Newborn Glucose Regulation
Preparation for Extrauterine Life

- In utero, fetus relies primarily on placental transfer of glucose and nutrients from mother to meet energy demands.
- Fetal glucose values are approximately 70 – 80% of maternal value.
- Fetus stores glucose in form of glycogen in 3rd trimester – especially the last month.
Preparation for Extrauterine Life

Glycogen Stores

Term

Preterm or SGA
After Birth

Glycogen Stores

- Enzymes activate breakdown of glycogen back into glucose molecules
- Glucose released into bloodstream to maintain blood sugar
After Birth

Glycogen Stores

- Enzymes activate breakdown of glycogen back into glucose molecules
- Glucose released into bloodstream to maintain blood sugar
Factors Impacting Glucose Levels

- Inadequate Glycogen Stores
- Hyperinsulinemia
- Increased Glucose Utilization
Inadequate Glycogen Stores

High Risk Infants

- Preterm
- Small for gestational age (SGA) - with asymmetric and symmetric growth
  - Risk for hypoglycemia in term SGA infants
  - Markedly ↑ risk in preterm SGA infants
Inadequate Glycogen Stores

Rapidly depleted …

Term

Preterm and SGA
Late Preterm Infant

- 34 – 36 completed weeks gestation
- Metabolically and physiologically immature
- Increased risk for:
  - Hypoglycemia
  - Feeding problems – delayed or problematic breastfeeding
  - Temperature instability
  - Respiratory distress, apnea
  - Hyperbilirubinemia
  - ↑ Hospital readmission rates
  - 3-fold higher mortality rate than term infants
Small for Gestational Age

- Birthweight < 10th percentile for gestational age
- Causes of SGA or intrauterine growth restriction:
  - Fetal factors → chromosomal, genetic, syndromes, metabolic disorders, intrauterine viral infection
  - Maternal factors → nutrition, chronic illness, uterine, placental, drug/toxin abuse, prescribed medications, genetic/familial, chronic stress
- A chronically stressed fetus uses most (or all) of placentally transferred glucose for growth and survival
Hyperinsulinemia

*Infant of a Diabetic Mother (IDM)*

- Elevated maternal glucose levels → glucose crosses placenta → increased fetal insulin production and release
- After umbilical cord cut → insulin level remains elevated → blood glucose drops rapidly → hypoglycemia
- Insulin is major growth hormone → increased levels cause fetal macrosomia (birthweight > 4000 grams)
Hyperinsulinemia

Infant of a Diabetic Mother (IDM)

- Macrosomic infants → increased risk for birth complications
  - Shoulder dystocia
  - Brachial plexus injury
  - Arm and clavicle fractures
  - Organ injury
  - Perinatal asphyxia
Hyperinsulinemia

Large for Gestational Age (LGA)

- Birthweight > 90th percentile for gestational age
- Causes:
  - Ethnic, genetic, or in case of males, a higher % lean body mass
  - Maternal glucose levels during pregnancy → maternal diabetes may be unrecognized
**Gestational Diabetes Mellitus (GDM)**

- Follow-up testing and evaluation 6 – 12 weeks postpartum is recommended
  - 7-fold increased risk for developing type 2 diabetes
  - Screening for diabetes every 3 years
- Increased risk for GDM in subsequent pregnancies
- Healthcare consequences for offspring include future diabetes, childhood obesity, cardiovascular disease, and hypertension
Maternal Diabetes

Gestational and Maternal Type 2 Diabetes

- Screening may include hemoglobin A1c (HbA1c)
  - Elevated plasma glucose level → excessive glucose enters RBC and attaches to hemoglobin A → HbA1c formed
  - Estimates average blood glucose over previous 3 months

<table>
<thead>
<tr>
<th>HbA1c Values</th>
</tr>
</thead>
<tbody>
<tr>
<td>Non-Diabetic</td>
</tr>
<tr>
<td>5%</td>
</tr>
</tbody>
</table>
Increased Glucose Utilization

