

Neonatal Hypoglycemia - Definition

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- Neonatal hypoglycemia is the most common metabolic problem in newborn infants and a readily preventable cause of brain injury in infancy. However, clinical thresholds for diagnosis and treatment of neonatal hypoglycemia are widely debated, with no universally accepted safe blood glucose concentration for newborns [1, 2].
- This uncertainty is largely due to a lack of evidence regarding the effect of low neonatal glucose concentrations on neurodevelopmental outcomes. Further, recent studies have suggested that higher glucose concentrations after hypoglycemia may also contribute to brain injury [3], thus adding complexity to this common clinical problem.

Table 1. Neonatal hypoglycemia definitions and or threshold for intervention:

Operational threshold by Cornblath et al.	<ul style="list-style-type: none">• That concentration of plasma or whole blood glucose at which clinicians should consider intervention, based on the evidence currently available in the literature.
NNF definition	<ul style="list-style-type: none">• A blood glucose value of < 40 mg/dL (plasma glucose < 45 mg/dL)
BAPM definition	<ul style="list-style-type: none">• Clinicians should intervene to raise blood glucose (BG) concentration in infants with risk factors for impaired metabolic adaptation but without abnormal clinical signs if BG concentration is <2.0 mmol/L (36 mg/dL) on two occasions.
WHO definition	<ul style="list-style-type: none">• Blood glucose level (BGL) of less than 45 mg/dL.
AAP definition	<ul style="list-style-type: none">• Intravenous treatment is not needed until glucose concentrations are < 25 mg/dL (1.4 mmol/L) within the first 4 h after birth, or < 35 mg/dL (2.0 mmol/L) from 4 to 24 h
PES definition	<ul style="list-style-type: none">• A blood glucose value of less than 50 mg/dL (2.77 mmol/L) in the first 48 hours after birth is being suggested as the threshold for neonatal hypoglycemia. In addition, the PES endorses a threshold of 60 mg/dL (3.33 mmol/L) in the first 48 hours if there is concern for a congenital hypoglycemia disorder.

- **Cornblath et al** suggested that ‘hypoglycemia’ is not readily defined for the individual neonate and that ‘operational threshold’ (concentration of blood glucose at which intervention should be considered) should be established. [4, 5]. Operational thresholds are different from therapeutic goals, do not define normal or abnormal but provide a margin of safety. Importantly however, such operational definitions do not address whether the threshold level of blood glucose for intervention represents the threshold level for neuronal injury. At present, no simple bedside measures exist that can determine these values and hence provide an absolute indication for an intervention in any individual infant
- **NNF** evidence based clinical practice guild lines state that for practical purposes and uniformity of definition, a blood glucose value of < 40 mg/dL (plasma glucose < 45 mg/dL) should prompt intervention for hypoglycemia in all newborns. There is no rational basis for the historical practice of distinguishing between term and preterm infants when setting threshold criteria for intervention.
- **British Association of Perinatal Medicine (BAPM)** Framework for Practice recommends that clinicians should intervene to raise blood glucose (BG) concentration in infants with risk factors for impaired metabolic adaption but without abnormal clinical signs if BG concentration is <2.0 mmol/L (36 mg/dL) on two occasions. This operational threshold was proposed by expert consensus in 2000, [4] and no evidence-based modifications to it have been proposed despite review of the literature on several occasions since.
- Children with Hypoglycemia and Their Later Development (CHYLD) study team published the neurocognitive outcomes at 4.5 years of a group of children who had risk factors for neonatal hypoglycaemia and received treatment aimed at raising the blood glucose to >2.6

mmol/L. [6] The group reported that blood glucose <2.6 mmol/L was associated with increased rates of executive and visual motor dysfunction. However, the observations do not support changing the operational threshold to 2.6 mmol/L (47mg/dL) for babies born at full term without abnormal signs.

- Findings from a large multicenter prospective study of preterm infants suggest that even moderate hypoglycemia (at least one daily value of plasma values <47 mg/dL) can have significant impact. There was a 30% incidence of neurodevelopmental sequelae if moderate hypoglycemia was present for 3 days or more and approximately 40% if present for 5 days or more. [7]
- **World Health Organization** defines hypoglycemia as “blood glucose level (BGL) of less than 45 mg/dL.” [8]
- Currently there is ongoing discussion between the AAP and PES regarding the management of hypoglycemia, including the blood glucose values that should prompt concern, particularly after 48 hours of age.
- **The AAP** concedes that the current “definition” of neonatal hypoglycemia (blood glucose <47 mg/dL [2.61 mmol/L]), but lower and higher thresholds have been recommended. For example, the American Academy of Pediatrics advises that intravenous treatment is not needed until glucose concentrations are < 25 mg/dL (1.4 mmol/L) within the first 4 h after birth, or < 35 mg/dL (2.0 mmol/L) from 4 to 24 h [9].
- **Per recent PES** recommendations, a blood glucose value of less than 50 mg/dL (2.77 mmol/L) in the first 48 hours after birth is being suggested as the threshold for neonatal hypoglycemia

[10]. In addition, the PES endorses a threshold of 60 mg/dL (3.33 mmol/L) in the first 48 hours if there is concern for a congenital hypoglycemia disorder. Such thresholds are based on the thresholds for observation of symptoms in older children and adults and are not specific to neonates. However, transitional neonatal hypoglycemia likely reflects a state of peripartum adaptation, and affected infants are likely not at risk for a congenital hypoglycemia disorder. These higher thresholds of blood glucose values increase concerns for overtreatment, especially in asymptomatic neonates. This lack of consensus reflects the paucity of evidence about long term outcomes after neonatal hypoglycaemia.

- *With the underlying risk of neurodevelopmental sequel with lower thresholds and concerns of over treatment by targeting higher thresholds AAP definition for hypoglycemia with blood glucose levels less than 47 mg/dl (2.6 mmol/L) seems to be promising for both term and preterm neonates.*

References-

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