Treatment of the Hypoglycemic Infant (and his Mother!)

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Past President, Academy of Breastfeeding Medicine
Founding Member, Sec/Treas, San Diego County Breastfeeding Coalition
Advisory Board, ILCA
Advisory Council, HMBANA
Reality Sets In:

Age 15

Age 16

Age 17
Age 24
Sharp Mary Birch Hospital For Women & Newborns
San Diego, California, USA

Deliveries (2013): 8891
Births (2013): 9178
NICU: Total 62 ➔ 84 beds
NICU Admissions: 1562
VLBW Admissions (<1500g): 191
11 Perinatologists
11 Neonatologists (cover 4 hosp)
1.6 FTE Lactation Consultants
1.6 FTE Perinatal Dieticians
1.6 FTE Occupational therapists
1.1 FTE Physical therapists
163 FTE RNs

No Industry Support to Declare
Treatment of the Hypoglycemic Infant: OBJECTIVES

At the conclusion of the presentation the participant will be able to:

- Describe the normal newborn breastfeeding course in regards to feeding behavior, weight loss and gain, and stool progression.
- Recognize the normal pattern of blood glucose in term, well newborns.
- List at least 3 indications for appropriate glucose screening.
- Describe a breastfeeding-supportive approach for treatment of hypoglycemia.
Treatment of the Hypoglycemic Infant:

- **Introduction**
  - Normal Transition & Energy Metabolism in the Newborn
  - Pathogenesis & Diagnosis of Hypoglycemia in the Newborn
  - Breastfeeding-Supportive Prevention & Treatment of Hypoglycemia
  - ABM Hypoglycemia Protocol (2014)
- Conclusions
Treatment of the Hypoglycemic Infant

Conclusions: (for those of you who would like to sleep)

- Healthy, full-term infants are programmed to make the transition from fetus to newborn through the normal breastfeeding process.
- Routine monitoring of blood glucose in asymptomatic term neonates is unnecessary (and may be harmful).
- Hypoglycemia can be minimized by early, frequent breastfeeding and skin-to-skin contact.
- The symptomatic hypoglycemic infant is the one of concern for long term neurologic sequelae and needs IV glucose, not forced feedings.
- Mothers of “hypoglycemic” infants need support and empowerment to request evidence-based options for treatment of their infants.
- Supplementation with heat-treated donor human milk meets JC criteria for “exclusive” breastmilk feeding.
Breastfeeding

- Breastfeeding natural but not instinctive
  - Learned response
  - Few positive role models / Nearly a lost art
  - Expectations vs. reality

- “Successful” Breastfeeding
  - Who defines?
  - Any breastfeeding better than none
  - Breastfeeding vs. breastmilk feeding

- Breastfeeding “Failures”
  - Shortened Duration
  - Readmissions
  - Tragedies
Supporting Breastfeeding & Dealing With Early Concerns

- Most mothers are capable of breastfeeding successfully
- Conspiracy of silence sometimes impedes understanding of the problem
- Lactation, like ALL physiologic functions, sometimes fails because of various medical causes
  - Primary lactation failure (? 5%)
  - Secondary lactation failure (many)
    - Breastfeeding never established
    - Breastfeeding established, then lost
“Clinicians must overcome the tendency to view the complications of mismanaged breastfeeding as an indictment of the process.

Instead, pediatric practitioners are obliged to confront the reality of breastfeeding failure, identify associated risk factors, and implement intervention strategies to prevent infant morbidity.”
Infants know what they want!
Treatment of the Hypoglycemic Infant

- Introduction
- **Normal Transition & Energy Metabolism in the Newborn**
- Pathogenesis & Diagnosis of Hypoglycemia in the Newborn
- Breastfeeding-Supportive Prevention & Treatment of Hypoglycemia
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- Conclusions
Physiology of Transition

- Infants well hydrated via placenta at birth
- Urine output exceeds intake days 1-3
- Small colostrum feedings (2-15 ml) physiologic
  - appropriate for size of infant’s stomach
  - sufficient to prevent hypoglycemia in healthy term infants
  - easy to manage as infant learns to coordinate suck, swallow, breathing
  - sucking needs greater than quantity needed
Infant Stomach Capacity

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


The small volume of colostrum and small newborn stomach correlate nicely!
Neonatal weight loss in breast and formula fed infants.


Maximal wt loss (%)  
BF  FF  Mixed  
6.6  3.5  5.9

Timing of loss (days)  
BF  FF  Mixed  
2.7  2.7  2.5

Regain B. Wt (days)  
BF  FF  Mixed  
8.3  6.5  7.9

Figure 1 Cumulative distribution curves for the breast and formula fed groups for (A) weight nadir, (B) maximum weight loss, and (C) time to regain birth weight.
Physiological weight loss in the breastfed neonate: a systematic review

- Meta-analysis of 11 studies
  - Mean weight loss 5.7% to 6.6% with standard deviations ~ 2%
  - Majority of infants regained birth weight within the 1st 2 weeks postpartum
  - Maximum weight loss days 2-3 of life

- Methods used to report weight loss were inconsistent
  - 7% allowable weight loss in 4 clinical practice guidelines based on mean weight loss, and does not take into account SD
  - More research needed to understand:
    - causes of neonatal weight loss
    - and implications for morbidity & mortality
Colostrum Intake During First Day of Life
Santoro et al. J Peds 2010; 156(1): 29-32

