# *Avoiding the pitfalls of hypoglycemia: Sweet Strategies for Success*

- Moderator: Lori FELDMAN-WINTER, MD, MPH
- Presenter: Renee Boynton-Jarrett, MD, ScD
- Physician Lead Champs
- Wednesday, February 10, 2016
- 11:00-12:00 CST

Cooper Medical School of Rowan University

BU Boston University School of Medicine

Cooper University Hospital

Boston Medical Center — Exceptional Care. Without Exception.

# Upcoming Wednesday Webinars

Webinars are held in collaboration with the Mississippi State Department of Health and are scheduled on Wednesdays from 11a-12p (CST)

ALL ARE WELCOME TO ATTEND! To register visit www.CHAMPSbreastfeed.org/webinars

## SCHEDULE

- March 16: *Nursing Staff Issues and Baby-Friendly Practices*
  Jennifer Ustianov, MS, BSN, RN, IBCLC
- April 6: *The CHAMPS Community and the Baby Cafe Model*
  Lucia Jenkins, RN, IBCLC, RLC; Kimarie Bugg, MSN, MPH, CLC; Danielle Lugrand, CLC
- May 18: *Creating a Prenatal Education Plan*
- June TBD: *Getting Hospital Leadership on Board*

# Blue Cross & Blue Shield of Mississippi's Baby-Friendly Regional Conference

**Location:** University of Southern MS, Gulf Park Campus, Long Beach, MS

**Date:** February 16th, 2016

**Speakers include:**

- Anne Merewood, PhD, IBCLC, MPH, CHAMPS Project Director
- Kimarie Bugg, MSN, MPH, CLC, CHAMPS Community Engagement Director
- Cathy Carothers, BLA, IBCLC, RLC, CHAMPS Mississippi Coordinator
- Lori Feldman-Winter, MD, MPH, CHAMPS Physician CHAMPion Lead

BlueCross BlueShield of Mississippi

It's good to be Blue.

# Upcoming: 4-hour Clinical Skills Trainings

- February 15th, Hancock Medical Center
- February 18th and 19th, Memorial Hospital at Gulfport
- February 23rd, King's Daughters Medical Center

For more information, visit: CHAMPSbreastfeed.org/events1



# Breastfeeding: The Gold Standard Conference 2016 Communities of Care

**Date:** March 16-18, 2016

**Location:** MSU Riley Center, Meridian, MS

Cathy Carothers BLA, IBCLC, RLC, CHAMPS Mississippi Coordinator, will be presenting a plenary session on CHAMPS and BFHI

# Second Indian Country Breastfeeds Conference: Sustainability and Support

**Date:** May 9-10, 2016

**Location:** Albuquerque, NM

**Topics Include:**

- Sustainability
- The Baby-Friendly Hospital Initiative
- Breastfeeding and clinician support
- Historical trauma and breastfeeding
- Illicit drug use and breastfeeding

## Keynote Speakers

Camie Goldhammer, MSW, LICSW, IBCLC (Sisseton-Wahpeton)

Susan Karol, MD, Chief Medical Officer, Indian Health Service

Bethany Moody, RN, MSN, CNM

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# *Avoiding the pitfalls of hypoglycemia: Sweet Strategies for Success*


MODERATOR: LORI FELDMAN-WINTER, MD, MPH

PRESENTER: RENEE BOYNTON-JARRETT, MD, SCD

PHYSICIAN LEAD CHAMPS


WEDNESDAY, FEBRUARY 10, 2016

11:00-12:00 CST

CHAMPS
COMMUNITIES AND HOSPITALS ADVANCING MATERNITY PRACTICES

# Disclosure

I have no relevant financial relationships with the manufacturer(s) of any commercial product(s) and/or provider of commercial services discussed in this CME activity.

I do not intend to discuss an unapproved/investigative use of a commercial product/device in my presentation.

I am funded as a consultant and Physician Lead for the CHAMPS Project

# Learning Objectives

1. Define neonatal hypoglycemia and the at-risk population
2. Reduce risk for hypoglycemia by avoiding unnecessary mother-baby separation.
3. Understand why supplementing interferes with breastfeeding

*What if every parent knew that immediate skin to skin care can offset transient hypoglycemia?*

# Case #1: LGA infant born to 28 year old mother with gestational diabetes

What is the best method of preventing neonatal hypoglycemia?

What are common risk factors for neonatal hypoglycemia?

What is the normal newborn blood glucose?

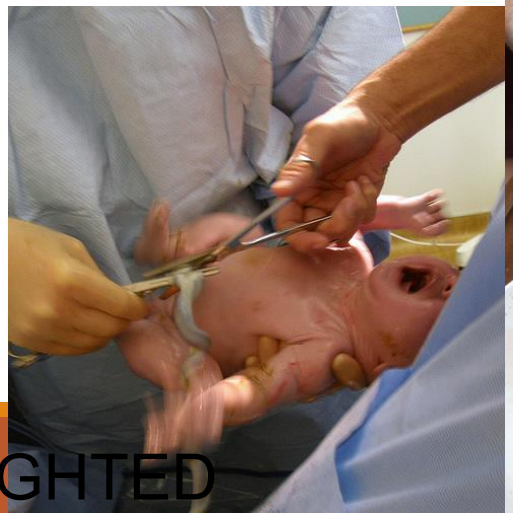
# Physiological hypoglycemia

- The term ‘‘hypoglycemia’’ refers to a low blood glucose concentration.
- Transient hypoglycemia in the first hours after birth is common
- Most neonates compensate through ‘‘counter-regulation”
  - endogenous fuel production through gluconeogenesis, glycogenolysis, and ketogenesis

# Transition from in utero fuel from mother to delivery

- In utero glucose, ketones, free fatty acids transferred to baby via umbilical cord
- Fetal glucose level is maintained around 54 mg/dL
- After delivery and cord is clamped the newborn's source of fuel is cut off abruptly and glucose level drops for the first 4-6 hours to levels around 45 mg/dL

Clamping too soon?!



