The Science of Secretory Activation: Implications for Breastfeeding Medicine Specialists

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Disclosures

Active Research and Training Awards

- NIH: *Reducing Disparity in the Receipt of Mothers' Own Milk in VLBW Infants: An Economic Intervention to Improve Adherence to Sustained Breast Pump Use: ReDiMOM Trial* (2020-2024; Patel and Johnson, PIs)
- NIH: *Early Childhood Neurodevelopmental, Economic and Nutritional Outcomes Among Former VLBW Infants from the ReDiMOM Trial* (2022-2026; Johnson and Patel, PIs)
- PCORI: *Clinically Integrated Breastfeeding Peer Counseling to Promote Breastfeeding Equity* (2021-2025; Borders, PI)
- NIH: *Effect of Gestational Age at Delivery on Lactation Outcomes in Pump-Dependent Mothers of Critically Ill Infants* (K23; Bendixen, 2023-2026)
- NIH: *Reducing the Disparity in the Receipt of Mothers' Own Milk in Black VLBW Infants: Understanding the Perceptions of Mothers and Maternal Matriarchs* (ReDiMOM Diversity Supplement; 2022-2024; DeVane-Johnson)
- AHRQ: *Optimizing Utilization of Lay Health Workers to Address Maternal and Child Health Disparities: Comprehensive Evaluation of a Clinically Integrated Breastfeeding Peer Counselor Program* (K01; Keenan-Devlin, 2022-2026).

Industry Research Funding and Consultation

- Medela AG, Baar, Switzerland

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The first month postpartum is the time of greatest risk for early, unplanned cessation of lactation

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The first month postpartum is the time of greatest risk for early, unplanned cessation of lactation

- Practitioners recommend “extra support” but without specific, evidence-based interventions to characterize effective “support” and evaluate outcomes
- Most interventions have been behavioral and/or motivational (additional education, visits with lactation care providers, use of peer counseling, economic incentives)
- Lost in all of this is leveraging the complex biology of the first 2-4 weeks postpartum to identify and mitigate predictable and unpredictable lactation problems in “healthy” and “at risk” dyads

Meier PP, Parker LA (2025). Overview of Special Issue, **Breastfeeding Medicine,**

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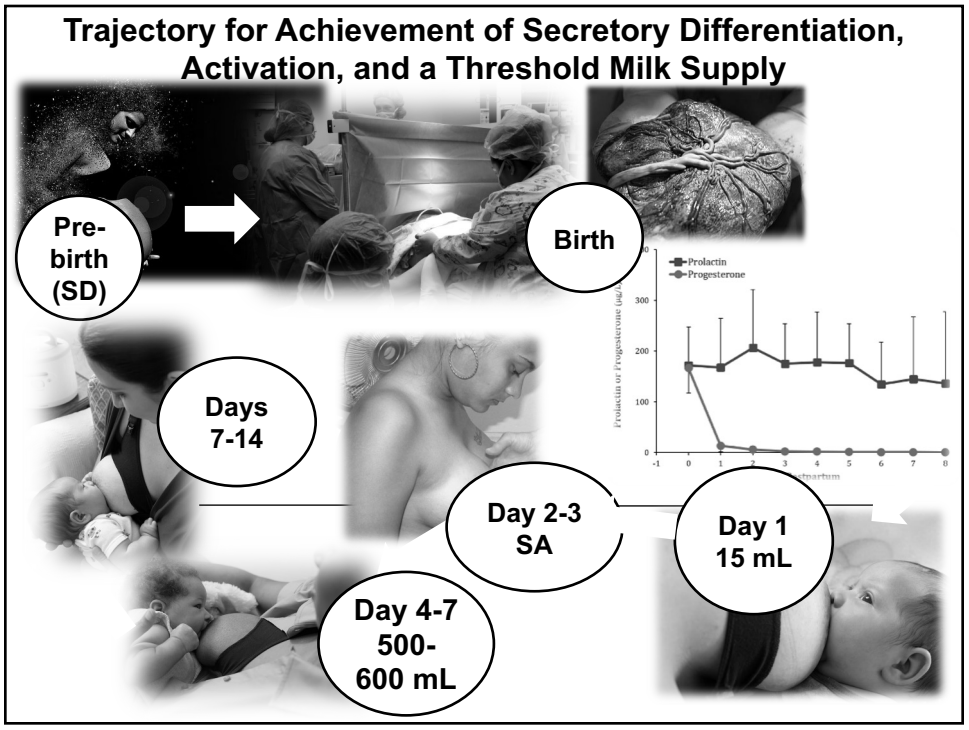

