Neonatal Hypoglycemia and the PES recommendations

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Conflict of interest

- I have no conflict of interest

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Objectives

- Evaluate your PES knowledge by reviewing 2 case studies of neonates with hypoglycemia
- Understand normal glucose regulation in the new born
- Outline the PES recommendations for evaluation and management of hypoglycemia

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Case Study Test

- "WWPD"

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Question 1

- 3.2 kg male baby
- 39 weeks born by SVD
- Apgar score 7@1 and 9@5
- Breast fed
- Doing well until apnea spell at 4 hours of life and he is transferred to NICU.
- They perform a sepsis screen and find glucose 36 mg/dL (2mmol/L)

In addition to starting antibiotics what is the next best step?

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WWPD Answers

A Feed and recheck glucose in 30 mins

B Draw critical sample (diagnostic evaluation) feed and recheck in 30 mins

C Give oral glucose gel and recheck in 30 mins

D Give 2ml/kg iv 10% glucose and start glucose drip @ 4-6 mg/kg min and recheck in 30 mins

F Draw critical sample (diagnostic evaluation), give 2ml/kg iv 10% glucose and start glucose drip @ 4-6 mg/kg min and recheck in 30 mins

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PES answer

A Feed and recheck glucose in 30 mins

B Draw critical sample (diagnostic evaluation) feed and recheck in 30 mins

C Give oral glucose gel and recheck in 30 mins

D Give 2ml/kg iv 10% glucose and start glucose drip @ 4-6 mg/kg min and recheck in 30 mins

F Draw critical sample (diagnostic evaluation), give 2ml/kg iv 10% glucose and start glucose drip @ 4-6 mg/kg min and recheck in 30 mins

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Question 2

- 48 hr cultures were negative
- 3 days IV fluids to keep glucose >70
- By day 5 weaned off IV and POC glucose levels were 52 mg/dl, 55 mg/dL and 59 mg/dl
- The baby is feeding well and mom feels the baby is ready for home.

What is the next best step?

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WWPD Answers

A. D/C home and standard f/u with pediatrician in 3-5 days
B. D/C home and have pediatrician check glucose levels in 3-5 days
C. Keep in hospital one more day
D. Do a six hour fasting study
E. Send off critical sample and make diagnosis of etiology of hypoglycemia

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PES Answers

A. D/C home and arrange f/u with pediatrician in 3-5 days
B. D/C home and have pediatrician check glucose levels in 3-5 days
C. Keep in hospital one more day
D. Do a six hour fasting study
E. Send off critical sample and make diagnosis of etiology

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Reasons Why a PES Hypoglycemia Guide is Needed

- High risk of permanent brain injury in pediatric hypoglycemia disorders due to delays in diagnosis and provision of adequate therapy
- Difficulties in distinguishing between neonates that have a persistent hypoglycemia disorder and those with self-limited transitional neonatal glucose homeostasis
- Currently we are seeing too many cases of missed hypoglycemia

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Definition of Hypoglycemia

- Diagnostic
  - $\leq$ 50 mg/dl Plasma Glucose in Lab
- Therapeutic
  - $\geq$ 70mg/dl
- Brain Damage
  - It depends

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Is that the same for the newborn

- Yes and No

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Normal Glucose Levels in the Newborn Period

Time	2 hours	24 hours	48 Hours	72 hours
Mean	56	63	66	67
Calculated 5%	≤28	≤40	≤41	≤48

Alkalay et al: Am J perinatology: 2006

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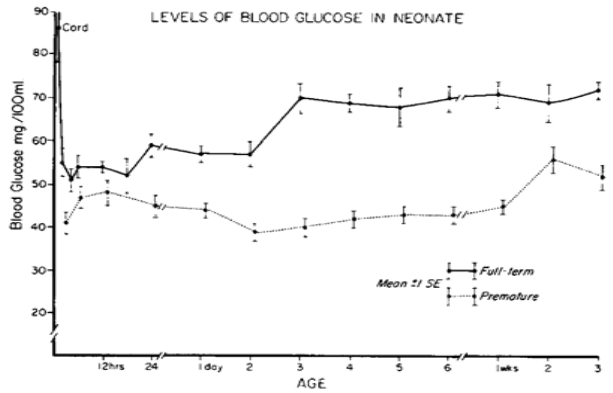

FIGURE 1. *Mean (±1 Standard Error) Capillary Whole-Blood Glucose Calculated from 206 Determinations in 179 Full-Sized Infants and from 442 Determinations in 104 Low-Birth-Weight Infants between Birth and Twenty-eight Days of Life.*

The blood was precipitated at the cribside, and the filtrate was analyzed with the use of glucose oxidase.

