OBJECTIVES

• Describe the physiologic glycemic transition from fetus to newborn
• Discuss the role of glucose gel in supporting neonates glycemia transition
Disclosures

I have no disclosures or conflicts of interest to report

Neonatal Hypoglycemia (NH) is the *metabolic* condition most responsible for infant admission to NICUs and is associated with:

- Perinatal Stress
- Preterm Births
- Gestational Diabetes
- Preeclampsia
Risk Factors

- Large for gestational age (LGA)
- Small for gestational age (SGA)
- Late Preterm infant (LPI) (34 0/7-36 6/7)
- Infant of diabetic mother
- Symptomatic
- Apgar < 7 at 5 minutes
- Infant requiring resuscitation

Dextrose Gel for Neonatal Hypoglycemia (the Sugar Babies Study): A randomized, double-blind, placebo-controlled trial

- Conducted at a tertiary center in New Zealand in 2010
- Dextrose gel reduced frequency of hypoglycemia
- Neonates receiving dextrose gel were less likely to:
  a. Be admitted to NICU for hypoglycemia
  b. Receive IV dextrose
  c. Have episodes of recurrent hypoglycemia
  d. Require supplementation
- No adverse effects noted

(Harris, Weston, Signal, Chase, & Harding, 2013)
Implementing a Protocol: Using glucose gel to treat neonatal hypoglycemia

**Quality Improvement Project:** Development and adoption of a nurse-driven protocol.
- Asymptomatic were given glucose gel (200 mg/kg of 40% dextrose) along with feeds.
- Transfers to NICU decreased by 75%
- Exclusive breastfeeding increased by 50%

(Bennett, Fagan, Chaharbakshi, Zamfirova, & Flicker, 2016)

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Oral Dextrose Gel Reduces the Need for Intravenous Dextrose Therapy in Neonatal Hypoglycemia

**Method:** A retrospective study conducted at the Women and Children’s Hospital of Buffalo, NY before and after implementation of the use of 40% dextrose gel in 2015.
- 248 infants were included in the pre-implementation group and 250 in the post group.
- Transfer to the NICU for IV dextrose was considered treatment failure.

Munmun Rawat, Praveen Chandrasekharan, Stephen Turkovich, Nancy Barclay, Katherine Perry, Eileen Schroeder, Lisa Testa, & Satyan Lakshminrusimha
Findings: Neonates receiving dextrose gel had:

- Lower incidence of transfers from the NBN to the NICU [35/1000 to 25/1000].
- Lower incidence of needing IV dextrose
- An increase in exclusive breast feeding [19-28%].
- Less separation from mother

Rawat et al, 2016

Innovations and Challenges of Implementing a Glucose Gel Toolkit for Neonatal Hypoglycemia

- Implemented a Management of Newborns at Risk for Hypoglycemia Toolkit
- 6.5% increase in exclusive breastfeeding
- 5% decrease in admissions to the Intermediate Care Nursery.

Hammer, D., Pohl, C., Jacobs, P., Kaufman, S., Drury, B.
Neonatal hypoglycemia occurs in up to 20% of newborns.

There is no agreement among experts as to the absolute threshold for normal and safe blood glucose levels during the first 24 hours of life.

Fetal glucose levels dependent on maternal glucose supply.

Fetal norm: about 50 mg/dl

Fetus excretes own insulin in response to the glucose from the mother

Neonatal low range: 20-50mg/dl during first 2 hours of life.
Are there advantages to these lower levels at birth?

- Stimulates appetite
- Enhances oxidative fat metabolism
- Stimulates physiologic processes required for postnatal life: promoting glucose production through gluconeogenesis and glycogenolysis.

Pathologic Hypoglycemia

Eunice Kennedy Shriver National Institute of Child Health and Human Development (NICHD) 2008 expert panel – findings:

- No true definition of NH
- No threshold values have been established relating glucose levels to pathological NH
How low is too low?