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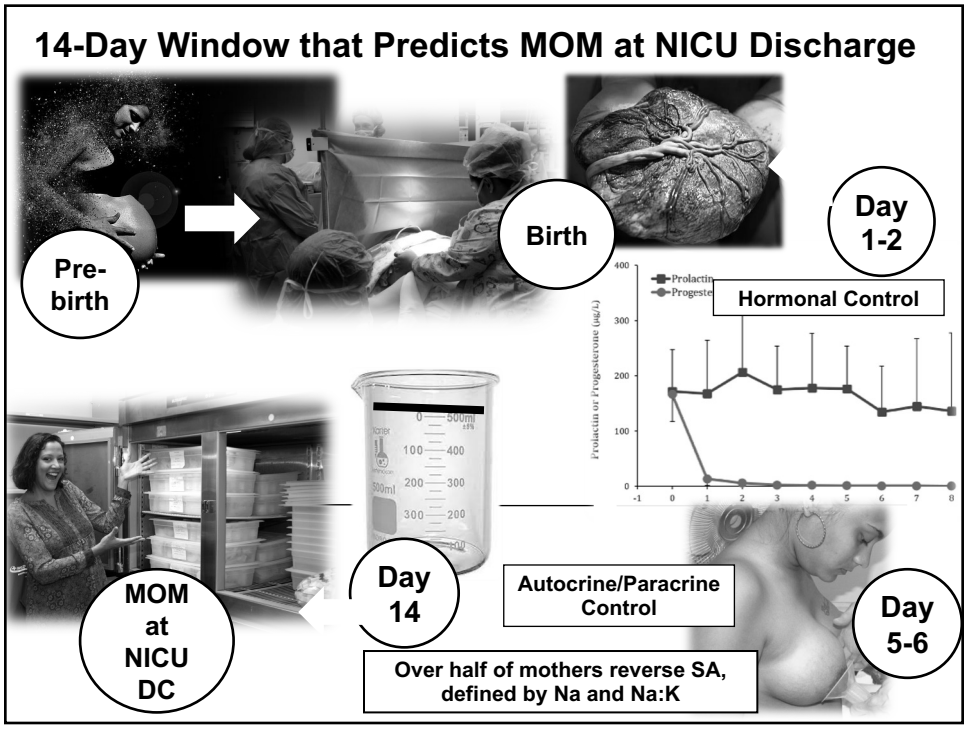

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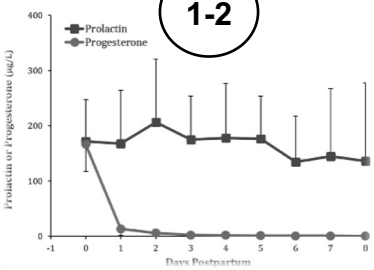
From Birth to SA Achievement

Birth

1-2



2-3

Day 5-6

- Affected by adiposity (Fat tissue harbors progesterone)
- Retained placental fragments
- Is the mechanism for concerns about early hormonal contraception (EHC)

- Affected by pumping/suckling frequency and effectiveness (optimal latch, LPT infant, incorrect suction pressures, breast shield sizes
- Affected by maternal metabolic disorders (obesity, hypertension, diabetes)
- May be affected by other co-morbidities attributable to disordered secretory differentiation

