum. (From Neville MJ. Lactogenesis in women. In: Jensen RD, Handbook of Milk Composition. San Diego, Academic Press, 1995, p 88; with permission.)
Definitions

- **Delayed lactogenesis II**
  - longer than usual interval between the colostrum phase and copious milk production, but whereby the mother has the ability to achieve full lactation.
- **Failed lactogenesis II**
  - a condition wherein the mother is either able to achieve full lactation but an extrinsic factor has interfered with the process, or one or more factors results in failure to attain an adequate milk production.
  - two types of conditions:
    - a primary inability to produce adequate milk volume
    - a secondary condition as a result of improper breastfeeding management and/or infant-related problems.

Delayed onset of lactation

- 17-44% of women experience delayed onset of lactation
- Defined as >72 hours postpartum & <9gm/feeding (30 gm = 1 oz) at 60 hours
- Milk synthesis occurs during first 3 days post birth, even in the absence of suckling or milk expression
- On ~day 4
  - non-breastfeeding mother’s milk reverts to composition of colostrum
  - breastfeeding mother’s milk changes to more mature milk composition
Why do we care?

- Delayed Lactogenesis II can contribute to early breastfeeding cessation!!

Breastfeeding outcomes at 4 weeks for women experiencing DLII.


Independent Risk Factors

- Type I diabetes
- Maternal age
- Parity
- Mode of delivery
- Prolonged 2nd stage of labor
- Labor pain medication
- Exogenous oxytocin use
- Maternal obesity
- Premature delivery
- Retained placenta
- Stress during labor and delivery
- Prenatal care provider
- Sheehan’s syndrome
- Infant birth weight
- Infant APGAR score <8
- Flat/inverted nipples
- Supplementation within 48 hours post partum
- Infant excess weight loss
- Nipple pain when breastfeeding
- Polycystic ovarian syndrome
- Insulin rx during pregnancy

Type I Diabetes

- Can delay onset of lactation by 15-28 h
- This can result in a decrease in milk volume over the first 3 days
- Breast contains insulin-sensitive tissue
- Hypoglycemia may ↓ glucose availability to lactocytes → ↓ lactose synthesis & ability to initiate lactation
- Insulin therapy during pregnancy (Matias 2014)
- Less optimal breastfeeding management may result in delays in baby going to breast

Parity
- Postnatal increases in milk volume occur later in primiparous women
  - 10-35 hours later in primips compared with multipips
- Increases potential for formula supplementation if mothers are unaware of this

Bar plot for estimation of physiological breast engorgement (described by the mothers as “breast fullness/tension”) during day 1 – day 3 in all mothers (means and SE). The perception of breast engorgement was significantly higher in multiparous mothers (repeated measures ANOVA F1,145 = 4.10, p value = 0.0446). Bystrova et al. International Breastfeeding Journal 2007 2:9 doi:10.1186/1746-4358-2-9

Mode of Delivery
- Unplanned cesarean section
- Emergency cesarean section
  - Fewer pulses in oxytocin
  - Lower prolactin concentration during feeding
- High levels of stress during labor and delivery
  - Prolonged stage II of labor
  - Duration of labor longer than 14 hours
- Maternal pain

Maternal Obesity
- Less likely to have increased prolactin concentration after breastfeeding in first 2 days
- Low milk transfer at 60 hours post birth
- High leptin (hormone secreted by fat that ↓ hunger) levels may inhibit milk ejection
- Mothers with later lactogenesis II had higher pre-pregnant BMI
- A one unit increase in BMI is associated with a 0.5 hour delay in lactogenesis
Maternal Obesity

- Breastfeeding durations decrease as maternal BMI increases
- Obesity alters the 24 hour spontaneous release of prolactin
- Prolactin response to sucking is blunted in obese mothers, decreasing by ~45ng/mL at 48 hours postpartum and 100ng/mL at 7 days, during the time period important for optimal milk production

Diet-induced obesity impairs mammary development and lactogenesis in murine mammary gland

- Mouse model showed that obesity impairs mammary gland development
- Obese mice exhibited marked abnormalities in alveolar development within the mammary gland
- Obesity also impaired lactogenesis; seen as lipid accumulation in the secretory epithelial cells, showing an absence of copious milk secretion