- Hay (2009): levels as low as 23mg/dL in healthy breastfed infants
- Adamkin (2011): levels of 30 mg/dL common in healthy infants during initial 1-2 hours of life.
- Neurologic damage has been associated with levels that are sustained at <10 mg/dL for more than 10 hours.
Adamkin: Neonatal Hypoglycemia: Is 60 the New 40? The Questions Remain the Same.

AAP values are derived from the range of values seen in healthy term newborn which can be as low as 20-25mg/dL during the first few hours of life.

The Pediatric Endocrine Society uses the mean plasma glucose levels of 55-65 mg/dL at birth and then increase to > 70mg/dl by 2-3 days.

“Overscreening, over diagnosing and over treating are the concerns when a ‘lower limit threshold’ is set too high”.

Congenital Hyperinsulinism

- Incidence: 1 in 50,000
- Caused by mutations in genes that regulate the release (secretion) of insulin, (http://ghr.nlm.nih.gov/condition/congenital-hyperinsulinism)
- Hypoketonemia
- Low free fatty acids
- Incomplete suppression of plasma insulin concentrations
Iatrogenic harm from increased intervention
- Decreased breastfeeding
- Altered cortical development from pain-induced stress with heel lancing.

Where did 47mg/dL come from??

Study in 1988 reported impaired motor and cognitive development at 18 months of age for infants weighing < 1850 at birth with recurrent asymptomatic hypoglycemia < 47 for > 3 day.

‘the association between modest hypoglycemia and poor neurodevelopment reported here might not be causal and might reflect our failure to adjust adequately for confounding factors’
**Journal of Pediatrics 2017**

°“Dextrose gel and breast feeding should be considered for first-line oral treatment of infants with hypoglycemia.” Journal of Pediatrics - Harris et al. 2017

°“40% dextrose gel offers an alternative to formula that actually improves breastfeeding rates at 2 weeks of age and reduces admission to the NICU for treatment of hypoglycemia with IV dextrose.” Journal of Pediatrics – Rozance et al. 2017

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

°**Conclusions and Relevance:** Early transient newborn hypoglycemia was associated with lower achievement test scores at age 10 years.

°Kaiser controlled for gestational age group, race, sex, multifetal gestation, insurance status, maternal educational level and socioeconomic status, and gravidity,
In response

Comment by Ruoyan Gai Tobe, MSc, PHD
◦ This study is facility based rather than population based.
◦ 81.5% of families had Medicaid or no insurance,
◦ 74.8% of mothers had an educational level below high school
◦ the incidence of the overall preterm labor was as high as 31.5% (440 of 1395).
◦ Both preterm labor and poor economic conditions are closely related to neonate hypoglycemia and school performance.

Association of Neonatal Glycemia With Neurodevelopmental Outcomes at 4.5 Years
◦ Conclusions and Relevance: Neonatal hypoglycemia was not associated with increased risk of combined neurosensory impairment at 4.5 years but was associated with a dose-dependent increased risk of poor executive function and visual motor function, even if not detected clinically, and may thus influence later learning
◦ Authors state that the highest risk was in children exposed to severe, recurrent hypoglycemia.
The Critical Assessment Question

Is the infant symptomatic?

Infants with clinical signs should be screened immediately.

Clinical Signs: Defining Symptomatic

- Jitteriness
- Cyanosis
- Seizures
- Apneic episodes
- Tachypnea
- Weak or high pitched cry
- Floppiness or lethargy
- Poor feeding
- Eye-rolling

Infants with clinical signs should be tested immediately.
We started using glucose gel in May, 2014
Since implementation we have decreased newborn transfers to NICU by 80%
**SCREENING AND MANAGEMENT OF ASYMPTOMATIC NEWBORNS AT RISK FOR HYPOGLYCEMIA DURING FIRST 48 HRS OF LIFE**