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Maternal Co-Morbidities Affect Pumping, Pumped MOM Volume, SA and CTV Achievements in Breast Pump-Dependent Mothers of Premature Infants

Integrating Biological, Behavioral, and Economic Factors in the Practice and Study of Early, Unplanned Lactation Cessation

Larelle H. Bookhart [1], Stephanie Devane-Johnson [2], Anita Esquerra-Zwiers [3], Yarden Golan Maor [4], Jessica Gomez [5], Katie T. Kivlighan [6], Clarisa Medina Poeliniz [7], Rachel Walker [8], Tricia J. Johnson [9], and Leslie A. Parker [10]

Maternal Complications of Pregnancy and Achievement of Secretory Activation and Coming to Volume in Breast Pump-Dependent Mothers of Preterm Infants

Rebecca Hoban [1,2], Qinglin Pei [3], Clarisa Medina Poeliniz [4], Yarden Golan Maor [5], Rachel E. Walker [6], Paula P. Meier [4,7], Angela Monk [3], and Leslie A. Parker [3]

Are these data generalizable to otherwise healthy dyads, especially with high maternal BMI?

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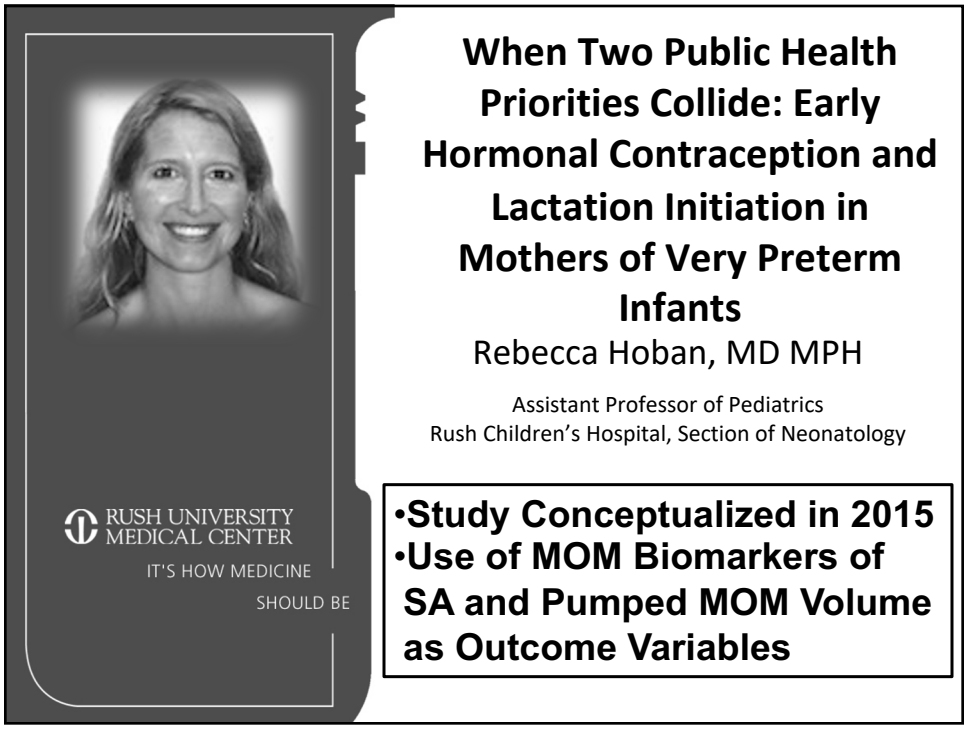