“During the first 24 hrs of life, newborns ingested 15 ± 11 g of milk.”
Effect of caesarean section on breast milk transfer to the normal term infant over the first week of life

Evans KC et al. Arch Dis Child Fetal neonatal Ed 2003; 88:F380-382

Table 2  Breast milk transfer (ml/kg body weight) for days 1–6

<table>
<thead>
<tr>
<th>Group</th>
<th>Day 1</th>
<th>Day 2</th>
<th>Day 3</th>
<th>Day 4</th>
<th>Day 5</th>
<th>Day 6</th>
<th>Total days 1–6</th>
</tr>
</thead>
<tbody>
<tr>
<td>NVD</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean (SE)</td>
<td>6 (1.4)</td>
<td>25 (2.2)</td>
<td>66 (3.6)</td>
<td>106 (3.9)</td>
<td>123 (4.5)</td>
<td>138 (3.9)</td>
<td>450 (30.4)</td>
</tr>
<tr>
<td>Number</td>
<td>26</td>
<td>88</td>
<td>88</td>
<td>88</td>
<td>88</td>
<td>88</td>
<td>26</td>
</tr>
<tr>
<td>CS</td>
<td></td>
<td></td>
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<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean (SE)</td>
<td>4 (0.6)</td>
<td>13 (1.1)</td>
<td>44 (2)</td>
<td>82 (3.5)</td>
<td>111 (3.5)</td>
<td>129 (3.2)</td>
<td>358 (22.1)</td>
</tr>
<tr>
<td>Number</td>
<td>23</td>
<td>97</td>
<td>97</td>
<td>97</td>
<td>97</td>
<td>97</td>
<td>23</td>
</tr>
</tbody>
</table>

Unadjusted significance: 0.151 <0.001 <0.001 <0.001 0.033 0.079 0.020
Adjusted significance: 0.031 <0.001 0.001 <0.001 0.046 0.118 0.001

NVD Mothers:
- More multiparas
- 1st breastfeed sooner
- More breastfeeding experience

Figure 1  Profile of breast milk transfer (BMT) over the first six postnatal days to infants born by caesarean section (CS) or normal vaginal delivery (NVD).

Conclusion: volumes of milk recommended in texts was excessive.
First-Day NBN Wt Loss Predicts In-Hospital Wt Nadir for BF Infants

Flaherman et al. Breastfeeding Med 2010

- 1,049 term infants
- Mean in-hospital weight nadir was 6.0 ± 2.6%
- Mean age of nadir: 38.7 ± 18.5 hrs
- While in hospital 6.4% of infants lost ≥ 10% of birth weight.
- Infants losing ≥ 4.5% birth wt at < 24 hrs had a greater risk of in-hospital weight loss of ≥ 10% (AOR 3.57)
- 76.1% infants did not have a documented weight gain while in the hospital
Sample of healthy, exclusively breastfed newborns from 3 Dutch studies (2359 infants)

Nadir weight:
- Occurred at 2 days of age
- Mean weight loss 6.2% of BWt
  - 4.1% of newborns lost ≥ 10% BWt at day 2
  - 0.9% of newborns still had Wt loss ≥ 10% by day 4
  - 0.6% of newborns still had Wt loss ≥ 10% by day 7

Regained BWt:
- 50% by 7 days
- 88% by 14 days
- 95% by 19 days

More Wt loss associated with:
- High maternal age
- G1
- C/S
- Female infant
- High birth-weight

Fig. 2. Standard deviation score lines of the reference chart for relative weight change in healthy breast-fed newborns (logarithmic-scale axes). The dots presents the weight change of the newborns.
Excess Weight Loss in First-Born Breastfed Newborns Relates to Maternal Intrapartum Fluid Balance

AUTHORS: Caroline J. Chantry, MD, a Laurie A. Nommsen-Rivers, PhD, b Janet M. Peerson, MS, c Roberta J. Cohen, PhD, c and Kathryn G. Dewey, PhD c

a Department of Pediatrics, University of California, Davis, Medical Center, Sacramento, California; b Department of Pediatrics, Cincinnati Children’s Hospital, Cincinnati, Ohio; and c Department of Nutrition, College of Agricultural and Environmental Sciences, University of California, Davis, California

KEY WORDS
excess weight loss, infant, breastfeeding, intrapartum fluid balance, neonate

ABBREVIATIONS
CI—confidence interval
EWL—excess weight loss

WHAT’S KNOWN ON THIS SUBJECT: Excess weight loss is relatively common in term breastfed infants, occurring in up to 16% of first-born infants in previous studies. Delayed onset of lactogenesis and suboptimal infant breastfeeding behavior were associated with excess weight loss in multivariate analyses.

WHAT THIS STUDY ADDS: This study describes an independent association between excess weight loss among breastfed infants and maternal intrapartum fluid balance. The prevalence of excess weight loss—19% of exclusively breastfed, demographically diverse, first-born, term infants—was higher than previously reported.

