PES Recommendations for Evaluation and Management of Hypoglycemia in Neonates, Infants, and Children

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On behalf of the Team

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PES HYPO Guide Committee

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Invited comments

- Professional organizations
  - AAP Committee on Fetus and Newborn
  - AAP Ped Endo group
  - PES Board
- World experts in Hypoglycemia
- World expert parents in management of hypoglycemia
  - CHI

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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
- Published guides do not exist for hypoglycemia in infants and children without diabetes;
- Guidelines exist for neonates in first 24 hours of life

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Etiology of hypoglycemia in newborn

- Transitional glucose homeostasis
- IUGR with depleted stores of glycogen
- Infants of diabetic mothers
- Perinatal Stress Hyperinsulinism
- Hypopituitarism
- Genetic Hyperinsulinism
- Glycogen Storage disease

Transitional glucose homeostasis

- Transitional period
  - First 12-48 hours of life
  - Change from fetal to neonatal glucose metabolism
    - In-utero: Constant insulin secretion
    - After birth: Intermittent insulin secretion and starts at glucose approximately 80 mgs/dl (4.4 mmol/L)

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 and to guide their expeditious diagnosis and effective treatment, and to prevent brain damage in at risk babies

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

Section 1 : Which neonates to evaluate for hypoglycemia

For those neonates who are suspected to be at high risk of having a persistent hypoglycemia disorder, we suggest evaluation when the infant is ≥ 48 hours of age so that the period of transitional glucose regulation has passed and persistent hypoglycemia may be excluded before discharge home (**GRADE 2++00)**.

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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

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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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

Section 2. Workup/investigation of persistent hypoglycemia in neonates

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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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

- No spontaneous glucose <50 mg/dL (2.8mmol/L)
  - Test by monitoring plasma glucose during a 6-hour fasting challenge
    - Skip a feed and measure POC glucose at 3,4 & 5 hours
    - Measure plasma glucose at 6 hours or if POC < 50 mg/dL (2.8 mmol/L)
- Consider further evaluation / treatment (including sub-specialist consultation) if unable to maintain plasma glucose > 60 mg/dL (3.3 mmol/L) for 6 hours after 3 days of age
- If there is a family history of a proven hypoglycemic disorder, a definitive test for the specific disorder should be performed

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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 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

- 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)**.
  - In these babies if they need IV glucose to treat then aim to keep glucose >60mg/dl (3.3mmol/L) while on IV glucose and wean off as tolerated

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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Summary

- We believe these recommendations will
  - Prevent unnecessary investigation and treatment of those babies undergoing transitional glucose homeostasis
  - Prevent babies with pathological hypoglycemia from being missed