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Transitional Hypoglycemia

- Transitional hypoglycemia is the normal physiological changes that occur in FT AGA infants (i.e., normal physiological infants) in the first 24-48 hrs of birth
- How common?

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Lubchenco and Bard 1971

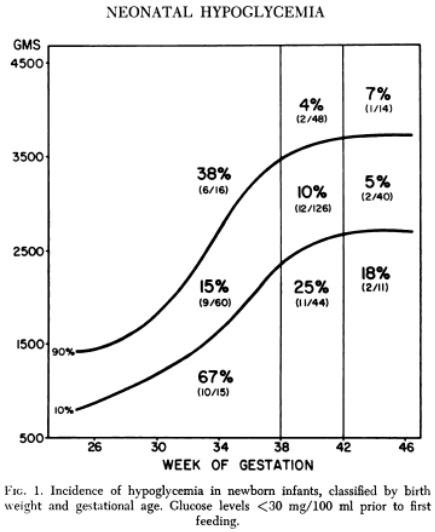

Fig. 1. Incidence of hypoglycemia in newborn infants, classified by birth weight and gestational age. Glucose levels <30 mg/100 ml prior to first feeding.

- 374 babies
- Before the first feed
- Glucose levels
  - <30mg/dL
  - 55 babies
  - 15%

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Lubchenco and Bard 1971

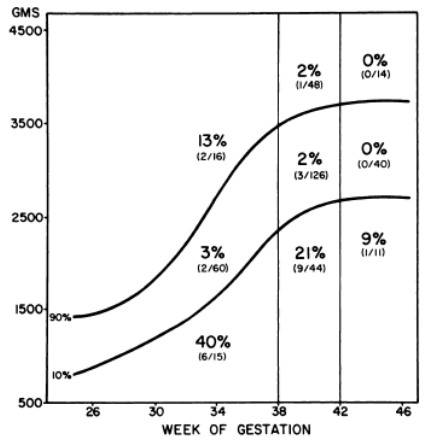

Fig. 2. Incidence of hypoglycemia in newborn infants, classified by birth weight and gestational age. Glucose levels <20 mg/100 ml prior to first feeding.

- 374 babies
- Before the first feed
- Glucose levels
  - **<20mg/dL**
  - 24 babies
  - 6%

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Lubchenco and Bard 1971

- When all babies were followed out to 72 hours 0.5% or 2/374 babies had glucose ≤ 50 mg/dl
- Of the 55 babies in the study with hypoglycemia, 2 (3.6%) still had hypoglycemia by 72 hrs
- Expected incidence of hypoglycemia <30mg/dl in a general Nursery Service is 11% in the first 24 hours

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Hypoglycemia in at risk babies

- 514 **at risk babies**
  - 260 (51%) glucose ≤ 47mg/dl
    - 81% occurred in the first 24 hours
    - 48% in ≤ 6H
  - 97 (19%) glucose ≤ 36mg/dl
  - 31 (6%) required IV glucose to treat hypoglycemia
  - 98 (19%) had > 1 episode
  - 79% were asymptomatic, 15% poor feeding and 16% jittery

Harris et al 2012. J Pediatrics

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Hypoglycemia in at risk babies

- Of the hypoglycemia babies
  - 95 (37%) had the first episode after 3 "normal" blood sugars.
  - 15 (6%) had the first hypoglycemia after 24 hours age.