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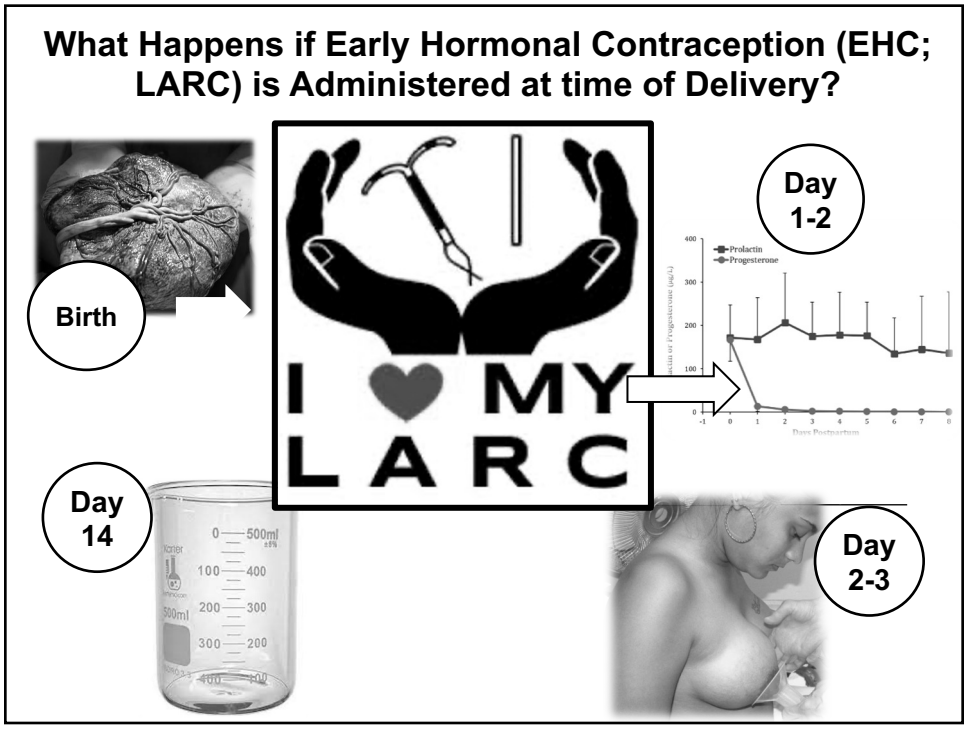

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Measures of Secretory Activation for Research and Practice: An Integrative Review

Breastfeeding Medicine, 2020

Clarisa Medina Poeliniz,[1] Janet L. Engstrom,[2] Rebecca Hoban,[3,4] Aloka L. Patel,[2,3] and Paula Meier[2,3]

Secretory Differentiation

- Growth in secretory cell number
- Ductal branching
- MOM synthesis held in check by circulating progesterone
- May be affected by inflammatory/metabolic morbidities

Birth

- Placenta delivery triggers SA by removing inhibition of progesterone

Secretory Activation
"milk coming in"
"Lactogenesis II"

- Upregulation of 4 transcellular pathways that synthesize MOM components
- Closure of 1 paracellular pathway
- Affected by stimulation from infant or pump

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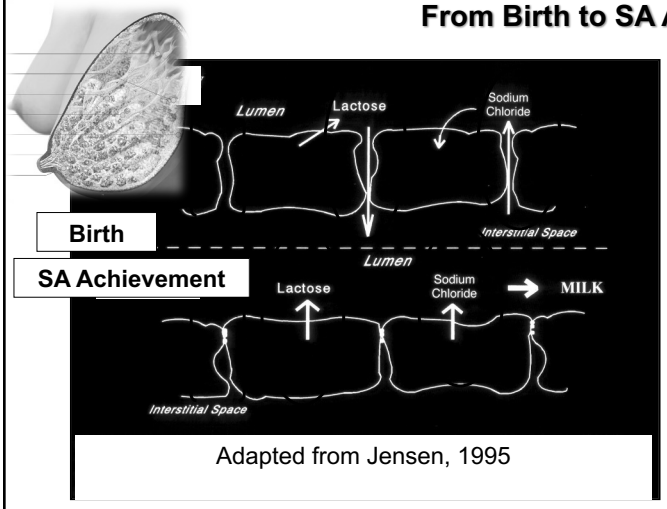
From Birth to SA Achievement