Chantry et al. Peds 2011; 127(1):e171-179
http://www.pediatrics.org/cgi/content/full/127/1/e171
Newborn Wet and Soiled Diaper Counts and Timing of Onset of Lactation as Indicators of Breastfeeding Inadequacy
Nommsen-Rivers LA et al. JHL 2008; 24(1):27-33

Analysis of data from Dewey et al. Peds 2003; 112:607-619

Most efficient predictor of breastfeeding inadequacy:
- < 4 soiled diapers on day 4
- onset lactation > 72 hrs
Comparison of Breast- and Formula-Fed Normal Newborns in Time to First Stool and Urine

Metaj M et al. J Perinatology 2003; 23:624-628

- Chart review of 1000 consecutive infants
  - ≥ 34 weeks gest age
  - Not admitted to NICU
  - Feeding groups: Breast-fed, Formula-fed, Mixed-fed

- Results:
  - Breast-fed infants fed earlier & more frequently
  - Breast-fed infants voided earlier (7.3 vs 8.5 hrs, p=0.03)
  - Type of feeding did not predict time to first stool
  - **Gestational age predicted time of first stool**

Figure 2. This graph depicts the average time to first stool for each gestational age. Each age plotted represents all infants at that week of gestational age; for example, 36 weeks represents infants 36 0/7 weeks to 36 6/7 weeks inclusive. Standard deviations were omitted from the graph but ranged from 3.8 to 9.9 hours.
Breastfeeding Within the 1st hr Compared to > 1 hr Reduces Risk of Early-Onset Feeding Problems in Term Neonates


FIG. 1. Rate ratios by timing of first feed for all women and stratified by parity and delivery demonstrating the increasing rate of poor feeding with increased interval to the first feed. Multip, multiparous; NVD, normal vaginal delivery; Primip, primiparous.
Enough Milk?

- Maximal weight loss of < 8% by day 3-4
  - Begins to gain weight day 4-5
  - Regains birth weight by day 10-14
- Stool yellow, seedy, curdy by day 5
  - 4-12 (every feeding OK) stools/24 hrs by 1 week
- Urine dilute, colorless
  - 6-8 wets/24 hrs by day 5
- Feeding every 2-3 hours on average (8-12 feeds/24 hrs) and satisfied
- Normal tone and activity
- Jaundice stable or decreasing

Linda M. Blum, “At The Breast”, Beacon Press, 1999
Fetal Glucose Metabolism

- Enzymes present, but normal fetus does not produce glucose:
  - Relies on maternal glucose
  - Fetal glucose levels 70-80% of maternal
- Fetal pancreas secretes insulin in response to maternal glucose levels by ~ 20 weeks gestation
- Glycogen (stored form of glucose in the liver) storage begins ~ 27 weeks gestation
  - Liver, heart, skeletal muscles
- Increased fetal insulin levels
  - Inhibits gluconeogenesis (production of glucose from precursors) in the fetus
  - Encourages fat and glycogen storage for metabolic needs after cord is cut.

References:
Cornblath M et al. NEJM 1965; 273:378-380
Neonatal Energy Regulation

**Insulin**
- Peptide hormone produced by *beta cells* in the pancreas.
- Regulates the metabolism of carbohydrates and fats by promoting the absorption of glucose from the blood to skeletal muscles and fat tissue and by causing fat to be stored rather than used for energy.
- As a central metabolic control mechanism, its status is also used as a control signal to other body systems (such as amino acid uptake by body cells).
- In addition, it has several other anabolic (building) effects throughout the body.

**Glucagon**
- Peptide hormone, produced by *alpha cells* of the pancreas, that raises the concentration of glucose in the bloodstream.
- Effect is opposite that of insulin, which lowers the glucose concentration.
- Pancreas releases glucagon when the concentration of glucose in the bloodstream falls too low.
- Glucagon causes the liver to convert stored glycogen into glucose, which is released into the bloodstream.
Neonatal Energy Regulation

- **Glycogenolysis**
  - Stored glycogen (liver) broken down to release glucose in response to epinephrine & glucagon (from low blood glucose)

- **Gluconeogenesis**
  - Synthesis of glucose from lactate, glycerol, pyruvate & alanine

- **Alternate energy sources**
  - Ketones from brown fat
  - Glycerol from lipolysis
  - Alanine from proteolysis
  - Neonatal brain better able to utilize alternative fuel sources than adult brain
  - 50% of energy in diet from fatty acids
Blood Glucose Homeostasis

Diet → Intestine → Blood Glucose 70 mg/100 ml → Liver → Muscle and other tissues

Amino Acids

Glycerol → Lactic acid

Kidney → Urine

Brain → Fat
The Cord is Cut: Rapid increase in regulatory enzymes at birth

- Blood glucose levels drop in the first few hours after birth
- Catecholamines (epinephrine, norepinephrine, dopamine) & cortisol are released by adrenal in response to:
  - Stress of labor and delivery
  - Low blood sugar
- Falling insulin level promotes release of glucagon (stimulates release of glucose from the liver)
- Net result is increased lipolysis (breakdown of fat to release glucose), glycogenolysis (breakdown of stored glucose in the liver) and gluconeogenesis (formation of glucose from precursors) which leads to increased blood glucose
- Full-term, healthy newborn produces 4-6 mg/kg/min glucose (2X adult)
Neonatal Hypoglycemia

- Feature of another illness OR
- Failure to adapt from fetal continuous transplacental glucose consumption to extra-uterine intermittent nutrient supply
- Transient hypoglycemia in the newborn is common
  - Occurs in almost all mammalian species
  - Self-limited: resolves within 2-3 hrs, even if feedings withheld (in normal term infants)
Breastfed Infants: Glucose & Ketone Bodies


- Breastfed term infants have:
  - lower blood glucose and
  - higher ketone bodies

than formula-fed infants.