Flint DJ, et al., Am J Physiol Endocrinol Metab 2005

Prematurity

- Chemical marker changes indicative of lactogenesis II are delayed in preterm mothers
- The volume of milk was reduced further when antenatal corticosteroids were administered between 28 and 34 weeks gestation and delivery occurred 3 to 9 days later
Retained placenta

- Viable placental fragments retained
- Continued secretion of progesterone by the retained fragments inhibits onset of lactation

Abnormal Placental Pathology

- **Placenta Accreta** - placenta attaches too deep in the uterine wall
- **Placenta Increta** - placenta attaches even deeper; penetrates into uterine muscle.
- **Placenta Percreta** - placenta penetrates through the entire uterine wall and attaches to another organ such as the bladder.
- Increased risk from previous cesarean deliveries

Stress during labor and delivery

- Mode of delivery
  - Delayed onset of milk production
  - Insufficient milk volume
  - Persistent insufficient milk
  - Difficult labor
  - Low infant suck

- Temporary insufficient milk
- Not Resolved
- Resolved

Dewey J Nutr 2001; 131:3012S-3015S
Stress during labor and delivery

- Duration of labor
- Time without sleep
- Maternal pain
- Urgent cesarean
- Prolonged stage II
- Excessive formula on day 2


Birth Trauma

- Traumatic birth experience
- Disturbing flashbacks to birth or previous traumatic birth experiences
- Psychosocial stress
- Post traumatic stress symptoms

MOTHER Diagram thanks to M Walker

PCOS: Polycystic ovarian syndrome

- ↑ androgens down-regulate estrogen & prolactin receptors
- Elevated estrogen
- Insulin resistance
- Low progesterone may impact ductile & lobuloalveolar development resulting in asymmetric or hypoplastic breasts
- Poor breast tissue development
- Low prolactin or ↓ prolactin receptors may interfere with breast growth during pregnancy & lactogenesis
More risk factors

- Postpartum hemorrhage with Sheehan’s syndrome
- Hypopituitarism
- Hypothyroidism
- Anatomic breast abnormalities
- Insufficient breast tissue
- Theca-lutein cyst (elevate testosterone levels)
- Conditions in the infant
- Maternal medications such as birth control methods containing estrogen or progestin only
  - Pseudofed

Infant Risk Factors

- Absent suckling
- Inefficient suckling
- Poor suckling

Effect of suckling on lactogenesis II

- Lactogenesis occurs in the absence of milk removal over the first 3 days
- Additional breast pumping prior to lactogenesis II has not been shown to hasten the event or result in increased milk intake at 72 hours
- Mothers who exclusively bottle-feed perceive lactogenesis II significantly later
Prenatal risk assessment

- History
  - Diabetes
  - Overweight/obesity
  - PCOS
  - Hypothyroid
  - Hypopituitarism

- History and Exam
  - Breast surgery
  - Growth during puberty and pregnancy

Diagnosis—Mom

- The breast is the only organ in the body without a diagnostic test to measure its adequacy! (Hartmann 2001)
  
- Biochemical markers can be measured to determine onset of lactation (Na, Cl, citrate, lactose)
  - Usually impractical

- Measurement of milk volume, especially if expressing for preterm infant
  - <9ml/feeding at 60 hours post birth

- No maternal perception of breast fullness, swelling, leaking >72 hours post birth
Diagnosis—Infant

- Uric acid crystals in diaper at 4 days
- Decreased diaper counts
  - <3 stools/day after day 4
  - <6 wet diapers/day after day 4
- Minimal or no weight gain
  - Weight loss >7%
- High bilirubin level

Assessment & Monitoring

- Anticipatory Guidance
  - Early feeding cues
  - Normal feeding patterns
  - Signs of effective milk transfer
  - Normal weight, voiding and stool patterns
  - Nipple tenderness
  - Breast engorgement
  - Include extended family in instruction