# The Neonatal Brain

- The neonatal brain has an enhanced capability to utilize ketone bodies, glucose-sparing fuel, protecting neurological function
- No evidence that treatment of asymptomatic hypoglycemia vs. no treatment leads to same or better neurological outcomes

A, Offringa M. Neurodevelopment after neonatal hypoglycemia: A systematic review and design of an optimal future study. Pediatrics 2006;117:2231–2243.

# What causes abnormal hypoglycemia in the newborn?

Hypoglycemia may be caused by conditions that:

- Lower the amount of glucose in the bloodstream
- Prevent or lessen storage of glucose
- Use up glycogen stores (sugar stored in the liver)
- Inhibit the use of glucose by the body

# Infants at risk for developing hypoglycemia

- Infants of diabetic mothers on oral hypoglycemic medications or insulin
- Large for gestational age infants (LGA)
- Small for gestational age infants (SGA)
- Premature infants < 34 weeks gestation
- Late preterm infants (LPT) > 34 weeks to 36.6 weeks gestation
- Post-term infants ( > 42 weeks gestation)
- Infants weighing < 2500 grams or > 4000 grams

# Associated Neonatal Conditions

- Inadequate maternal nutrition in pregnancy
- Excess insulin produced in a baby of a diabetic mother
- Severe hemolytic disease of the newborn (incompatibility of blood types of mother and baby)
- Birth defects and congenital metabolic diseases (such as hyper-insulinism)
- Birth asphyxia
- Cold stress (conditions that are too cold)
- Liver disease
- Infection

# Symptoms of Hypoglycemia

- Jitteriness
- Cyanosis (blue coloring)
- Apnea (stopping breathing)
- Hypothermia (low body temperature)
- Poor body tone
- Poor feeding
- Altered consciousness: Lethargy, irritability, abnormal cry, stupor
- Seizures

*Heel prick blood tests are used to monitor hypoglycemia in newborns.*

# Whipple's Triad

1. A reliable low blood glucose measurement
2. Clinical signs and symptoms consistent with hypoglycemia
3. Resolution of clinical signs and symptoms after restoring glucose to normal values

Whipple AO, Fratz DK. Adenoma of islet cells with hyperinsulinism: a review. Ann Surg 1935;101:1299e310.
Cornblath M, Ichord R. Hypoglycemia in the neonate. Semin Perinatol 2000;24:136e49.

# Uncontrolled Gestational Diabetes

# Measurement


- Screening test:
  - Glucose stripes easy, inexpensive, and available but NOT reliable
- Gold standard:
  - serum testing done at lab
- Other:
  - Bedside rapid tests with reflective colorimetry may be more accurate but not widely available

# Thresholds by Hour

TABLE 1. POPULATION LOW THRESHOLDS: PLASMA GLUCOSE LEVEL[40]

| *Hour(s) after birth* | *≤ 5th percentile plasma glucose level* |
|---|---|
| 1–2 (nadir) | 28 mg/dL (1.6 mmol/L) |
| 3–47 | 40 mg/dL (2.2/mmol/L) |
| 48–72 | 48 mg/dL (2.7 mmol/L) |

ABM Protocol #1 Revised 2014;
Alkalay et al. American Journal of Perinatology 2006

# Definition Controversial

| Basis for Definition | Blood Glucose Values by Birthweight Class (mg/dL in serum or plasma) | | |
|---|---|---|---|
| | *Term AGA* | *LBW* | *VLBW* |
| Symptoms | * | * | * |
| Population survey (values 2 SD below population mean) | | | |
| 1960s[60] | <35 | <25 | <25 |
| 1987 <24 hr[32] | <30-35 | | |
| >24-48 hr | | | |
| Functional correlations | | | |
| Altered brain electrophysiology[37] | <30 | | |
| Endocrine counter-regulatory responses[40] | <30 | | |
| Cerebral blood flow responses[40] | <30 | | |
| Adverse long-term outcome | | | |
| Infants <1,850 g BW[35] | | 47 | |
| SGA premature infants[67] | | 47 | |
| Proposed treatment guidline | | | |
| Alkalay et al[38] | | | |
| <24 hr age | 45 | 45 | 45 |
| 24-72 hr age | 50 | 50 | 50 |
| >72 hr age | 60 | 60 | 60 |
| Stanley and Baker[33] | 60 | 60 | 60 |

* Extreme individual variation, defined by symptoms associated with low blood glucose, which resolves after administration of glucose. Almost all were <20-30 mg/dL [1.2-1.7 mmol/L] whole blood glucose.

Corblath M, Ichord R. Hypoglycemia in the neonate. Semin Perinatol . 2000 Apr;24(2):136-49.