- Those infants who lose the most weight postnatally have the highest ketone body concentrations.

- Which suggests:
  - Provision of alternate fuels constitutes a **normal adaptive response** to transiently low nutrient intake during the establishment of breastfeeding.
  - Breastfed infants may well tolerate lower plasma glucose levels without any significant clinical manifestations or sequelae.
Miss Piggy Wardrobe malfunction
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Four Approaches to the Definition of Hypoglycemia

- Epidemiologic approach
- Clinical manifestations
- Acute changes in metabolic and endocrine responses and neurologic function
- Long term neurologic outcome
Epidemiologic Approach: What are NORMAL glucose levels?

- **It depends!** No Consensus re Definition of Hypoglycemia/Normoglycemia
- Values different in whole blood, plasma, serum
  - Glu concentration in plasma or serum 10-15% higher than in whole blood
- Varying study methodologies (age of infant, feeding regimens, time from last feeding)
Normal Pattern of Glucose Levels


\[
\begin{align*}
20 &= 1.1 \\
30 &= 1.7 \\
40 &= 2.2 \\
50 &= 2.8 \\
60 &= 3.3 \\
80 &= 4.4 \\
100 &= 5.6 \\
180 &= 10
\end{align*}
\]

\[\text{mg/dL} = \text{mmol/L}\]
Definitions of Neonatal Hypoglycemia

Age 0-3 hrs < 35 mg/dL (<2.0 mmol/L)
3-24 hrs < 40 mg/dL (<2.2 mmol/L)
> 24 hrs < 45 mg/dL (<2.5 mmol/L)


Age 0-24 hrs < 30 mg/dL (<1.7 mmol/L)
24-48 hrs < 40 mg/dL (<2.2 mmol/L)


Age < 24 hrs < 45 mg/dL (< 2.5 mmol/L)
24-72 hrs < 50 mg/dL (< 2.8 mmol/L)
> 72 hrs < 60 mg/dL (< 3.3 mmol/L)


Any age < 60 mg/dL (< 3.3 mmol/L)

No Consensus re Definition of Hypoglycemia/ Normoglycemia

- At < 40 mg/dL - 20.6-43% “hypoglycemic” \(^1,2\)
- At < 30 mg/dL - 4-11.4% “hypoglycemic” \(^1,3,4\)

“Significant hypoglycemia is not and can never be defined by a single number that can be applied universally to every individual patient. Rather, it is characterized by a value(s) that is unique to each individual and varies with both their state of physiologic maturity and the influence of pathology.”
Definition of Neonatal Hypoglycemia

“ At present there is neither a rational basis nor sufficient evidence to identify a specific value or range of plasma glucose concentrations that would define “hypoglycemia” as a pathologic entity.”


“In addition, there is no single concentration or range of plasma glucose concentrations that is associated with clinical signs.

Therefore, there is no consensus regarding ........ which concentration of glucose requires therapeutic intervention in the asymptomatic infant.

The generally adopted plasma glucose concentration that defines NH (neonatal hypoglycemia) for all infants (< 47 mg/dL) is without rigorous scientific justification.”

Adamkin DH and the Committee on Fetus and Newborn. Clinical Report – Postnatal Glucose Homeostasis in Late-Preterm and Term Infants. 2011; 127(3):575-579
## Operational Thresholds

**Operational thresholds for: Plasma Glucose**

<table>
<thead>
<tr>
<th>Intervention</th>
<th>&lt; 36 mg/dL (2.0 mmol/L)</th>
</tr>
</thead>
<tbody>
<tr>
<td>IV Glucose</td>
<td>&lt; 20-25 mg/dL (1.1-1.4 mmol/L)</td>
</tr>
<tr>
<td>Therapeutic objective</td>
<td>&gt; 45 mg/dL (2.5 mmol/L)</td>
</tr>
<tr>
<td>Therapeutic objective (profound/persistent ↓ Glu)</td>
<td>&gt; 60 mg/dL (3.3 mmol/L)</td>
</tr>
<tr>
<td>Preterm infants</td>
<td>Same as term</td>
</tr>
<tr>
<td>Infants on TPN</td>
<td>&gt; 45 mg/dL (2.5 mmol/L)</td>
</tr>
</tbody>
</table>
Operational Thresholds

- **1st 24 hrs:**
  - healthy term or preterm 34-37 wks, formula-fed: < 30-35 mg/dL (<1.7-2.0 mmol/L)
  - sick, LBW, preterm <34 wks:
    - < 45-50 mg/dL (<2.5-2.8 mmol/L)
- **> 24 hrs:**
  - < 40-50 mg/dL (<2.2-2.8 mmol/L)
- **Any age:**
  - <20-25 mg/dL (<1.1-1.4 mmol/L)
Population Meta-Analysis of Low Plasma Glucose Thresholds in Full-Term Normal Newborns