Adapted from Jensen, 1995

- Secretory Activation necessitates closure of paracellular pathways between the mammary epithelial cells
- Pumping behaviors (frequency, minutes, long inter-pump intervals) likely influence this timing

- Paracellular pathways are open at birth and must close before full lactation is possible. Closure essential for achievement of secretory activation
- Na in early MOM is high due to transfer from maternal circulation. As PCPs close, Na gradually decreases
- Lactose in early MOM is low because it is produced by the breast, escapes into maternal circulation and is excreted in urine

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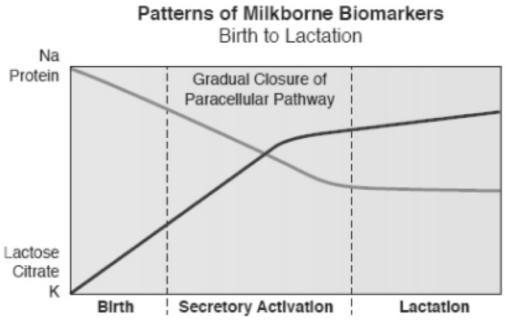
MOM Biomarkers of Secretory Activation (SA)

•Reflect the upregulation of 4 transcellular pathways and closure of a single paracellular pathway in the mammary gland



- WNL for all 4 biomarkers (Na, citrate, protein, lactose, Na:K ratio)
  - Dose-response between number of biomarkers WNL and MOM volume (Hoban, 2020)
- Na and/Na:K ratio only
  - Na ≤ 12, Na:K < 0.6
  - Na ≤ 16, Na:K < 0.8
  - Na ≤ 20, Na:K < 1.0

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Clarisa Medina Poeliniz,[1] Janet L. Engstrom,[2] Rebecca Hoban,[3,4] Aloka L. Patel,[2,3] and Paula Meier[2,3]

Breastfeeding Medicine, 2020

Milk Biomarkers of Secretory Activation in Breast Pump-Dependent Mothers of Preterm Infants: An Integrative Review

Leslie A. Parker,[1] Rebecca Hoban,[2] Marion M. Bendixen,[1] Clarisa Medina-Poeliniz,[3] Tricia L. Johnson,[4] and Paula P. Meier[5]

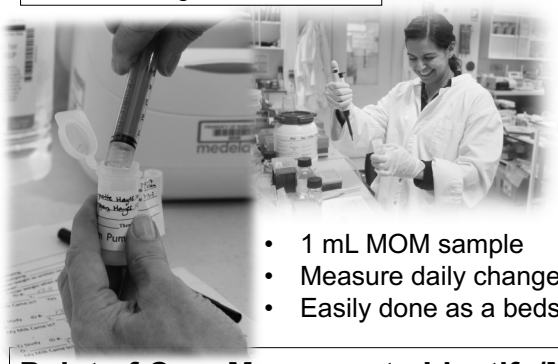
Breastfeeding Medicine, 2024

Reviews Open Access

Point-of-Care Techniques to Identify Risks for Early, Unplanned Lactation Cessation Among Term Mother/Infant Dyads: An Integrative Review

Larelle H. Bookhart[1], Stephanie Devane-Johnson[2], Katie T. Kivlighan[3], Clarisa Medina-Poeliniz[4], Leslie A. Parker[5], and Anita L. Esquerra-Zwiers[6]

Breastfeeding Medicine, 2025



- 1 mL MOM sample
- Measure daily change for Na or for Na:K ratio
- Easily done as a bedside POC test

Point of Care Measures to Identify/Manage at Risk Mothers

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Use of Horiba Ion Selective Electrodes as POC Technique to Measure Achievement of SA

Early postpartum pumping behaviors, pumped milk volume, and achievement of secretory activation in breast pump-dependent mothers of preterm infants