# Complications Associated with Hypoglycemia

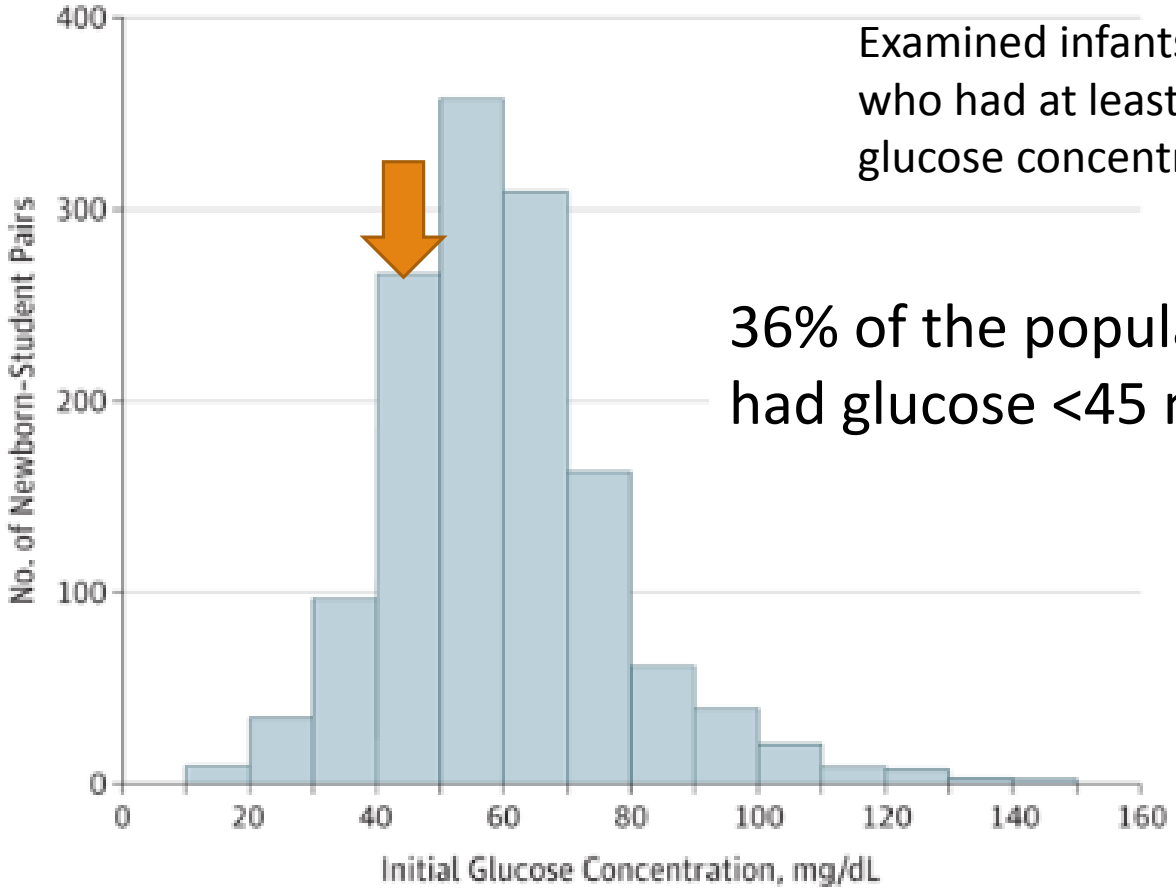
*How Low is Too Low?*

# Concerns About Transient Hypoglycemia

- Retrospective study examining long term cognitive effects of transient hypoglycemia within 3 hours of life (The UAMS universal newborn glucose screening policy was to obtain an early glucose concentration from all newborns, compliance exceeded 99%)
- Glucose level less than 35 mg/dL (primary) and less than 40 and 45 mg/dL (secondary) were investigated (policy to intervene at 35 mg/dL with early feed or dextrose IV).
- Primary outcome was proficiency on fourth-grade literacy and mathematics achievement tests at age 10 years
- Study conducted in AK (no Baby-Friendly hospitals)

Kaiser J, et al. *JAMA Pediatr*. 2015

# Retrospective Study of Hypoglycemia




Examined infants from 1998 who had at least 1 recorded glucose concentration

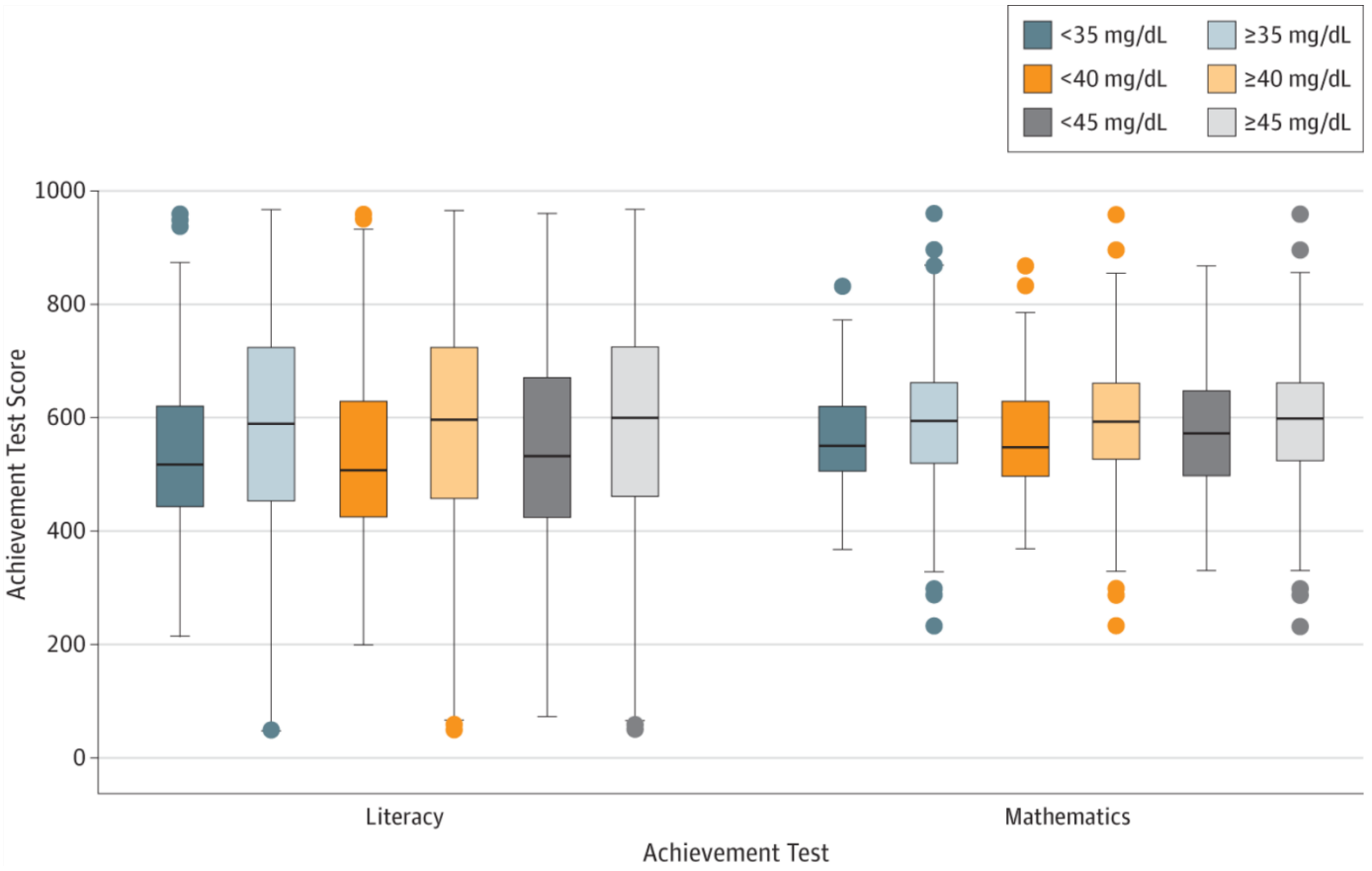
36% of the population had glucose <45 mg/dl