Population:
- Studies published 1986-1994 (BF less prevalent than today)
- 723 infants from 6 studies: 35% breastfed
- Whole blood studies converted to plasma values (plasma values higher by 13.5%)
- Exclusively breastfed study excluded
  - Known lower glucose levels than formula-fed
  - **Low thresholds for exclusively breastfed might be lower**

<table>
<thead>
<tr>
<th>Results: Rec Low Thresholds</th>
<th>Hour after birth</th>
<th>≤5%tile PGL mg/dL (mmol/L)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1-2 (nadir)</td>
<td>28 (1.56)</td>
<td></td>
</tr>
<tr>
<td>3-23</td>
<td>40 (2.22)</td>
<td></td>
</tr>
<tr>
<td>24-47</td>
<td>41 (2.28)</td>
<td></td>
</tr>
<tr>
<td>48-72</td>
<td>48 (2.67)</td>
<td></td>
</tr>
</tbody>
</table>
Definitions of Hypoglycemia:
Clinical Signs Associated with Hypoglycemia – Non-specific!

- Changes in levels of consciousness
  - irritability
  - lethargy
  - stupor
- Apnea, cyanotic spells
- Coma
- Feeding poorly, after feeding well
- Hypothermia
- Hypotonia, limpness
- Tremor
- Seizures

Clinical signs should be alleviated with correction of plasma glucose levels.

Pathogenesis of Hypoglycemia in Neonates: Excess Utilization

- XS insulin
- XS glucose use for thermoregulation
- XS use for muscle activity
- XS anaerobic metabolism
- XS glucose-dependent tissues
- Inborn errors of metabolism
- Acute brain injury
Pathogenesis of Hypoglycemia in Neonates: Inadequate Production or Substrate Delivery

- Inadequate or delayed feedings
- Aberrant hormonal regulation of glucose or lipid metabolism
- Transient developmental immaturity of critical metabolic pathways
- Deficient metabolic reserves of precursors or glucose-sparing substrates
- Deficient brain glucose transporters
- Suppression of gluconeogenesis, glycogenolysis and hepatic glucose release
Pathogenesis of Hypoglycemia in Neonates: Main Causes

- Decreased substrate availability (low stores)
- Increased energy use (long labor, cold stress, resp. distress, etc.)
- Hyperinsulinism
  - IDM
  - Beckwith-Wiedemann
  - Islet cell hyperplasia; tocolytic drugs, etc.
- Other causes: erythroblastosis, ExTx, PC/HV, sepsis, CHD, metabolic disorders, etc.
Definitions of Hypoglycemia:

Acute Physiologic Changes

- Research has failed to define “safe” blood glucose concentration or “threshold” for neurologic damage using: EEG, VEP, BAER
- 4 times # HUS/MRI abnormalities in 18 SYMPTOMATIC full-term infants as normoglycemic controls. All but 1 resolved. (Kinnala, Pediatr, 1999)
- Neural damage attributed to hypoglycemia is not just inadequate energy stores:
  - Result of accumulation of toxic substances (e.g., aspartic acid)
  - Because this takes time:
    - BRIEF PERIODS OF HYPOGLYCEMIA ARE UNLIKELY TO CAUSE NEUROLOGIC DAMAGE.
Definitions of Hypoglycemia: Long Term Neurologic Outcome

- Limited data:
  - Lack of suitable non-hypoglycemic controls
  - Failure to consider other pathology
  - Small number of asymptomatic hypoglycemic infants followed

- Factors to consider
  - How low?
  - How long?
  - Varies from infant to infant
  - Other factors important

- Immature brain incredibly resistant to hypoglycemic damage (many mechanisms)
Acute Changes/Long Term Outcome

Rat Studies:

- Neuronal necrosis occurred with:
  - glucose < 18 mg/dL (< 1 mmol/L) **PLUS**
  - long enough to induce a flat EEG for ≥ 30 min

  Siesjo, Diabetes Metab Rev 1988; 4:113-144
  Auer et al, Diabetes 1984; 64:177-191
Symptomatic Hypoglycemia in Otherwise Healthy, Breastfed Term Newborns
Moore AM, Perlman M. Pediatrics 1999; 103:837-839

- 3 cases that presented at home with seizures or apnea, day 3
  - 3 cases admitted between 1993-1997; all 3 male
  - Geographic area with 65,000 annual births
  - Full-term with no recognized perinatal risk factors for hypoglycemia
  - 2 of 3 primips; all normal pregnancy and SVD
  - All three feeding poorly at and after discharge

- Outcomes: 2 normal; 1 delayed in special school
- All 3: No urinary ketones → defective ketogenic response
“Evidence from studies of humans and other animals suggests that cortical damage and long-term sequelae occur after prolonged hypoglycemia sufficiently severe to cause neurologic signs.”
Long term outcome of asymptomatic hypoglycemia

“No studies have demonstrated harm from a few hours of asymptomatic hypoglycemia during this normal postnatal period of establishing “physiological glucose homeostasis”.”


“...little or no evidence exists to indicate that asymptomatic neonatal hypoglycemia at any concentration of plasma glucose in the first days of life results in any adverse sequelae in growth or neurologic development.”

HYPOGLYCEMIA IN THE BREASTFED NEWBORN

- Introduction
- Normal Transition & Energy Metabolism in the Newborn
- Pathogenesis & Diagnosis of Hypoglycemia in the Newborn
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- ABM Hypoglycemia Protocol (2014)
- Conclusions
Early and exclusive breastfeeding meets the nutritional requirements of healthy, full-term newborn infants.