Rebecca Hoban, Clarisa Medina-Poeliniz

J Perinatology, 2024

THE JOURNAL OF PEDIATRICS • www.jpeds.com

J Pediatrics, 2020

Mother's Own Milk Biomarkers Predict Coming to Volume in Pump-Dependent Mothers of Preterm Infants

Rebecca Hoban, MD, MPH, Clarisa Medina Poeliniz, MSN, PhD(c), Emily Somerset, MSc, Ching Tat Lai, PhD, Judy Janes, RN, IBCLC, Aloka L. Patel, MD, Donna Geddes, PhD, and Paula P. Meier, PhD

Milk Biomarkers of Secretory Activation in Breast Pump-Dependent Mothers of Preterm Infants: An Integrative Review

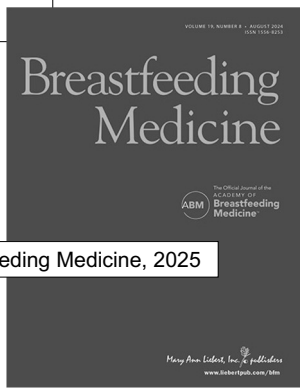
Leslie A. Parker, Rebecca Hoban, Marion M. Bendixen, Clarisa Medina-Poeliniz, Tricia J. Johnson, and Paula P. Meier

Breastfeeding Medicine, 2024

Measures of Secretory Activation for Research and Practice: An Integrative Review

Clarisa Medina Poeliniz, Janet L. Engstrom, Rebecca Hoban, Aloka L. Patel, and Paula Meier

Breastfeeding Medicine, 2020



Breastfeeding Medicine, 2025

Human Milk Biomarkers of Secretory Activation in Breast Pump-Dependent Mothers of Premature Infants

Rebecca Hoban, Judy Janes, Donna Geddes, and Paula P. Meier

Breastfeeding Medicine, 2018

Prepregnancy Body Mass Index Is Associated with Time-Dependent Changes in Secretory Activation Measures During the First 7 Days Postpartum in Breast Pump-dependent Mothers of Premature Infants

Clarisa Medina Poeliniz, Aloka L. Patel, and Paula Meier

Breastfeeding Medicine, 2021

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•Embedded gram scale that weighed to nearest 0.1 gram

Custom-designed interactive app for mothers to weigh milk:

- separately for the two breasts
- using any of 4 different size storage containers
- app programmed to subtract container weight
- Data stored within this pumping session

•Data logger captured and stored pumping behavior data

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What is the best measure of paracellular pathway permeability in the mammary gland?

- Lactose and citrate are the most relevant components, signaling upregulation of transcellular pathways and closure of paracellular pathway
  - 24-hour urinary lactose measures used as SA identification in older studies
  - Citrate, the "harbinger of lactogenesis", is not affected by paracellular pathway patency
- Na has been used for decades and is the oldest measure in both humans and animals
  - Measures are unaffected by maternal diet (Ereman,1987) nor which breast sampled, or whether sampled pre-or post-feed (*during established lactation*)* Koo, 1982). Which breast and inter-feed/pump interval may be important for SA
- Na:K ratio first credited to Filtreau (1999) to detect subclinical mastitis in Bangladeshi women
  - Proposed standardizing the Na only measure by K to control for measurement variation and changes in biomarkers over longer lactation (goal to detect mastitis)
- Some studies have used both Na and Na:K ratio or only Na:K for early lactation outcomes, based on Filtreau's rationale
  - LeMay (2014), Murase (2017), Wang (2025), Hoban (2018, 2020, 2024), Esquerra-Zwiers (2022)