Kaiser J et al. *JAMA Pediatr.* 2015

# Association Between Transient Newborn Hypoglycemia and Fourth-Grade Achievement Test Proficiency: A Population-Based Study

JAMA Pediatr. 2015;169(10):913-921. doi:10.1001/jamapediatrics.2015.1631



## eTable 2. Variables Associated With Literacy and Mathematics Achievement-Test Proficiency by Hypoglycemia Cutoffs: <35, <40, and <45 mg/dL Excluding ELGANS[a]

| | Literacy | | | Mathematics | | |
|---|---|---|---|---|---|---|
| **Variable** | **<35 mg/dL [b]** | **<40 mg/dL [c]** | **<45 mg/dL [c]** | **<35 mg/dL [b]** | **<40 mg/dL [c]** | **<45 mg/dL [c]** |
| | **aOR (95% CI)** | **aOR (95% CI)** | **aOR (95% CI)** | **aOR (95% CI)** | **aOR (95% CI)** | **aOR (95% CI)** |
| Hypoglycemia | 0.51 (0.30-0.87) | 0.45 (0.29-0.70) | 0.62 (0.44-0.86) | 0.49 (0.29-0.82) | 0.51 (0.33-0.78) | 0.72 (0.52-1.003) |
| Gestational age group | | | | | | |
| FT | Ref | Ref | Ref | Ref | Ref | Ref |
| LPT | 0.83 (0.58-1.20) | 0.86 (0.60-1.25) | 0.86 (0.60-1.25) | 0.88 (0.61-1.28) | 0.91 (0.63-1.32) | 0.90 (0.62-1.30) |
| PT | 0.88 (0.58-1.34) | 0.96 (0.63-1.47) | 0.88 (0.58-1.34) | 0.76 (0.50-1.16) | 0.79 (0.52-1.21) | 0.73 (0.48-1.10) |
| Race | | | | | | |
| Black | Ref | Ref | Ref | Ref | Ref | Ref |
| White | 2.88 (2.20-3.77) | 2.90 (2.21-3.81) | 2.87 (2.19-3.76) | 2.87 (2.18-3.78) | 2.89 (2.19-3.81) | 2.85 (2.17-3.75) |
| Other | 4.13 (2.23-7.68) | 4.12 (2.22-7.66) | 4.15 (2.23-7.71) | 2.82 (1.52-5.22) | 2.78 (1.50-5.15) | 2.78 (1.50-5.14) |
| Male | 0.53 (0.41-0.68) | 0.53 (0.41-0.69) | 0.53 (0.41-0.69) | 0.83 (0.64-1.08) | 0.84 (0.65-1.09) | 0.84 (0.64-1.08) |
| Multifetal gestation | 0.50 (0.26-0.95) | 0.48 (0.25-0.93) | 0.47 (0.25-0.92) | 0.68 (0.36-1.27) | 0.66 (0.35-1.24) | 0.65 (0.35-1.22) |
| Insurance | | | | | | |
| Medicaid | Ref | Ref | Ref | Ref | Ref | Ref |
| Other | 0.87 (0.50-1.50) | 0.87 (0.50-1.51) | 0.89 (0.52-1.54) | 1.27 (0.72-2.25) | 1.28 (0.72-2.26) | 1.30 (0.74-2.29) |
| Private | 1.74 (1.17-2.61) | 1.74 (1.16-2.60) | 1.73 (1.16-2.60) | 1.80 (1.18-2.75) | 1.79 (1.17-2.73) | 1.79 (1.17-2.73) |
| Maternal education | | | | | | |
| <High school | Ref | Ref | Ref | Ref | Ref | Ref |
| High school graduate | 1.58 (1.17-2.13) | 1.56 (1.16-2.11) | 1.57 (1.16-2.12) | 1.32 (0.98-1.79) | 1.32 (0.98-1.78) | 1.33 (0.99-1.80) |
| >High school | 2.90 (1.98-4.25) | 2.86 (1.95-4.19) | 2.87 (1.96-4.21) | 2.20 (1.49-3.23) | 2.17 (1.48-3.20) | 2.18 (1.48-3.21) |
| Gravity | | | | | | |
| 1 | Ref | Ref | Ref | Ref | Ref | Ref |
| 2-3 | 0.57 (0.42-0.77) | 0.58 (0.43-0.79) | 0.57 (0.42-0.77) | 0.81 (0.60-1.09) | 0.82 (0.60-1.11) | 0.79 (0.59-1.07) |
| >3 | 0.40 (0.27-0.58) | 0.41 (0.28-0.60) | 0.40 (0.27-0.58) | 0.51 (0.35-0.74) | 0.52 (0.36-0.75) | 0.50 (0.35-0.73) |

