# NEWBORN GLUCOSE REGULATION

Kelli Satnes DNP, APRN, NNP-BC

## 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 3<sup>rd</sup> trimester – especially the last month

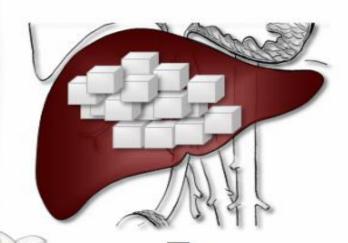




### After Birth

#### Glycogen Stores

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



Glycogen

Glucose

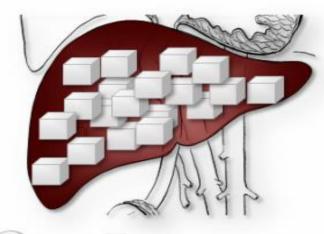


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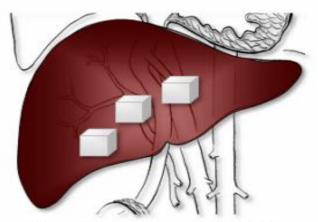
## Preparation for Extrauterine Life

Glycogen Stores

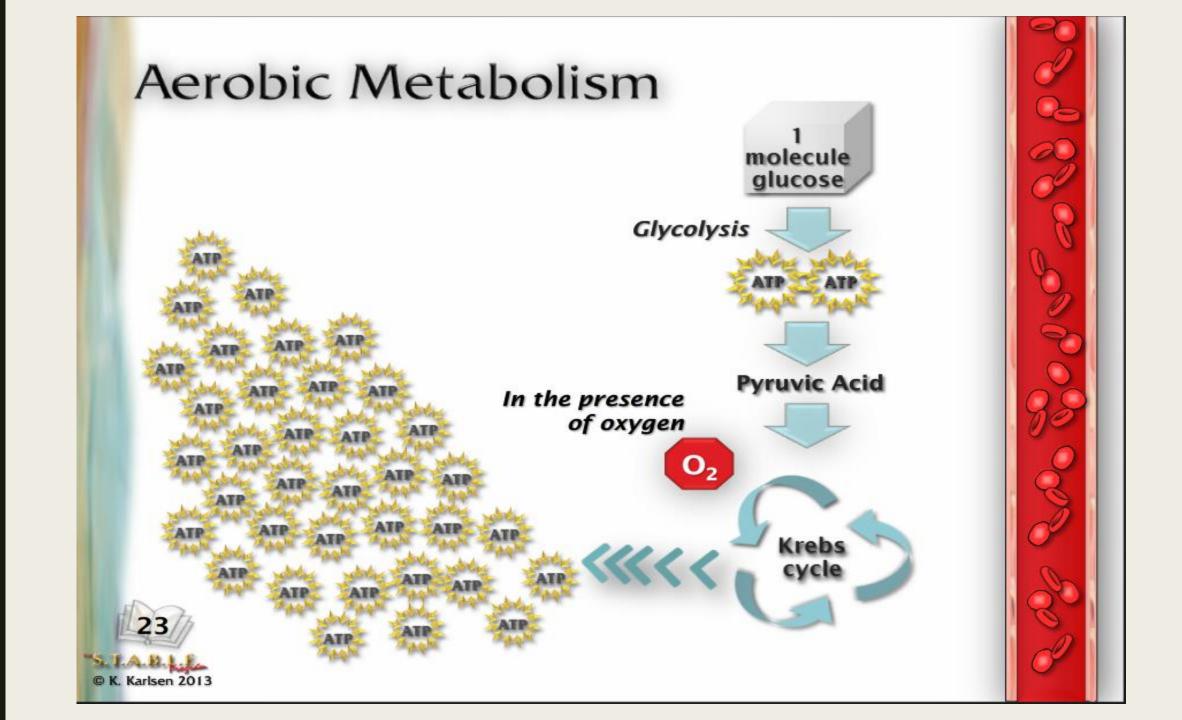








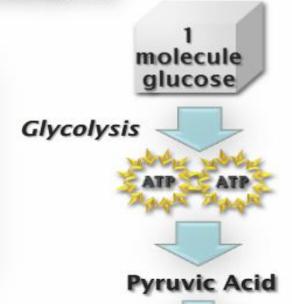
Preterm or SGA



## Anaerobic Metabolism

# Consequences of anaerobic metabolism:

- Accelerated glucose utilization
- Metabolic acidosis
- Cellular dysfunction



In the ABSENCE of oxygen



Lactic Acid



# Neonatal Hypoglycemia

- Common issue in the newborn period
  - May occur in up to 10% of healthy newborn infants
  - Risk for neurological injury
- Infants at highest risk for neonatal hypoglycemia are:
  - preterm infants <37 weeks; IDM, SGA, and LGA infants</li>
- Significant source of patient medical cost
- Common cause of admission to NICUs
  - -disruption of parent and infant bonding
  - -stress on parents
  - -utilization of limited NICU resources

## Factors Impacting Glucose Levels



Inadequate Glycogen Stores



Hyperinsulinemia



Increased Glucose Utilization



## 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
  - - 3-fold higher mortality rate than term infants



## Small for Gestational Age

- Birthweight < 10<sup>th</sup> 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

36 week 5.2 kg IDM

(birthweight > 4000 grams)



## Hyperinsulinemia

#### Large for Gestational Age (LGA)

- Birthweight > 90<sup>th</sup> 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