- **AT RISK**: SGA, LGA, IDM, Late PT (34 wks to 36 wks Birth GA), other clinical situations per physician discretion
- **Bedside Glucose (BG)**: Screening is based on bedside glucose “BG” (whole blood glucose; typically 10-18% lower than plasma glucose)
- Throughout the algorithm, “feed” refers to maternal preference – breast feeding alone is considered sufficient if this is mother’s choice
- Assess for symptoms before every BG measurement and document in medical record.
  - Contact Neonatal Provider immediately for symptomatic infants and administer OGG if necessary.
  - Symptoms include: poor feeding, jitteriness, tremors, flappiness, lethargy, high pitched cry, irritability, grunting, cyanosis, apnea
- **Oral Glucose Gel (OGG)**: dose is 0.5ml/kg → see reverse side for dosing chart

Target glucose levels are >35 mg/dl from Birth → 4 hrs and >45 mg/dl from 4 → 24 hrs, ≥50 mg/dl from 24-48 hours

- Begin feeding within 60 min of birth
- BG screen #1 at 30 min after completion of first feed
- If ≥35: continue feeds q2-3hrs and perform pre-feed BG screen
- If <35:
  - Administer OGG immediately
  - Place skin-to-skin and feed
  - Repeat BG 1 hr after OGG dose (not 1 hr after feed)

- BG screen #2: Target ≥35 (birth to 4 hrs) >45 (4-24 hrs)
- If ≥Target: Continue feeds q2-3hrs and perform pre-feed BG screen
- If <Target: Notify Neonatal Provider for consult & administer OGG
- If 25 to < Target:
  - Administer OGG immediately
  - Place skin-to-skin and feed
  - Repeat BG 1 hr after OGG dose

Continue feeds q2-3 hrs with BG screens prior to feeds:
- If ≥ Target: continue feeds q2-3hrs and perform pre-feed BG screen
- If < Target: administer OGG, place skin to skin and repeat BG in 1 hr

BG ≥35-44 when between 4 and 24 hours of age
- Administer OGG immediately
- Place skin-to-skin and feed
- Repeat BG 1 hr after OGG dose
- Notify Neonatal Provider if ≥ 24 hr of age

BG ≥45 when between 4 and 24 hours of age
- OGG dose not needed
- Continue feeds q2-3hrs and perform pre-feed BG screen

STOP: When 4 consecutive values (including post gel screen) in target range for age in hrs:

<table>
<thead>
<tr>
<th>Target range for age in hrs:</th>
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</thead>
<tbody>
<tr>
<td>&lt;4 hr</td>
</tr>
<tr>
<td>&gt;4-24 hr</td>
</tr>
<tr>
<td>≥50</td>
</tr>
</tbody>
</table>

- Notify Neonatal Provider and give OGG immediately if:
  - Infant is symptomatic
  - Infant requires total THREE doses OGG since birth
  - BG below the notification threshold (below):
    - <35 at any time after the first OGG dose
    - <35 from > 4 -24 hrs of age
    - <30 at 24-48 hrs

Revised: 7.17.2017

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**How to administer glucose gel**

*https://www.facebook.com/cathy.bennett.925/videos/10218463313805471/*
## Advocate Lutheran General Data

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<th>Year</th>
<th>2014</th>
<th>2015</th>
<th>2016</th>
<th>2017</th>
<th>2018</th>
<th>2019 to date</th>
<th>Grand Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number of at risk infants</td>
<td>502</td>
<td>944</td>
<td>805</td>
<td>799</td>
<td>826</td>
<td>475</td>
<td>4351</td>
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<tr>
<td>Number who received gel</td>
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<td>254</td>
<td>245</td>
<td>270</td>
<td>278</td>
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<td>1315</td>
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<tr>
<td>Number to NICU</td>
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<td>18</td>
<td>25</td>
<td>32</td>
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<td>16</td>
<td>141</td>
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<td>Percentage to NICU</td>
<td>3.39%</td>
<td>1.91%</td>
<td>3.11%</td>
<td>4.01%</td>
<td>4.01%</td>
<td>3.4%</td>
<td>3.25%</td>
</tr>
</tbody>
</table>

### 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 Moro reflex, high pitched cry, seizures, lethargy, floppiness, cyanosis, apnea and poor feeding, tachypnea