Healthy, full-term infants do not develop symptomatic hypoglycemia simply as a result of underfeeding.
Glucose Screening

- Routine screening and monitoring of blood glucose concentration is not needed in healthy term newborn infants after an entirely normal pregnancy and delivery.

- Blood glucose concentration should only be measured in term infants who have clinical manifestations or who are known to be at risk.

  - Adamkin DH and Committee on Fetus and Newborn, Pediatrics 2011; 127(3):575-579
Hypoglycemia: Clinical Management

- Monitoring infants at highest risk
- Confirming plasma glucose low
- Demonstrating that symptoms resolve after restoring plasma glucose to normal
- Observing and documenting all these events
Assessment of Glucose Levels

- Bedside glucose testing strips
  - Inexpensive and practical
  - Not reliable (Ho et al, Arch Dis Child Fetal Neonatal Ed, 1996)
    - ~ 20% false positive (low value when true glucose higher)
    - Not satisfactory as sole measuring device

- Newer point-of-care devices – still not as accurate as laboratory measurement
  - glucose electrode (YSI)
  - glucose oxidation optical method (Hemo-Cue)

- Use bedside devices for screening
- Confirm and treat on laboratory value (esp. in case of asymptomatic infant)
To Prevent/Minimize Hypoglycemia

- Assess Hx, PE for risk factors for ↓ Glu
- Very selective glucose screening
- Mother and infant continuously together
- Early and frequent breastfeeding - nurse within 30-60 mins of birth
Transition: Cot vs Skin-to-Skin Care

- RCT of immediate post-partum care of 50 term healthy newborns during first 90 minutes
- Skin-to-skin intervention improves:
  - Axillary and skin temperature
  - Blood glucose levels
  - Recovery from negative base deficit
  - Infant crying
- “Keeping the baby skin-to-skin with the mother preserves energy and accelerates metabolic adaptation and may increase the well-being of the newborn”
- Similar RCT of skin-to-skin by fathers after C-section showed significant benefit


Christensson K et al. Lancet 1998; 352(9134:1115
Mother-Baby Separation

- 1-2 hours after birth, infants separated from their mothers exhibit “separation distress crying”
  - Stops upon reunion with the mother
  - Cries are distinctly different from newborn hunger and pain crying
- Infants placed in a cot for the first 90 minutes after birth cried 10x more than those placed skin-to-skin with mother

Selective Screening for Hypoglycemia

- SGA (<10th %tile)
- Discordant (smaller) twin
- LGA (>90th %tile, in certain populations)
- IDM
- LBW (<2500 gm)
- Post-asphyxia
- Erythroblastosis fetalis
- Polycythemia/hyperviscosity
- Cold stress/hypothermia
- Presence of microphallus or midline defect
- Beckwith-Wiedemann Syndrome or other endocrine or inborn errors of metabolism
- Other stressors, such as RDS, sepsis, etc.
Treatment of Symptomatic Hypoglycemia

- IV glucose: 2cc/kg 10% glucose bolus, followed by continuous infusion of 6-8 mg/kg/min (approx 100 cc/kg/d)
- Encourage frequent breastfeeding after relief of symptoms
- Adjust IV rate by blood glucose concentration
- Gradually wean IV rate as feeding resumed, checking glucose concentrations before feedings until off IV fluids
- Document signs, physical exam, screening values, laboratory values, treatment and response
Treatment of **Asymptomatic Hypoglycemia**

- Continue breastfeeding q1-2 hrs or feed expressed breastmilk or breastmilk substitute (approx 5-15 ml)
  - Recheck blood glucose before subsequent feedings until value is stable in the normal range
  - If neonate is unable to suck, avoid intragastric feeding and begin intravenous therapy. Such an infant is not normal and requires careful examination and evaluation.
  - If enteral feeding is not tolerated, begin IV glucose

![Decision tree with suggested guidelines for the management of infants with hypoglycemia. * Levels arbitrary and not ‘normal’ or ‘hypoglycemic’](image-url)
Clinical Report—Postnatal Glucose Homeostasis in Late-Preterm and Term Infants

David H. Adamkin, MD and COMMITTEE ON FETUS AND NEWBORN

KEY WORDS
newborn, glucose, neonatal hypoglycemia, late-preterm infant

ABBREVIATIONS
NH—neonatal hypoglycemia
D\textsubscript{10}W—dextrose 10\% in water

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abstract

This report provides a practical guide and algorithm for the screening and subsequent management of neonatal hypoglycemia. Current evidence does not support a specific concentration of glucose that can discriminate normal from abnormal or can potentially result in acute or chronic irreversible neurologic damage. Early identification of the at-risk infant and institution of prophylactic measures to prevent neonatal hypoglycemia are recommended as a pragmatic approach despite the absence of a consistent definition of hypoglycemia in the literature. *Pediatrics* 2011;127:575–579
Abstract
This report provides a practical guide and algorithm for the screening and subsequent management of neonatal hypoglycemia. Current evidence does not support a specific concentration of glucose that can discriminate normal from abnormal or can potentially result in acute or chronic irreversible neurologic damage. Early identification of the at-risk infant and institution of prophylactic measures to prevent neonatal hypoglycemia are recommended as a pragmatic approach despite the absence of a consistent definition of hypoglycemia in the literature.