### Increased Glucose Utilization

#### Sick Infants

- Infection
- Birth stress

Rapid depletion of glycogen stores

- ▶ Hypoxia → anaerobic glycolysis
- ▶ Shock → anaerobic glycolysis
- Respiratory disease
- Cardiac disease
- Hypothermia
- Limited stores are rapidly depleted
  - Preterm
  - Small for gestational age





Review Infants at Risk for Hypoglycemia

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





# Definition of Neonatal Hypoglycemia

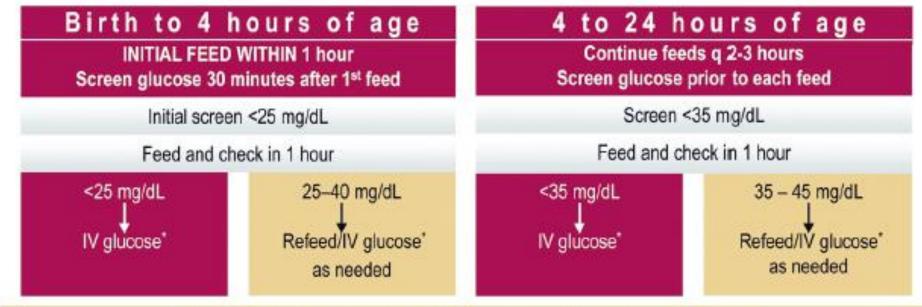
- American Academy of Pediatrics (AAP) vs Pediatric Endocrine Society (PES)
- PES -> recommends intervention for glucose levels
  - <50mg/dL in the first 48 hours of life
  - <60mg/dL after 48 hours of life
- AAP -> recommends intervention for glucose levels
  - <40mg/dL in the first 4 hours of life
  - <45mg/dL in the first 4-48 hours of life</p>
- Continuous glucose monitoring

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

(LPT) Infants 34 - 3657 weeks and SGA (screen 0-24 hrs); IDM and LGA ≥34 weeks (screen 0-12 hrs)]

Symptomatic and <40 mg/dL → IV glucose

#### **ASYMPTOMATIC**



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

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

<sup>\*</sup> 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.

## Signs / Symptoms of Hypoglycemia

# General Findings

- Abnormal cry weak, high-pitched
- Poor feeding poor suck and coordination
- Hypothermia
- Diaphoresis

#### Neurologic Signs

- Tremors
- Jitteriness
- Irritability
- Hypotonia
- Lethargy
- Seizures

#### Cardiorespiratory Signs

- Tachypnea
- Respiratory depression
- Apnea
- Cyanosis



# Screening

- Who to screen?
  - Infants at risk:
    - IDM
    - Preterm
    - SGA
    - LGA
  - Any infant who is symptomatic
- Point of Care versus Serum glucose
  - Don't wait for results of serum testing for treatment!