#### Initial Screen < 40mg/dL

- Glucose Gel immediately
- Place skin-to-skin and feed
- Repeat BG 1 hr after Gel dose

#### Initial Screen ≥ 40mg/dL

- Continue feeds q 2-3 hours
- Screen glucose level prior to each feed

#### 2nd screen < 25mg/dL

- Notify Provider
- Administer Gel
- Continue skin-to-skin

#### 2nd screen 25-40mg/dL

- Glucose Gel immediately
- Place skin-to-skin and feed
- Repeat glucose 1 hr after Gel dose

#### 2nd screen ≥ 40mg/dL

- Continue feeds q 2-3 hours
- Screen glucose level prior to each feed

#### 1st Screen after 4 hours of age < 45mg/dL

- Glucose Gel immediately
- Place skin-to-skin and feed
- Repeat BG 1 hr after Gel dose

#### 1st Screen after 4 hours of age ≥ 45mg/dL

- Continue feeds q 2-3 hours
- Screen glucose level prior to each feed

#### 2nd screen < 35mg/dL

- Glucose Gel
- Place skin-to-skin and feed
- Repeat glucose 1 hr after Gel dose
- Notify Provider

#### 2nd screen 35-44 mg/dL

- Glucose Gel
- Place skin-to-skin and feed
- Repeat glucose 1 hr after Gel dose

#### 2nd screen ≥ 45mg/dL

- Continue feeds q 2-3 hours
- Screen glucose level prior to each feed

### 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

Adapted from AAP, 2011
Advocate System-Wide Success

More of this

Less of this

Glucose Gel Reminders

Once gel is administered, the baby should be placed skin to skin and encouraged to breastfeed.

Skin to skin supports increased glucose levels, thermoregulation, and decreases the neonatal physiologic stress response.

An ac bedside glucose (BG) should not be obtained sooner than 2 hours after the last normal level.

It is important to look at the big picture when assessing the need to administer gel or continue with glucose checks.
What’s next?

- Prophylactic Oral Dextrose Gel for Newborn Babies at Risk of Neonatal Hypoglycaemia: A Randomised Controlled Dose-Finding Trial (the Pre-hPOD Study)
- The incidence of neonatal hypoglycaemia can be reduced with a single dose of buccal 40% dextrose gel 200 mg/kg.
- A large randomised trial (Hypoglycaemia Prevention with Oral Dextrose [hPOD]) is under way to determine the effects on NICU admission and later outcome.


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Prophylactic Dextrose Gel Does Not Prevent Neonatal Hypoglycemia: A Quasi-Experimental Pilot Study

Clinical Trial

“To test the hypothesis that prophylactic dextrose gel administered to newborn infants at risk for hypoglycemia will increase the initial blood glucose concentration after the first feeding and decrease neonatal intensive care unit (NICU) admissions for treatment of asymptomatic neonatal hypoglycemia compared with feedings alone.”

- 236 subjects (72 prophylactic, 164 controls).
- First glucose concentration was not different between the prophylactic and control
- Rates of NICU admission for treatment of transient neonatal hypoglycemia were 9.7% (prophylactic) and 14.6% (controls).

- Insta-Glucose (77%) may have caused a hyperinsulinemic response
Has your hospital implemented the use of 40% glucose gel to treat transitional neonatal hypoglycemia?

Yes: 95  Not yet: 14  No: 7

Since the implementation of glucose gel, has your hospital had a decrease in the number of infants (with the primary diagnosis of hypoglycemia) admitted to NICU, SCN or needing IV dextrose?

Yes: 72  No: 17
Implemented Use of Gel in 2014

Advocate Lutheran General Hospital

Women's and Children's Hospital of Buffalo

Implemented Use of Gel in 2016
Implemented Use of Gel in 2017

Elmendorf AFB Alaska

Implemented Use of Gel in 2018
KEEP THE NEW FAMILY TOGETHER WHENEVER POSSIBLE

References