**Sick Infants**
- Infection
- Birth stress
- Hypoxia $\rightarrow$ anaerobic glycolysis
- Shock $\rightarrow$ anaerobic glycolysis
- Respiratory disease
- Cardiac disease
- Hypothermia
- **Limited stores** are rapidly depleted
  - Preterm
  - Small for gestational age

Rapid depletion of glycogen stores
Aerobic Metabolism

1 molecule glucose

Glycolysis

ATP

Pyruvic Acid

In the presence of oxygen

O₂

Krebs cycle
Anaerobic Metabolism

Consequences of anaerobic metabolism:

- Accelerated glucose utilization
- Metabolic acidosis
- Cellular dysfunction

In the ABSENCE of oxygen
Review Infants at Risk for Hypoglycemia

- SGA - Small for Gestational Age
- Premature
- LGA - Large for Gestational Age
- IDM - Infant of Diabetic Mother
- Stressed
- Sick

↓ Glycogen stores
↓ Hyperinsulinism
↑ Glucose utilization
Blood Glucose Monitoring

- Glucose is the major source of metabolic fuel for newborns
  - Transported to organs and tissues in blood → “blood sugar”
- Gold standard for monitoring level of blood sugar is plasma glucose value
- Infants with risk factors or who have signs/symptoms of hypoglycemia → evaluate blood sugar
Blood Glucose Screening

- Whole blood glucose bedside test → estimates plasma glucose level
- May be 10 – 18% lower than plasma value
- Obtain every 15 – 30 minutes until > 50 mg/dL (2.8 mmol/L) on at least 2 consecutive tests
- If low, obtain a plasma glucose level
  - But do not delay treatment!
### Signs / Symptoms of Hypoglycemia

<table>
<thead>
<tr>
<th>General Findings</th>
<th>Neurologic Signs</th>
<th>Cardiorespiratory Signs</th>
</tr>
</thead>
<tbody>
<tr>
<td>Abnormal cry – weak, high-pitched</td>
<td>Tremors</td>
<td>Tachypnea</td>
</tr>
<tr>
<td>Poor feeding – poor suck and coordination</td>
<td>Jitteriness</td>
<td>Respiratory depression</td>
</tr>
<tr>
<td>Hypothermia</td>
<td>Irritability</td>
<td>Apnea</td>
</tr>
<tr>
<td>Diaphoresis</td>
<td>Hypotonia</td>
<td>Cyanosis</td>
</tr>
<tr>
<td></td>
<td>Lethargy</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Seizures</td>
<td></td>
</tr>
</tbody>
</table>
Definition of Hypoglycemia

Glucose delivery or availability which is inadequate to meet glucose demand

Exact glucose value which defines hypoglycemia remains controversial

- Lack of definitive evidence:
  - Which glucose values and under what conditions neurologic damage occurs
  - Impact of asymptomatic hypoglycemia on neurodevelopmental outcome
ABM Clinical Protocol #1: Guidelines for Blood Glucose Monitoring and Treatment of Hypoglycemia in Term and Late-Preterm Neonates, Revised 2014

Nancy Wight, Kathleen A. Marinelli, and The Academy of Breastfeeding Medicine

A central goal of The Academy of Breastfeeding Medicine is the development of clinical protocols for managing common medical problems that may impact breastfeeding success. These protocols serve only as guidelines for the care of breastfeeding mothers and infants and do not delineate an exclusive course of treatment or serve as standards of medical care. Variations in treatment may be appropriate according to the needs of an individual patient.