## Interventions

#### **■** Treatments:

- Early skin to skin care
- Early initiation of feeds (within 1h of life)
- May require supplementation of DHM or formula
- 40% glucose gel
- IV glucose
- NICU admission

## 40% Glucose Gel

- Supplement is give by buccal dose
  - rapidly absorbed
- Infant can stay skin to skin with mother, <u>no</u> interruption in feeding or bonding
- Ingredients
  - Purified water
  - Dextrose 40%
  - Glycerin
  - Grape flavor
  - Preservatives



## 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 Lancet 2013; 382: 2077-83 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.

Published Online September 25, 2013 http://dx.doi.org/10.1016/ 50140-6736(13)61645-1

See Comment page 2045

September 25, 2013. The Lancet, Volume 382, Issue 9910, 2077 - 2083

# How to administer glucose gel

o https://www.facebook.com/cathy.bennett.925/videos/10218463313805471/



## IMPROVING NEONATAL HYPOGLYCEMIA PROTOCOL ADHERENCE IN AT RISK INFANTS

Kelli Satnes DNP, APRN, NNP-BC, Department of Neonatology DNP Project, Fran and Earl Ziegler OU College of Nursing

#### Improving Neonatal Hypoglycemia Guideline Adherence in At-Risk Neonates





Kelli Satnes, DNP, APRN, NNP-BC, Section of Neonatal-Perinatal Medicine, Oklahoma Children's Hospital Renee Leasure, PhD, RN, CNS, CCRN, Fran and Earl Ziegler College of Nursing Susan Bedwell, DNP, APRN, CCNS-N, Section of Neonatal-Perinatal Medicine, OU Health Sciences Center

**Q**Health

#### **Background**

- Transient neonatal hypoglycemia in at-risk neonates is common in the immediate postnatal period.
- Interventions such as early breastfeeding, skin-toskin immediately after birth, and the use of 40% glucose gel in hypoglycemic infants has decreased the number of avoidable NICU admissions.
- Lack of parental awareness of the risks, causes, and treatments for neonatal hypoglycemia is common and may contribute to a delay in treatment.
- This puts infants at risk for neurological damage and contributes to avoidable NICU admissions.

#### **Objectives**

 Decrease the burden of avoidable NICU admissions for transient neonatal hypoglycemia in at-risk neonates by empowering and educating parents on transient neonatal hypoglycemia and ensuring early and timely determination of oral feeding supplementation in at-risk neonates.

#### **Methods**

- A parent education handout was added to the current neonatal hypoglycemia guideline.
- At-risk infants were defined as infants born premature at 35-37 weeks' gestation, small for gestational age, large for gestational age, or infants of diabetic mothers.
- Parents of at-risk infants were provided a parent education handout by a trained transition nurse at the time of the initial oral feeding.
- Parent handout provided easy-to-understand information on hypoglycemia, benefits of early intervention and adherence to an every 3-hour feeding schedule, and the importance of additional oral supplementation, if needed.
- A convenience sample was used. Data was collected through retrospective chart review.

#### Results

- No statistical differences between pre- and postintervention groups
- Mean gestational age: Pre-37.2, Post -37.8
- Use of glucose gel was lower in the post-intervention group (p.008).
- Incidence of hypoglycemia between 4-24 hours of age was lower in post-intervention group (p.081).
- Fewer short term NICU stays were noted in the postintervention group, although not statistically significant (p.216).