Interventions

- Two or more risk factors present a high level of suspicion and should be used as signal for close surveillance following discharge
- Underlying cause drives the plan of care
- Maximize breast stimulation and assure adequate infant growth
- A wait and see approach may delay appropriate interventions and result in more serious sequelae
- Avoid use of Depo Provera prior to discharge
Breastfeeding management in hospital for at risk mothers/babies

- Skin-to-skin
- Baby to breast within first hour after birth
- Breastfeed 12 times/24 hours
  - Especially if mother is diabetic or obese
- Feed hourly for 3-4 feedings until blood glucose is stable
  - q 2-3 hours until 12 hours

Infant Stomach Capacity

- Anatomic Capacity = stretched stomach capacity at autopsy
- Physiologic Capacity = amount taken per feeding


Feed the Baby!: Supplementation

- Most infants well hydrated via placenta at birth
- Urine output exceeds intake days 1-3
- Small colostrum feedings (5-15 ml) physiologic
  - appropriate for size of infant’s stomach
  - sufficient to prevent hypoglycemia
  - easy to manage as infant learns to coordinate suck, swallow, breathing
- Some infants will need some supplementation
Antenatal expression of colostrum

Diabetic mothers may wish to express colostrum, freeze it, and bring to hospital in case supplementation is needed for hypoglycemia

© K. Marinelli MD 2014

Immature sucking patterns in infants of mothers with diabetes

- Poorer sucking patterns seen among infants of insulin-managed mothers with diabetes
  - Insulin group averaged 5.2 fewer sucking bursts and 42 fewer sucks per 5 minute interval (on artificial nipple)
  - 42 x .14ml/swallow = ~9ml ↓ /5min sucking
  - 36ml ↓ /20 minute feeding
  - 360ml/day ↓ (10 feeds) = 13oz deficit/day


Breastfeeding Baby’s First Immunization

From birth and on up for many decades, it is important that they receive immunizations. Neonates are not able to receive food, water, or medications by mouth. Neonates are not able to be safely vaccinated by giving the vaccine directly into their mouth or giving it through a feeding tube. It is “Breastfeeding Immunization.”

© K. Marinelli MD, IBCLC, FABM 2014

K. Marinelli MD, IBCLC, FABM
What if baby cannot transfer colostrum/milk?

- Early and frequent sucking helps assure maximum milk production and transition to mature milk composition following lactogenesis II
- Babies who may be in trouble:
  - Sleepy baby
  - Late preterm infant/preterm infant
  - Oral anomalies
  - Birth trauma

Ineffective Latch

- Low tone
- Does not draw nipple/areola deep into mouth
- Younger infants exert lower vacuum
- Vacuum is primary force used to remove milk from the breast

Alternate Massage/Breast Compressions

- Breast is massaged and compressed during pauses between sucking bursts
- Creates improved pressure gradient between breast and baby’s mouth
- Can increase volume and fat content of feeds
Adequate intake during prolonged colostral phase

- Increased number of feedings maximizes colostrum intake
  - Prevents dehydration
  - Prevents excessive weight loss
  - Prevents hyperbilirubinemia (especially important for late preterm infants)

- More effective feedings
  - Improve latch
  - Alternate massage
  - Assure mother knows when baby is swallowing

---

Improve flat nipples

1. Cut along this line with blade
2. Insert palatal from cut end
3. Mother applies the smooth end to her breast and gently pulls the nipple

---

Helping with Latch

- Nipple shield
  - 20 mm size
  - 16 mm may be too small and 24 mm may be too large
  - Teat height should not exceed distance from infant's lips to juncture of hard and soft palate
  - Compensates for relatively weak suck
  - Properly fitted
  - Reverse pressure softening for edematous areola

---
Determine the need for supplementation

- Weight loss >7%
  - continued weight loss after day 3
- Inadequate diaper count
  - <3 stools/day after day 4
  - <6 wet diapers/day after day 4
- Minimal breast changes by day 5 post birth
- Rising bilirubin levels
- ABM supplementation protocol (www.bfmed.org)

AAP Clinical Practice Guideline:
Management of Hyperbilirubinemia in the Newborn Infant 35 or More Weeks of Gestation

Nomogram for designation of risk in 2840 well newborns at 36 or more weeks' gestational age with birth weight of 2000 g or more or term newborns' gestational age and birth weight of 2500 g or more based on the hour-specific serum bilirubin values.

