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**PES Guidelines : “Recommendations for Evaluation and Management of Hypoglycemia in Neonates, Infants, and Children”**

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**Disclosures**

- I have no conflict of interest to declare

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**Objectives**

1. To outline why new guidelines are needed
2. To discuss the etiology of transitional hypoglycemia
3. To discuss the PES Recommendations

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## Guideline Committee

**Co-Chair:** Charles Stanley

**Members:**

Diva D. De Leon	Mark A. Sperling
Joseph I. Wolfsdorf	Morey Haymond
Khalid Hussain	Lynne L. Levitsky
David A. Weinstein	Neil White

Mohammad Hassan Murad

Paul Rozance                      Rebecca Simmons  
Deborah L. Harris

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## Invited comments

- Professional organizations
  - AAP Committee on Fetus and Newborn
  - AAP Ped Endo group
  - PES Board
  - Congenital Hyperinsulinism International
- World experts in Hypoglycemia

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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
- Pediatric hypoglycemia disorders have unique features
- Difficulties in distinguishing between neonates that have a persistent hypoglycemia disorder and those with self-limited transitional neonatal glucose homeostasis

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## Late Presenting "Congenital Hypoglycemia"

- Retrospective review of patients seen in hypoglycemia center in last 4 years with forms of hypoglycemia that could have been present at birth
  - Genetic forms of Hyperinsulinism
  - Hypopituitarism with pituitary malformations
- Presented after d/c from birth hospital
- Incidence
  - HI 1: 30 - 50,000
  - Hypopit 1: 25-50,000

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## Results

- 18 patients
- 12 had genetic forms of hyperinsulinism
  - 5 had IV glucose to treat hypo 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 hypo 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 not
- Hypopituitarism
  - 100% (6 of 6) of late diagnosed patients had an opportunity to be diagnosed in NICU and were not

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## Cook Children's ER Study

- 224,125 patients
- 19,507 patients had a glucose test (8.7%)
- 160 had hypoglycemia (0.82%)
  - 0.07% of total ER patients
  - 1:1400 ER patients
- 85 had complete evaluation (53%)
  - 75 had confirmed true hypoglycemia
    - 17 had serious endocrine cause (20%)

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## Etiology of Hypoglycemia

Serious Underlying Disorders	8	Non Serious Underlying Disorders	51
Nissen	8	Idiopathic Ketotic Hypoglycemia	51
Fundoplication		No Hypoglycemia	10
Adrenal Insufficiency	4	Beta Blocker Use	1
Hyperinsulinism	4	Sepsis	1
Hypopituitarism	1	<b>Total</b>	<b>63</b>
<b>Total</b>	<b>17</b>		

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## Normal Glucose Levels in the Newborn Period

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

Alkalay et al: Am J perinatology: 2006

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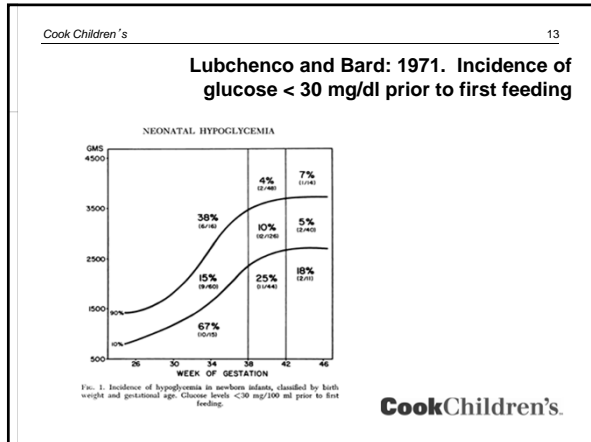
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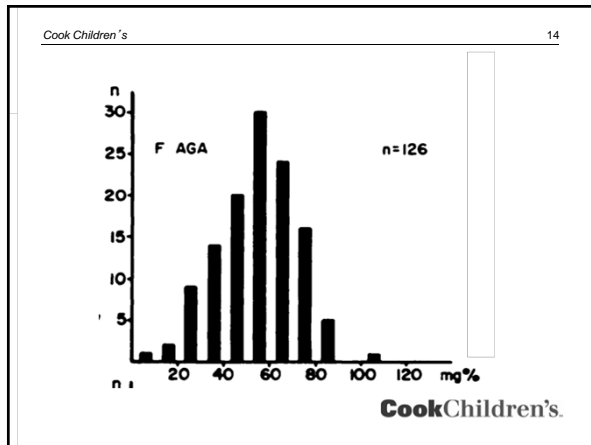
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**Are all neonates equal?**

- When all babies were re-screened at 72 hours <1% or 2/374 babies had glucose  $\leq$  50 mg/dl
- Of the 55 babies in the study with hypoglycemia, 2 (3.6%) still had glucose <50 mg/dl by 72 hr

Lubchenko and Bard 1971

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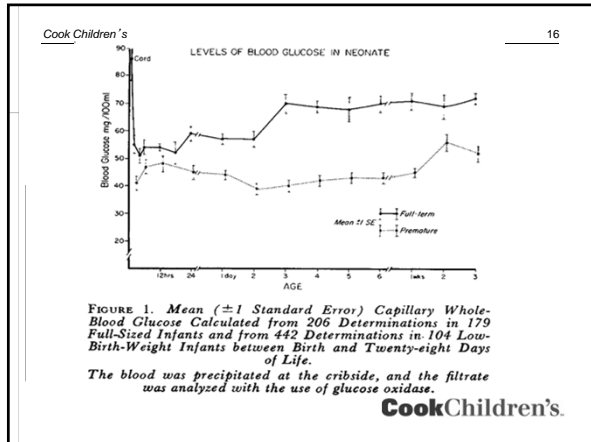
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## Committee objectives

- To provide recommendations for the diagnosis and management of hypoglycemia disorders in neonates, infants and children.
  - Prevent unnecessary investigation of normal neonates
  - To assist physicians to recognize persistent hypoglycemia disorders, to guide their rapid diagnosis and effective treatment, and to prevent brain damage in at risk babies

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## Outline of Recommendations

- **Section 1:** Which neonates, infants and children to evaluate for 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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## 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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## 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. Workup/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. **SCORE 1++++**

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## When to work-up

- 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

- 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)**.<sup>1</sup>

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### Section 3 Management

- For neonates with a suspected congenital hypoglycemia disorder and older infants and children with a confirmed 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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### Section 3 Management

- **We recommend** an individualized approach to management in which treatment is tailored to the specific hypoglycemia disorder, taking into account patient safety and family preferences.

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## Conclusions

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

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