	(n=12).n(%)	(n=37), n(%)	x	P
Process				
Initia Glucose 10-25 26-39 40-65 >65	2(17) 3(25) 7(58) 0(0)	5(14) 10(27) 15(40) 7(19)	33.678	.434
Glucose level < 40 in first 4 hours Yes No	6(50) 6(50)	15(40) 22(60)	3.228	.199
H yes, lowest glucose level recorded 10-25 26-39 NA	2(17) 4(33) 6(50)	7(19) 8(22) 22(59)	28.271	*800.
initiel Glucose <25 Yes No	2(17) 10(83)	4(11) 33(89)	.626	.591
Glucces level <45 from 4-24h of life Yes No	8(67) 4(33)	14(38) 23(62)	3.044	.081
If yes, lowest glucose level recorded 10-25 26-39 40-44 NA	0(0) 6(50) 2(17) 4(33)	2(5) 7(19) 5(14) 23(62)	22.932	.116
Outcomes Required NKU admission Yes No	2(17) 10(83)	3(8) 34(92)	.584	.395
Required NICU admission with LOS > 48h with IV glucose supplementation Yes No	1(8) 11(92)	4(11) 33(89)	1.0	.805
Total length of NICU stay (in days): 0 1-2 3-5 >5	9(75) 2(17) 1(8) 0(0)	32(87) 0(0) 2(5) 23(8)	8.311	.216
Number of gluccee gels administered 0 1 2 3	1(8) 3(25) 8(67) 0(0)	14(38) 15(41) 6(16) 2(5)	11.893	.008*
Time (in minutes) glucose obtained after administration of glucose gel and start of feeding				
Dose 1 NA <30 30 60 min 61:40 min 91:120 min	1(8) 0 (0) 0 (0) 8(67) 3(25)	14(38) 0(0) 5(13) 15(41) 3(8)	41.29	0.029*
Dose 2 NA <30 min 30-80 min 61-80 min 91-120 min	4(33) 0(0) 1(8) 7(58) 0(0)	29(76) 1(3) 1(3) 5(14) 1(3)	30.073	0.018*
Dose 3 NA 430 min 30-60 min 61-90 min	12(100) 0(0) 0(0) 0(0) 0(0)	35(95) 0(0) 0(0) 2(5) 0(0)	.676	.713

#### **Discussion**

- The discrepancy between the size of the pre- and post- intervention group was attributable to the difficulty of identifying qualifying participants from retrospective data collection.
- Theoretically, the lower need for the use of glucose gel appears to be attributable to better guideline adherence and appropriate feeding supplementation in the enhanced guideline group.
- At the core of this quality improvement initiative is the belief that parent education and involvement are essential to optimal outcomes for infants.

#### Conclusion

- The data remains scarce on how parent understanding of neonatal hypoglycemia and early determination of supplemental feeds could significantly improve patient outcomes and decrease need for advanced intervention.
- While the data in this quality initiative does show a statistically significant lower need for the use of glucose gel in the post-intervention group, the sample sizes remain small and the exact mechanism of the decreased need for intervention remains uncertain.
- Enhancing the standard hypoglycemia guideline by adding a parent handout was a simple intervention that required minimal change in workflow and required low financial investment with preliminary data showing the potential for significant cost savings.



Special thanks to the Newborn Transition Nurses at the Oklahoma Children's Hospital at OU Health!

## Results

- -Mean gestational age: Pre-37.2, Post -37.8
- -Maternal BMI: Pre-34.92, Post-35.97
- -Most common risk factors for hypoglycemia: Pre-prematurity and LGA, Post -IDM and LGA
- -Number of glucose gels administered lower in post intervention group, statistically significant (p .008)
- Incidence of hypoglycemia between 4-24 hours of age lower in post-intervention group, although not statistically significant (p .081)
- -Longer LOS for NICU admissions in the post-intervention group, although not statistically significant (*p* .216)

## Discussion

- NICU admissions were longer in the enhanced protocol group
  - Overall NICU admission rates were low in both groups
- Post-intervention participants were less likely to require more than one dose glucose gel than the pre-intervention group
- Unable to obtain all data initially planned, missing data on supplementation
- Difficulties identifying pre-intervention group participants
- Would be interesting to obtain additional data on parental understanding of neonatal hypoglycemia before and after intervention

## Conclusion

- Commonly encountered issue in the newborn nursery
- No actual consensus on how to define hypoglycemia
  - Commonly used thresholds are:
    - >40 in first 4h of life
    - >45 at 4-24h of life
    - >60 by 48h of life
- Most commonly noted in at risk newborns:
  - Preterm <37 weeks</li>
  - IDM
  - SGA or LGA
- Treatments:
  - Early skin to skin care
  - Early initiation of feeds (within 1h of life)
  - May require supplement via DHM or formula if breastfeeding
  - 40% Glucose Gel
  - IV glucose