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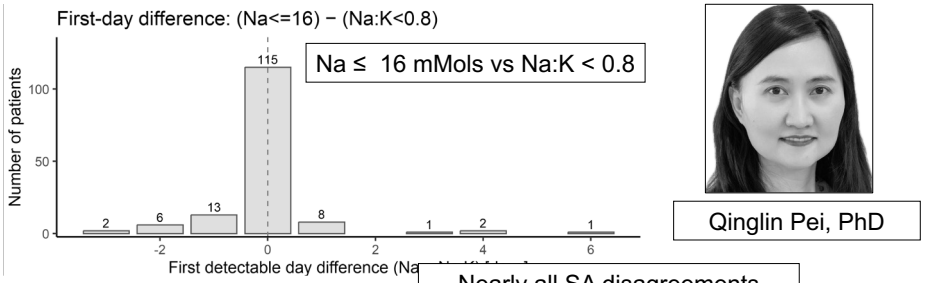
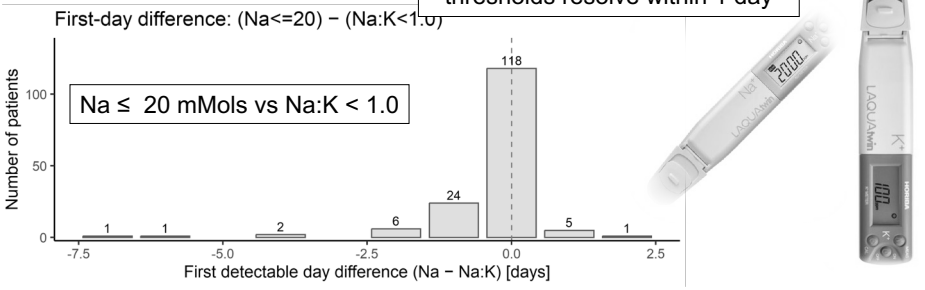
Is the Na:K ratio needed in practice and research?



Qinglin Pei, PhD

Nearly all SA disagreements between Na and Na:K ratio thresholds resolve within 1 day



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What about mastitis and return of menses?

Sodium and Potassium Concentrations and Somatic Cell Count of Human Milk Produced in the First Six Weeks Postpartum and Their Suitability as Biomarkers of Clinical and Subclinical Mastitis

Nutrients, 2022

Ryan M. Pace [1,*], Christina D. W. Pace [1], Bethaney D. Fehrenkamp [1,2], William J. Price [3], Meghan Lewis [4], Janet E. Williams [4], Mark A. McGuire [4] and Michelle K. McGuire [1,*]

Breastfeeding and Reproduction in Women in Western Australia — A Review

Birth and Family Journal, 1981

P. E. Hartmann
J. K. Kulski
S. Rattigan
C. G. Prosser
L. Saint

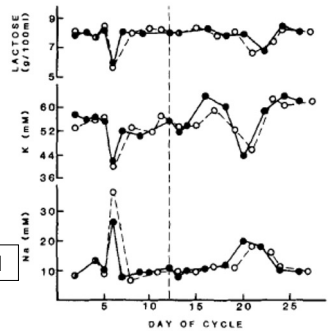

Figure 7. Changes in the concentration of lactose, potassium and sodium in milk from the right (•) and left (○) breast of a woman throughout the menstrual cycle. Ovulation is indicated by the dashed line.

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Summary and Next Steps

- Na alone is an accurate biomarker of paracellular pathway patency to detect SA
  - Na:K ratio is not needed for clinical practice
  - If Na:K ratio is used for research, threshold values need to be altered for the K Horiba ion electrode
- Na alone does NOT truly measure SA achievement
  It is the best default, and likely detects most problems
  - Achievement per se may be having all biomarkers WNL (lactose, citrate, sodium, total protein, potassium)
  - This scenario may characterize problems with SD that present as problems with SA
- Current Na thresholds for SA are likely just placeholders until we can model trajectories between various Na thresholds, postpartum day and pumped MOM volume
  - In other words, trends versus absolute values (similar to managing bilirubin post-birth) will likely be the future algorithm for interventions

- Case studies from your practices, especially if in collaboration with our research team, will be important to this work.

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