Abbreviations: aOR, adjusted odds ratio; CI, confidence interval; FT, full-term; LPT, late preterm; PT, preterm; ELGAN, extremely low gestational age newborn.

SI conversion factors: To convert glucose to mmol/L, multiply values by 0.0555.

[a] Multivariate regression analysis displayed as adjusted odds ratios and 95% CI.

[b] Primary hypoglycemia cutoff.

[c] Secondary hypoglycemia cutoff.

JAMA Pediatr. 2015;169(10):913-921. doi:10.1001/jamapediatrics.2015.1531

# Concerns About Transient Hypoglycemia

- Transient newborn hypoglycemia was common:
  - (glucose level <35, <40, and <45 mg/dL) was observed in 6.4%, 10.3%, and 19.3% of infants, respectively.
- After controlling for multiple perinatal factors, early transient hypoglycemia was associated with "*decreased probability* of proficiency on literacy and mathematics fourth-grade achievement tests."
  - Probabilities of exposure more extensive for lower levels (<35 mg/dL)
  - Glucose levels 40-45 did not correlate with worse outcomes for math only for literacy,
- Recommendation:
  - "Given that the findings are serious and contrary to expert opinion, the results need to be validated in other populations before universal newborn glucose screening should be adopted."

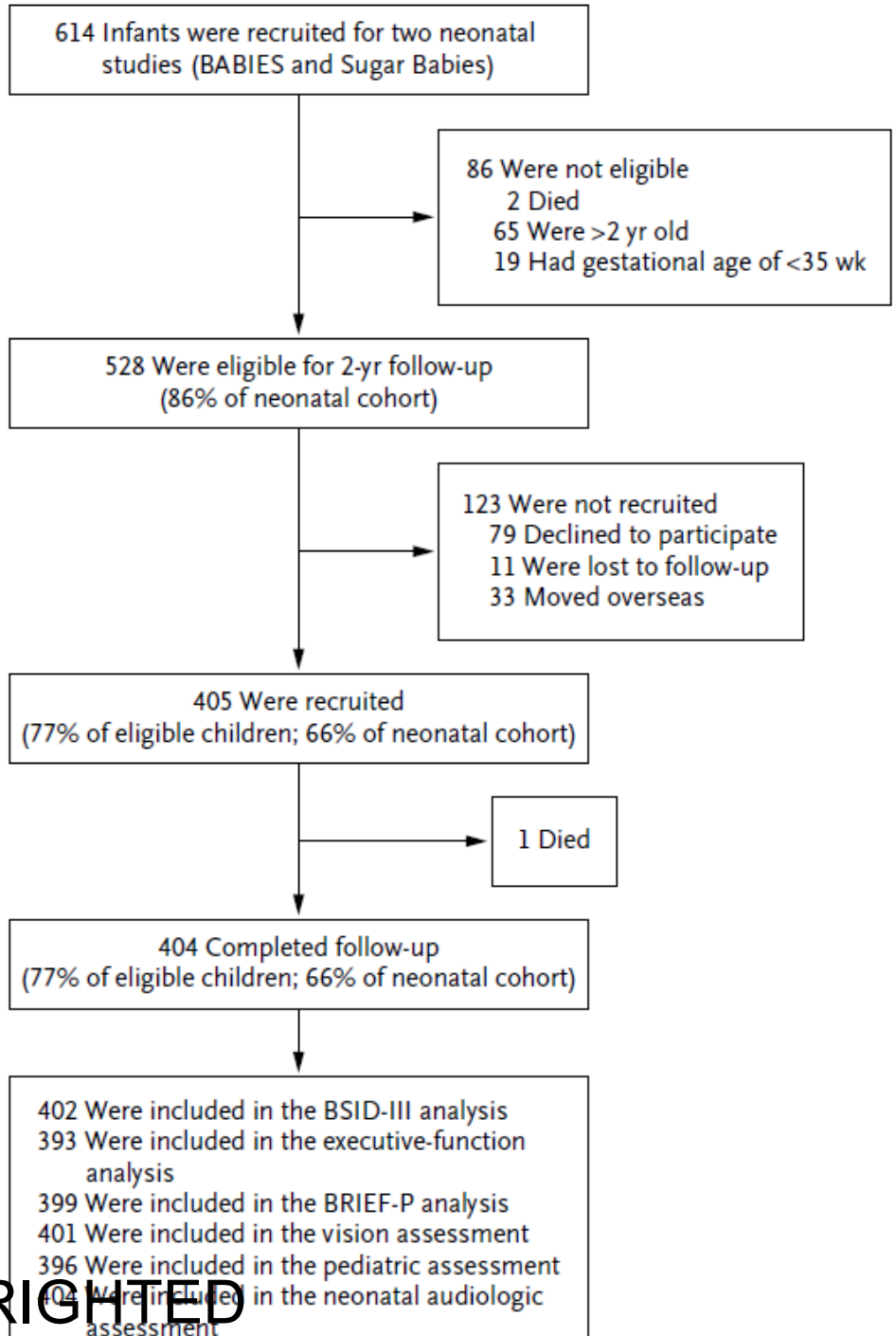
Kaiser J et al. *JAMA Pediatr.* 2015

# Limitations of Kaiser Study

- All newborns were tested, not at-risk newborns
- No analysis according to risk stratification
  - Did those at-risk for hypoglycemia, have worse outcomes in neurodevelopment?
- No controls for feeding (breastfeeding), skin to skin, or interventions to hypoglycemia