Harris et al, J Pediatrics: 2012

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Missed hypoglycemia Study

- Cook Children's Hypoglycemia Clinic
- Retrospective chart review of patients seen in our center in last 4 years who had hypoglycemia presenting after discharge from newborn hospital
  - Genetic forms of Hyperinsulinism
  - Hypopituitarism with pituitary malformation
- Should these patients have been diagnosed in the newborn period if the PES guidelines were followed

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Results

- 18 patients presented between 1 week and 8 years of age
- 12 had genetic forms of hyperinsulinism
  - 5 had IV glucose to treat hypoglycemia in NICU
  - 2 had a family history of AD genetic HI in Dad
  - 5 completely normal newborn period
- 6 had hypopituitarism with malformation
  - 6 had IV glucose to treat hypoglycemia in NICU

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Conclusion

- Hyperinsulinism
  - 58% (7 of 12) of late diagnosed patients had an opportunity to be diagnosed in NICU and were missed during the newborn period
- Hypopituitarism
  - 100% (6 of 6) of late diagnosed patients had an opportunity to be diagnosed in NICU and were missed during the newborn period

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PES Hypoglycemia Committee objectives

- Prevent unnecessary investigation of normal neonates
- To assist physicians to recognize persistent hypoglycemia disorders,
- To guide their rapid diagnosis and effective treatment
- To prevent brain damage in at risk babies

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Recommendations from the Pediatric Endocrine Society for Evaluation and Management of Persistent Hypoglycemia in Neonates, Infants, and Children

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Outline of Recommendations

- **Section 1:** Which neonates, infants and children to evaluate for hypoglycemia
  - Who to screen
  - Who to evaluate for etiology of hypoglycemia
- **Section 2.** Workup/investigation of persistent hypoglycemia in neonates, infants, and children
- **Section 3.** Management of neonates, infants, and children with a documented persistent hypoglycemia disorder

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Section 1a: Who to screen

Neonates with signs of hypoglycemia

Infants of diabetic mothers

Large-for-gestational-age birth-weight

Premature or post-mature delivery

IUGR

Neonates who had perinatal stress:

- Birth asphyxia/ischemia; C-section for fetal distress
- Maternal pre-eclampsia/eclampsia or hypertension
- Meconium aspiration syndrome,

Family history of a genetic form of hypoglycemia

Congenital syndromes such as BWS/Hypopit

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Section 1b: Who to investigate

- Neonates with **severe hypoglycemia** (e.g., an episode of symptomatic hypoglycemia or **requiring iv dextrose to treat hypoglycemia**)
- Neonates unable to consistently maintain pre-prandial plasma glucose concentrations **> 50 mg/dL by day 3**
- **Family history** of a genetic form of hypoglycemia
- **Congenital syndromes** (e.g., Beckwith-Wiedemann), abnormal physical features (e.g., midline facial malformations, microphallus)

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Section 2. Investigation of persistent hypoglycemia in neonates, infants, and children

2.1 We recommend that investigations be carried out to diagnose the underlying mechanism of hypoglycemia in order to provide specific management. Grade 1++++

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When to investigate

- After 48 hours of life
  - Transitional period of glucose regulation has passed and a critical sample at the time of diagnosis will allow the etiology to be determined.
- When glucose <50mg/dL

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How to investigate

- Review the History
- Review family history
- Perform a careful physical exam
- Obtain critical sample
  - blood and urine tests when the glucose is low (<50mg/dl)
- Make a diagnosis of the etiology of hypoglycemia

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Critical Sample

- Plasma Glucose
- Insulin, C-Peptide
- Lactate
- Free fatty acids, beta-hydroxybutyrate
- Cortisol and GH
- Urine organic acids
- Acyl-carnitine profile
- ACTH, Ammonia, Amino Acids

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Section 3. Management of neonates, infants, and children with a documented persistent hypoglycemia disorder.

- For high-risk neonates without a suspected congenital hypoglycemia disorder, **we suggest** the goal of treatment be to maintain PG >50 mg/dL (>2.8 mmol/L) for those who are < 48 hours of age and >60 mg/dL (>3.3mmol/L) for those who are > 48 hours of age. (**GRADE 2+000)**.↑

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Section 3. Management of neonates, infants, and children with a documented persistent hypoglycemia disorder.

- For neonates with a suspected congenital hypoglycemia disorder **we recommend** that the goal of treatment be to maintain PG above 70 mg/dL (3.9 mmol/L). (**GRADE 1++00)**

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Conclusions

- The PES Recommendations
  - Prevent unnecessary investigation and treatment of those babies undergoing transitional glucose homeostasis
  - Prevent neonates infants and children with pathological hypoglycemia from being missed

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Guideline Committee

Co-Chair: Charles Stanley

Members:

Endocrinology

- Diva D. De Leon
- Joseph I. Wolfsdorf
- Khalid Hussain
- David A. Weinstein
- Mark A. Sperling
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