Purpose

To provide guidance in the first hours/days of life to:
## Table 1. Population Low Thresholds: Plasma Glucose Level

<table>
<thead>
<tr>
<th>Hour(s) after birth</th>
<th>$\leq 5^{th}$ percentile plasma glucose level</th>
</tr>
</thead>
<tbody>
<tr>
<td>1–2 (nadir)</td>
<td>28 mg/dL (1.6 mmol/L)</td>
</tr>
<tr>
<td>3–47</td>
<td>40 mg/dL (2.2 mmol/L)</td>
</tr>
<tr>
<td>48–72</td>
<td>48 mg/dL (2.7 mmol/L)</td>
</tr>
</tbody>
</table>
No studies have shown that treating transiently low blood glucose levels results in better short-term or long-term outcomes compared with no treatment, and in fact there is no evidence at all that hypoglycemic infants with no clinical signs benefit from treatment.\textsuperscript{11,12} Increases in neurodevelopmental abnormalities have been found in infants who have hypoglycemia associated with abnormal clinical signs, especially those with severe, persistent hyperinsulinemic hypoglycemia.\textsuperscript{11–16} Rozance and Hay\textsuperscript{17} have delineated the conditions that should be present before considering that long-term neurologic impairment might be related to neonatal hypoglycemia. Transient, single, brief periods of hypoglycemia are unlikely to cause permanent neurologic damage.\textsuperscript{18–21} Therefore, the monitoring of blood glucose concentrations in healthy, term, appropriately grown neonates is unnecessary and potentially harmful to parental well-being and the successful establishment of breastfeeding.\textsuperscript{18–23}
No studies have shown that treating transiently low blood glucose levels results in better short-term or long-term outcomes compared with no treatment, and in fact there is no evidence at all that hypoglycemic infants with no clinical signs benefit from treatment.\textsuperscript{11,12} Increases in neurodevelopmental abnormalities have been found in infants who have hypoglycemia associated with abnormal clinical signs, especially those with severe, persistent hyperinsulinemic hypoglycemia.\textsuperscript{11–16} Rozance and Hay\textsuperscript{17} have delineated the conditions that should be present before considering that long-term neurologic impairment might be related to neonatal hypoglycemia. Transient, single, brief periods of hypoglycemia are unlikely to cause permanent neurologic damage.\textsuperscript{18–21} Therefore, the monitoring of blood glucose concentrations in healthy, term, appropriately grown neonates is unnecessary and potentially harmful to parental well-being and the successful establishment of breastfeeding.\textsuperscript{18–23}
No studies have shown that treating transiently low blood glucose levels results in better short-term or long-term outcomes compared with no treatment, and in fact there is no evidence at all that hypoglycemic infants with no clinical signs benefit from treatment.\textsuperscript{11,12} Increases in neurodevelopmental abnormalities have been found in infants who have hypoglycemia associated with abnormal clinical signs, especially those with severe, persistent hyperinsulinemic hypoglycemia.\textsuperscript{11–16} Rozance and Hay\textsuperscript{17} have delineated the conditions that should be present before considering that long-term neurologic impairment might be related to neonatal hypoglycemia. Transient, single, brief periods of hypoglycemia are unlikely to cause permanent neurologic damage.\textsuperscript{18–21} Therefore, the monitoring of blood glucose concentrations in healthy, term, appropriately grown neonates is unnecessary and potentially harmful to parental well-being and the successful establishment of breastfeeding.\textsuperscript{18–23}
Clinical Report—Postnatal Glucose Homeostasis in Late-Preterm and Term Infants

BACKGROUND

Blood glucose concentrations as low as 30 mg/dL are common in healthy neonates by 1 to 2 hours after birth; these low concentrations, seen in all mammalian newborns, usually are transient, asymptomatic, and considered to be part of normal adaptation to postnatal life.
Screening and Management of Postnatal Glucose Homeostasis in Late Preterm and Term SGA, IDM/LGA Infants

(LPT) Infants 34 – 36\(^{+7}\) 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**

- Initial feed within 1 hour
- Screen glucose 30 minutes after 1st feed
  - Initial screen <25 mg/dL
    - Feed and check in 1 hour
      - <25 mg/dL → IV glucose*
      - 25–40 mg/dL → Refeed/IV glucose* as needed