Diapers of the Breastfed Baby

- The baby's diaper should be kept dry but never wet.
- The nappy should be kept clean and dry.
- The diaper should be changed when soiled.
- The baby's bottom should always be exposed to the air.
- The baby's bottom should be kept dry.
Determine the need for supplementation

- Uric acid crystals on day 4
- Swallowing absent for majority of feeding
- Milk transfer less than what is expected for day post birth
  - Pre and post feeds weights
  - 38mL/feeding on day 3 (an ounce +)
  - 58mL/feeding on day 4 (2 ounces)

What to supplement?

- "Where it is not possible for the biological mother to breastfeed, the first alternative, if available, should be the use of human breastmilk from other sources." WHO & UNICEF 1980
- "Human milk is the preferred feeding for all infants, including premature and sick newborns, with rare exceptions." AAP Policy Statement 2012
Milk Expression

“What’s hands-on pumping?”

Photos thanks to Jane Morton
© K. Marinelli MD 2014

What to supplement?

- Mother’s own milk first if available
- Hand express colostrum into a spoon and spoon feed baby
  - Teaspoon is 5ml
- If using a pump, can draw the drops up into a syringe
- Banked human milk

Alternative feeding methods

© K. Marinelli MD 2014
If do not have human milk

- Sugar water should not be given by mouth due to its rapid absorption and poor nutrition
- Cereal should not be given to an infant <3mo of age as it ↑ the risk for diabetes in susceptible families (Norris et al, 2003)
- If formula becomes temporarily necessary, consider using a hydrolyzed formula
  - Bilirubin levels fall faster

Supplementation of Breastfeeding

- If need to supplement with formula, strongly consider use of protein-hydralysate
  - More effective in lowering bilirubin
    - Contains β-glucuronidase inhibitor (as does HM, not regular formula) (Gourley 2005)
  - Less likely to induce allergy
  - Tastes bad!
  - Seen as medicine
  - Expensive
  - ...so less likely to give up breastfeeding!

Examples of Hydrolyzed Protein and Amino Acid–Based Infant Formulas Available in the United States

- Extensively hydrolyzed casein (cow milk protein)
  - Enfamil Nutramigen® with Enflora™ (Mead Johnson Nutritionals)
  - Enfamil Purémo (Mead Johnson Nutritionals)
  - Enfamil Progestam (Mead Johnson Nutritionals)
  - Similac Expert Care Alimentum (Ross Products)
- Partially hydrolyzed whey (cow milk protein)
  - Gerber Good Start Gentle Formula (Nestlé USA)
  - Gerber Good Start Protect Formula (Nestlé USA)
- Partially hydrolyzed whey/casein (cow milk protein)
  - Enfamil Gentlease (Mead Johnson)
- Partially Hydrolyzed Soy (Soy Protein)
  - Good Start Supreme Soy (Nestlé USA)
- Free amino acid–based
  - Neocate (and Neocate 1 for children 12 mo) (Nutricia North America)
  - EleCare (Ross Pediatrics)
  - Nutramigen AA Lipil (Mead Johnson)

Interventions for mother

- Assess and correct any potential infant suckling problems
  - E.g. poor latch or tight frenulum
- Breast engorgement or nipple trauma/pain present
  - proper treatment to alleviate symptoms and promote maternal comfort and milk flow necessary
- Mechanical breast pumping with an effective hospital-grade breast pump following each breastfeeding should be initiated

Interventions for mother

- Galactagogues have been shown to increase prolactin levels and milk production in some cases
  - ABM Galactagogue protocol www.bfmed.org
- Test weighing
- Record of daily feeding, pumping, and infant stooling and urination patterns to monitor progress
Recognizing Reaching Maternal Lactation Potential

- Assessment of proportion of daily breastfeeding, supplements, and expressed breast milk volumes obtained from pumping
  - May not reach exclusive breastfeeding
  - Can be very emotional
  - Emphasize success

Thank You!!!

Contact me: Kathleen.marinelli@cox.net