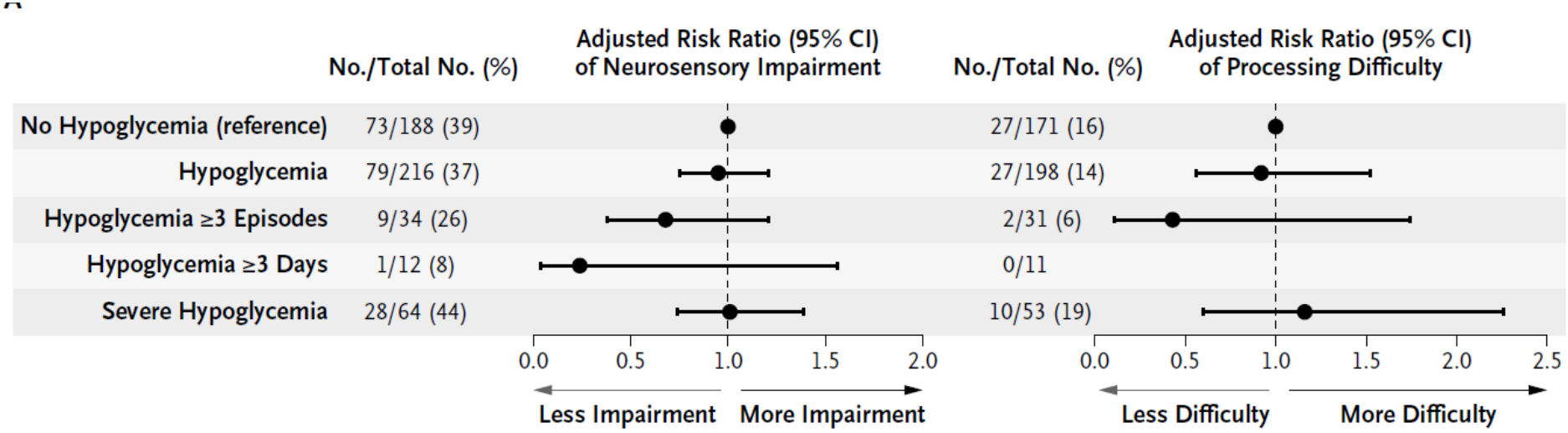
# Is treatment of asymptomatic hypoglycemia necessary?

>35 weeks gestation and
at risk for hypoglycemia
Treated to maintain glucose
Level >47 mg/dL




McKinlay et al NEJM October 2015

# No Effect of Treatment Group on Cognitive Performance




But they treated all blood sugars of 47 mg/dL or lower

McKinlay et al NEJM October 2015

# Caveat:
# Study Limitations

- Were healthy non-at-risk newborns included?
- Feeding method is NOT reported.
- Could have used expressed colostrum, but NOT part of the protocol.
- Skin-to-skin care NOT reported.
- Data do not define a threshold for safety or point when treatment is needed.

# Can Hypoglycemia Be Prevented?

# Can Hypoglycemia be Prevented?

- Strongest existing evidence:
  - Immediate and continuous skin-to-skin care

# Early skin-to-skin contact for mothers and their healthy newborn infants (Review)

2012 May 16;5:CD003519

Moore ER, Anderson GC, Bergman N, Dowswell T

## Summary

- 34 RCT's (2177 dyads)
- **Increased glucose 70-90 minutes, mean increase of 11 mg/dL (95% CI 8-13)**
- Increased breastfeeding 1-4 months AOR=1.27 (95% CI 1.06-1.53)
- Increased duration of breastfeeding mean difference 43 days (p=0.06)

# Baby-friendly USA STEP 4

- **Help mothers initiate breastfeeding within one hour**
  - *"Place babies in skin-to-skin contact with their mothers immediately following birth for at least an hour and encourage mothers to recognize when their babies are ready to breastfeed, offering help if needed."*
- This step applies to **all babies**, regardless of feeding method.

# Screening and Management of Postnatal Glucose Homeostasis in Late Preterm and Term SGA, IDM/LGA Infants

[(LPT) Infants 34 – $36^{6/7}$ weeks and SGA (screen 0-24 hrs); IDM and LGA ≥34 weeks (screen 0-12 hrs)]

**Symptomatic and <40 mg/dL ⟶ IV glucose**

## ASYMPTOMATIC

| Birth to 4 hours of age | 4 to 24 hours of age |
|---|---|
| INITIAL FEED WITHIN 1 hour<br>Screen glucose 30 minutes after 1st feed | Continue feeds q 2-3 hours<br>Screen glucose prior to each feed |
| Initial screen <25 mg/dL | Screen <35 mg/dL |
| Feed and check in 1 hour | Feed and check in 1 hour |
| <25 mg/dL ↓ IV glucose* | 25–40 mg/dL ↓ Refeed/IV glucose* as needed |
| <35 mg/dL ↓ IV glucose* | 35 – 45 mg/dL ↓ Refeed/IV glucose* as needed |

**Target glucose screen ≥45 mg/dL prior to routine feeds**

* Glucose dose = 200 mg/kg (dextrose 10% at 2 mL/kg) and/or IV infusion at 5–8 mg/kg per min (80–100 mL/kg per d). Achieve plasma glucose level of 40-50 mg/dL.