**4 to 24 hours of age**

- Continue feeds q 2-3 hours
- Screen glucose prior to each feed
  - Screen <35 mg/dL
    - Feed and check in 1 hour
      - <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.
40% Glucose Gel

- Supplement is given by buccal dose
  - rapidly absorbed
- Infant can stay skin to skin with mother, **no** interruption in feeding or bonding
- Ingredients
  - Purified water
  - Dextrose 40%
  - Glycerin
  - Grape flavor
  - Preservatives
Poll Everywhere

- https://www.polleverywhere.com/multiple_choice_polls/bdGOFV7tDdHp rxNmdYwZn
Dextrose gel for neonatal hypoglycaemia (the Sugar Babies Study): a randomised, double-blind, placebo-controlled trial

Deborah L Harris, Philip J Weston, Matthew Signal, J Geoffrey Chase, Jane E Harding

Summary

Background Neonatal hypoglycaemia is common, and a preventable cause of brain damage. Dextrose gel is used to reverse hypoglycaemia in individuals with diabetes; however, little evidence exists for its use in babies. We aimed to assess whether treatment with dextrose gel was more effective than feeding alone for reversal of neonatal hypoglycaemia in at-risk babies.
How to administer glucose gel

Management of At Risk Newborns for Hypoglycemia (First 24 Hrs of life)

“At-risk” defined as: Late Preterm (35-36 6/7 weeks) or ≤ 37 weeks, LGA (>4000gms), SGA (<2500gms), IDM and/or GDM, Apgar ≤ 6 at 1 minute, Maternal Beta Blocker

Symptomatic and BS <40mg/dL → Notify Provider

**SYMPTOMS OF HYPOGLYCEMIA:** Irritability, tremors, jitteriness, exaggerated More careful, high-pitched cry, seizures, lethargy, floppiness, cyanosis, apnea and poor feeding, hypoglycemic convulsions

**ASYMPTOMATIC**

Provide uninterrupted skin to skin care and initiate first feed WITHIN 1 hour of life

### Birth to 4 hours of age

**Target glucose ≥ 40mg/dL**

Screen glucose 30 minutes after 1st feeding
- not before 90 minutes of life

<table>
<thead>
<tr>
<th>Initial Screen &lt; 40mg/dL</th>
<th>Initial Screen ≥ 40mg/dL</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Glucose Gel immediately</td>
<td>• Continue feeds q 2-3 hours</td>
</tr>
<tr>
<td>• Place skin-to-skin and feed</td>
<td>• Screen glucose level prior to each feed</td>
</tr>
<tr>
<td>• Repeat BG 1 hr after Gel dose</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>2nd screen &lt; 25mg/dL</th>
<th>2nd screen 25-40mg/dL</th>
<th>2nd screen &gt; 40mg/dL</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Notify Provider</td>
<td>• Glucose Gel immediately</td>
<td>• Continue feeds q 2-3 hours</td>
</tr>
<tr>
<td>• Administer Gel</td>
<td>• Place skin-to-skin and feed</td>
<td>• Screen glucose level prior to each feed</td>
</tr>
<tr>
<td>• Continue skin-to-skin</td>
<td>• Repeat glucose 1 hr after Gel dose</td>
<td></td>
</tr>
</tbody>
</table>