Adamkin DH and Committee on Fetus and Newborn, Pediatrics 2011; 127(3):575-579 (FREE download from Pediatrics and AAP)
Adamkin D et al. Committee on the Fetus and Newborn, AAP, Pediatrics, March 2011

- Very similar to ABM statement (used many similar references and statements)

- Had to “fight off” endocrinologists who wanted 60 mg/dl (3.3 mmol/L) as lowest acceptable value

- Compromised at 40 mg/dL (2.2 mmol/L)
New AAP Policy Statement

Very similar to ABM statement (used many similar references and statements)

Had to “fight off” endocrinologists who wanted 60 mg/dl (4.4 mmol/L) as lowest acceptable value

Compromised at 40 mg/dL (3.3 mmol/L)

- Prospective determination of hypoglycemia defined as < 47 mg/dL (< 2.6 mM/L) in 514 Pts
  - ≥ 35 wks + SGA, LGA, IDM, late preterm or other
  - Standard protocol for timing and method of sampling
  - Bedside glucose oxidase method (Blood gas)
  - Part of prospective trial of treatment trial

Results

- Median number of Glu measurements per baby was 9 (1-22)
  - 51% had Glu < 47 mg/dL (< 2.6 mM)
  - 19% had Glu < 36 mg/dL (< 2.0 mM)
  - 37% had first low glucose after 3 normal measurements

- No difference in incidence, timing or severity of low glu concentrations between the 4 groups
  - Babies with ≥ 3 risk factors were more likely to have severe decreased glucose

- No evidence that ANY numerical cutoff is more valid than any other.

- Description of condition:
  - NOT – a low blood glucose measurement
  - BUT – “impaired metabolic adaptation”

- Unrealistic task to assign one number in an area that contains so many variables,
  - Therefore, use Cornblath’s thresholds and therapeutic goals (Peds 2000)

Most appropriate definition:

- “A persistently low blood glucose level measured with an accurate device in a baby at risk for impaired metabolic adaptation but no clinical signs,
- OR
- A single low blood glucose in a baby presenting with abnormal clinical signs.”

- No difference in preterm infants with and without transient low blood glucose in Developmental Quotient at 2 and 15 years (Tin, Peds 2012; 130:497-503)

Key Points:
- Frequently observed transient low blood glucose is reflection of normal metabolic adaptation, not pathology.
- No single “cut-off” blood glucose level defines clinical significance (ie. DON’T USE 47!)
- Use operative thresholds per Cornblath in at risk newborns
HYPOGLYCEMIA IN THE BREASTFED NEWBORN

- Introduction
- Normal Transition & Energy Metabolism in the Newborn
- Pathogenesis & Diagnosis of Hypoglycemia in the Newborn
- Breastfeeding-Supportive Prevention & Treatment of Hypoglycemia
- ABM Hypoglycemia Protocol (2014)
- Conclusions
ABM Hypoglycemia Protocol, 2014

**General Management Recommendations**


- Early and exclusive breastfeeding meets the nutritional and metabolic needs of healthy term infants
  - Routine supplementation unnecessary (harmful)
  - Initiate breastfeeding within 30-60 min of life and continue on demand
  - Promote skin-to-skin contact
  - Frequent feeds: 10-12 X/24 hrs first few days

- Glucose screening only on at-risk and symptomatic infants
  - Routine monitoring unnecessary (harmful)
  - Screen at-risk with frequency and duration relevant to specific risk factors
  - Continue monitoring until pre-prandial levels consistently normal
  - Bedside glucose screening must be confirmed in laboratory
ABM Hypoglycemia Protocol, 2014
Management of Documented Hypoglycemia

Symptomatic Infants or Plasma glucose < 20-25 mg/dL (<1.1-1.4 mmol/L)

- Initiate 10% glucose solution IV with bolus
- Do not rely on forced po or NG feedings
- Maintain glucose > 45 mg/dL (> 2.5 mmol/L)
- Adjust IV rate by blood glucose
- Encourage frequent breastfeeding after relief of symptoms
- Monitor pre-prandial glucose concentrations as the IV is weaned, until values are stable off IV fluids
- Carefully document signs, PE, screening values, lab values, Rx and response to Rx
Asymptomatic Infant

- Continue breastfeeding (~ q 1-2 hrs) or feed 3-5 ml/kg (up to 10 ml/kg) of expressed breastmilk or substitute nutrition
- Recheck pre-prandial blood glucose until acceptable and stable
- Avoid forced (NG) feedings if the infant is not able to suck
- If glucose remains low despite feedings, begin IV therapy
- Breastfeeding may continue during IV therapy
- Carefully document signs, PE, screening values, lab values, Rx and response to Rx
ABM Hypoglycemia Protocol, 2014
Supporting the Mother

- Maternal anxiety
  - She has done something wrong
  - Her milk is not adequate/good
  - Supplementation will ruin breastfeeding

- Maternal Support
  - Overcome maternal feelings of inadequacy
  - Help establish a full milk supply
    - Stimulate the breasts by manual or mechanical expression to mimic normal infant
    - Keep infant at breast or return to breast ASAP
    - Skin-to-skin care
Acceptable Medical Reasons for the Use of Breast-Milk Substitutes