Symptoms of hypoglycemia include: Irritability, tremors, jitteriness, exaggerated Moro reflex, high-pitched cry, seizures, lethargy, floppiness, cyanosis, apnea, poor feeding.

AAP Committee on Fetus and Newborn. Pediatrics.*127(3); 2011:575 -579*

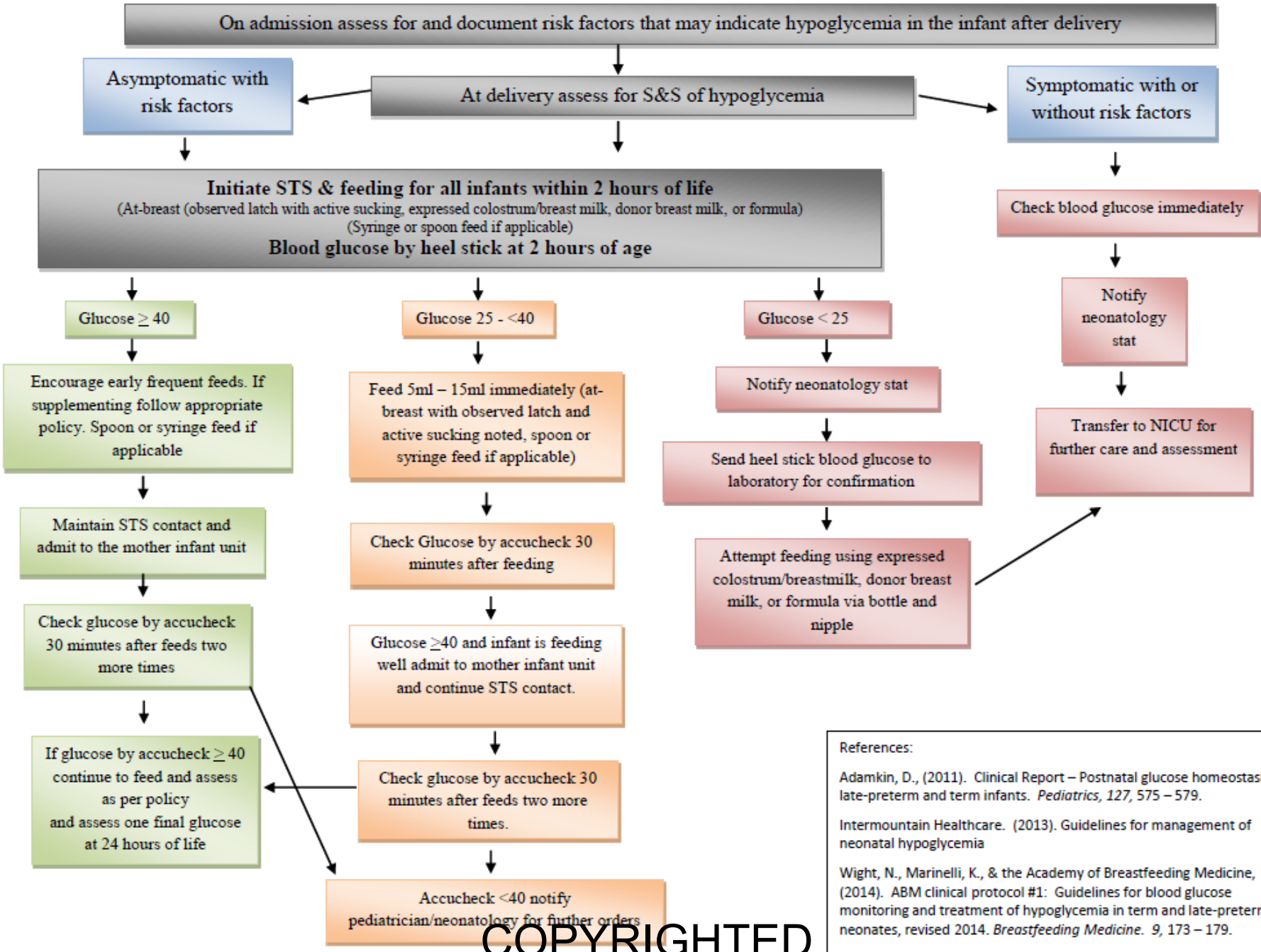
# First Steps of Protocol

- **Try to feed at risk newborns immediately, but by no later than 30 to 60 minutes of life**. Allow the infant to breastfeed or feed 3-5 ml/kg expressed colostrum (or formula if colostrum or donor milk unavailable)
- Obtain the **first** heel-stick blood **glucose** on all at-risk newborns no sooner than **30 minutes AFTER completion of the first feeding** but by no later than 2 hours of life. Check immediately if infant symptomatic.

# ABM Protocol #1

A. Early and exclusive breastfeeding meets the nutritional and metabolic needs of healthy, term newborn infants.
   1. Routine supplementation is unnecessary.
   2. Initiate breastfeeding within 30–60 minutes of life and continue on demand.
   3. Facilitate skin-to-skin contact of mother and infant.
   4. Feedings should be frequent, 10–12 times per 24 hours in the first few days after birth.

B. Glucose screening is performed only on at-risk infants or infants with clinical signs.
   1. Routine monitoring of blood glucose in all term newborns is unnecessary and may be harmful.
   2. At-risk infants should be screened for hypoglycemia with a frequency and duration related to the specific risk factors of the individual infant.
   3. Monitoring continues until normal, prefeed levels are consistently obtained.
   4. Bedside glucose screening tests must be confirmed by formal laboratory testing.