### 4 to 24 hours of age

**Target glucose ≥ 45mg/dL**

Feed newborn every 2-3 hours

Check blood glucose before each feed

<table>
<thead>
<tr>
<th>1st Screen after 4 hours of age ≤ 45mg/dL</th>
<th>1st Screen after 4 hours of age ≥ 45mg/dL</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Glucose Gel immediately</td>
<td>• Continue feeds q 2-3 hours</td>
</tr>
<tr>
<td>• Place skin-to-skin and feed</td>
<td>• Screen glucose level prior to each feed</td>
</tr>
<tr>
<td>• Repeat BG 1 hr after Gel dose</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>2nd screen &lt; 35mg/dL</th>
<th>2nd screen 35-44mg/dL</th>
<th>2nd screen ≥ 45mg/dL</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Glucose Gel immediately</td>
<td>• Place skin-to-skin and feed</td>
<td>• Continue feeds q 2-3 hours</td>
</tr>
<tr>
<td>• Place skin-to-skin and feed</td>
<td>• Repeat glucose 1 hr after Gel dose</td>
<td>• Screen glucose level prior to each feed</td>
</tr>
<tr>
<td>• Notify Provider</td>
<td>• Repeat glucose 1 hr after Gel dose</td>
<td></td>
</tr>
</tbody>
</table>

**Goal:** To obtain 3 consecutive glucose values in target range for age in hours: Birth to 4 hours of age ≥ 40 and 4 to 24 hours of age ≥ 45
A Quality-Improvement Initiative to Reduce NICU Transfers for Neonates at Risk for Hypoglycemia

Sherry LeBlanc, NNP-BC, Jamie Haushalter, CPNP-PC, IBCLC, Carl Seashore, MD, Karen S. Wood, MD, Michael J. Steiner, MD, MPH, Ashley G. Sutton, MD

BACKGROUND AND OBJECTIVE: Neonatal hypoglycemia is a common problem, often requiring management in the NICU. Nonpharmacologic interventions, including early breastfeeding and skin-to-skin care (SSC), may prevent hypoglycemia and the need to escalate care. Our objective was to maintain mother-infant dyads in the mother-infant unit by decreasing hypoglycemia resulting in NICU transfer.

METHODS: Inborn infants ≥35 weeks’ gestation with at least 1 risk factor for hypoglycemia were included. Using quality-improvement methodology, a bundle for at-risk infants was implemented, which included a protocol change focusing on early SSC, early feeding, and obtaining a blood glucose measurement in asymptomatic infants at 90 minutes. The primary outcome was the overall transfer rate of at-risk infants to the NICU. Secondary outcomes were related to protocol adherence. Balancing measures,
Neonatal Hypoglycemia

Symptomatic Hypoglycemia (BG <40 mg/dL) – Notify LIP STAT

Asymptomatic Infant with Risk Factors*

**Birth through 4 hours of life:**
- First hour: Uninterrupted SSC
- Initiate first feed by 1 hour of life.
- Obtain BG at 90 minutes of life.

- **<25mg/dL:** Continue skin to SSC and feed measurable amount and notify NBN LIP
- **≤40mg/dL:** Continue SSC
  - Feed measureable amount and recheck
  - See box to right
- **≥41mg/dL:** Routine care

If after second feeding the blood glucose is <25mg/dL, notify NBN LIP to facilitate transfer to NCCC. Continue SSC.

**After 4 hours of life:**
- Feed at least every 2-3 hours
- Check BG before to each feeding

- **<35mg/dL** feed measurable amount
  - and call NBN LIP 35-45mg/dL feed and recheck after 1 hour. If no improvement notify newborn LIP ≥46mg/dL feed on demand minimum q2 to 3 hours

Three normal consecutive preprandial
- BGs = Pass ^
- Call NBN LIP if infant has not passed protocol by 12 hours of life.

---

**Hypoglycemia | Key Learning Points:**

*Risk Factors:* IDM and/or GDM, <37 weeks' gestation, SGA (<2500 g), LGA (>4000 g)

†Measurable factors: 3-5mL/kg of expressed colosrum, donor milk, or formula

**Symptoms:** poor feeding, irritability, tremors, jitteriness, exaggerated Moro reflex lethargy, seizure, poor tone, persistent hypothermia

**Interventions to minimize hypoglycemia:** SSC, avoid cold stress, warm heel before obtaining BG, help with latch and/or feeding. ^If BG values during birth to 4 hours of life are ≥41, they may be included in the 3 consecutive passing values.
Results

- Decreased NICU Admissions
- Savings of >$100,000
- Keeps Moms and Babies Together