WHO/UNICEF 2009

**Infant Conditions**
- Infants who should not receive breastmilk or any other milk except specialized formulas (eg. classic galactosemia)
- Infants for whom breastmilk remains the best feeding option but who may need other food for a limited period in addition to breastmilk (eg. hypoglycemia, LBW)

**Maternal Conditions**
- Mothers who should avoid breastfeeding permanently (eg. chemotherapy)
- Mothers who should avoid breastfeeding temporarily (eg. herpes on breast, rare medications)
- Mothers for whom breastfeeding is not contraindicated, although they present health problems of concern (eg. TB, substance abuse)
What to Supplement

Quantity (term newborn):
- 2-10 ml 1st 24 hrs
- 5-15 ml 24-48 hrs
- 15-30 ml 48-72 hrs

Quality
- Expressed Mom’s Breastmilk
- Pasteurized Donor Human Milk
- Elemental/Hypoallergenic formulas
- Regular infant formula
- Soy formula
- Glucose water
How to Supplement: Current Alternative Feeding Techniques

- Most common techniques:
  - Developing countries: CUP
  - Developed countries: BOTTLE

- Other techniques:
  - Finger-feeding
  - Dropper, spoon
  - Syringe
  - SNS
Alternative Feeding Methods

- Goal of ANY Alternative Feeding Method:
  - To establish or restore full direct breastfeeding

- Why the Concern About Bottle Feeding?
  - The main advantage of supplementing without a bottle is the non-verbal message to the parents that the alternative method is temporary.
  - Bottle-feeding is physiologically very different than breastfeeding.
Randomized Clinical Trial of Pacifier Use and Bottle-Feeding or Cupfeeding and Their Effect on Breastfeeding.

- Supplemental feedings, regardless of method (cup or bottle), had a large detrimental effect on BF duration.
- For those infants delivered by C-section, cupfeeding significantly prolonged exclusive, full and overall duration (by 10 wks!) of BF.
- For those infants receiving > 2 supplements, cupfeeding prolonged exclusive and full BF.
- For those infants receiving >3 supplements, cupfeeding prolonged exclusive, full and overall duration of BF.
- Infants fed by bottle received significantly more volume (121 vs 67 mL) than cupfed infants.
- Early pacifier use significantly shortened overall breastfeeding duration.
Selection Criteria for Alternative Methods:

- Cost and Availability
- Ease of use and ease of cleaning
- Stress to infant
- Whether an adequate volume of milk can be fed to the infant in 20-30 minutes
- Whether use will be short or long term
- **Whether the method enhances the development of breastfeeding skills**
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Working Within the Hospital & Healthcare System

- Develop key physician support
  - Enlist (or create) a breastfeeding knowledgeable physician champion
  - Summarize issues (elevator speech)
- Develop key nursing support
  - Nurse manager(s)
  - Nurse educators/clinical specialists
- Create evidence-based hypoglycemia policy and procedure (and summary algorithm)
  - Use what you have learned here
  - AAP and ABM references are key
  - Make the new P & P a mandatory competency
Joint Commission releases standard to measure exclusive breastfeedings in birth hospital

by Lori Feldman-Winter, M.D., M.P.H., FAAP, and Susan Landers, M.D., FAAP

Persistently low rates of exclusive breastfeeding in the United States have been observed over the past several decades. In addition, the gap is expanding between the numbers of mothers who initiate any breastfeeding vs. mothers who give nothing but human milk to their infants.

According to the latest data from the Centers for Disease Control and Prevention’s National Immunization Survey, nearly one in four breastfed infants receives formula supplements before hospital discharge, despite little evidence that these supplements are medically indicated, and the rate is rising (www.cdc.gov/breastfeeding/data/NIS_data).

Because of the huge contributions to infant and maternal health and wellness from exclusive breastfeeding, and to address the concern of excessive formula use, the Joint Commission has revised the Pregnancy and Related Conditions core measure. The new Perinatal Care Core Measures set was released in April and includes the following measures:

1. elective delivery,
2. Caesarean section,
3. antenatal steroids,
4. health care-associated bloodstream infections in newborns.

A new measure will require hospitals to track breastfeeding rates among healthy newborns in the nursery. Adoption of the AAP-endorsed “Ten Steps to Successful Breastfeeding” can help increase exclusive breastfeeding.
Conclusions: (for those of you who would like to sleep)

- Healthy, full-term infants are programmed to make the transition from fetus to newborn through the normal breastfeeding process.
- Routine monitoring of blood glucose in asymptomatic term neonates is unnecessary (and may be harmful).
- Hypoglycemia can be minimized by early, frequent breastfeeding and skin-to-skin contact.
- The symptomatic hypoglycemic infant is the one of concern for long term neurologic sequelae and needs IV glucose, not forced feedings.
- Mothers of “hypoglycemic” infants need support and empowerment to request evidence-based options for treatment of their infants.
- Supplementation with heat-treated donor human milk meets JC criteria for “exclusive” breastmilk feeding.
Treatment of the Hypoglycemic Infant: Selective References

- AAP, Committee on Fetus and Newborn, Postnatal Glucose Homeostasis in Late Preterm and Term Infants. *Pediatrics* 2011; 127:575-579