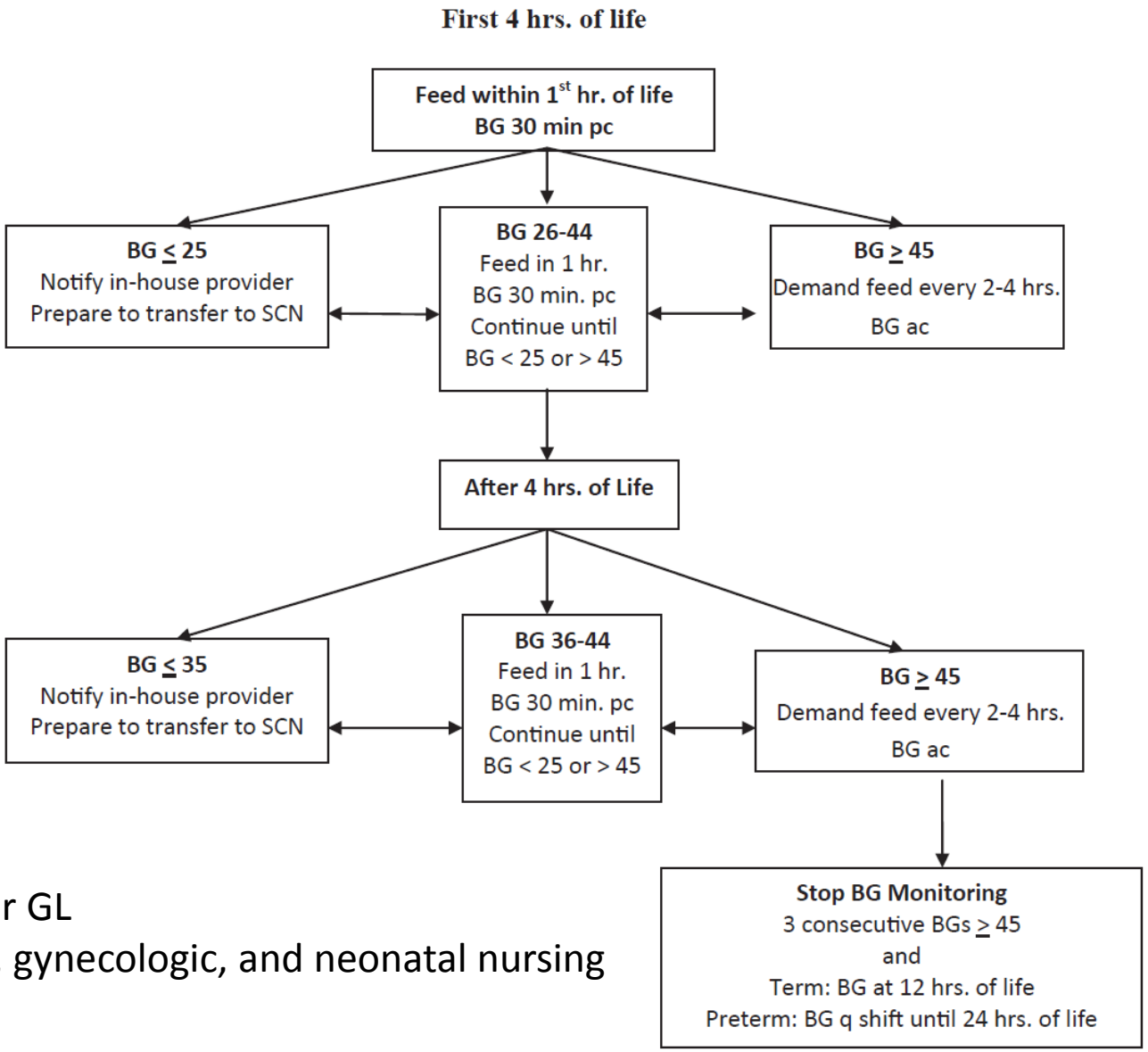



References:

Adamkin, D., (2011). Clinical Report – Postnatal glucose homeostasis in late-preterm and term infants. *Pediatrics, 127,* 575 – 579.

Intermountain Healthcare. (2013). Guidelines for management of neonatal hypoglycemia

Wight, N., Marinelli, K., & the Academy of Breastfeeding Medicine, (2014). ABM clinical protocol #1: Guidelines for blood glucose monitoring and treatment of hypoglycemia in term and late-preterm neonates, revised 2014. *Breastfeeding Medicine. 9,* 173 – 179.




Csont, G, Lowmaster GL
Journal of obstetric, gynecologic, and neonatal nursing
2014

**Figure 1.** Simplified algorithm for blood gas protocol. BG = blood gas; SCN = special care nursery; pc = after feedings; ac = before feedings.

# What are the Risks of Supplementation?

**Effects on Mom**

- Decreases confidence
- Decreases milk removal leading to increased autocrine control and decreased milk synthesis
- Leads to premature weaning

**Effects on Baby**

- Increases risk of short and long term disease
- Changes microbiology and immuno-biology of gut

**Effects on Dyad**

- Interferes with effective latch
- Decreases hormonal stimulation via afferent nerve receptors

# Take Away Messages

- Neonatal hypoglycemia may have a lasting impact on development
- Immediate skin-to-skin care within the first hour of life can help offset transient hypoglycemia
- Screening:
  - At-risk and symptomatic infants should be screened
  - Test feeds are unnecessary

*What if every parent knew that immediate skin to skin care can offset transient hypoglycemia?*