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Low blood sugar levels in the newborn infant: Do changing goal posts matter?

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ABSTRACT

Glucose supply and metabolism are essential for growth and normal brain development in both the fetus and newborn. Disorders of glucose availability and metabolism can result in either hypoglycemia or hyperglycemia. The first section of this manuscript will contrast recommendations from the American Academy of Pediatrics and the Pediatric Endocrine Society on the approach to defining neonatal hypoglycemia. Recent studies will be reviewed which add to the controversy. This review aims to discuss the evidence-based guidelines, definitions, pathogenesis, outcomes and management options in this field. The current variations in practices and possibilities of future trials are also addressed.

1. Introduction

Using thresholds for at – risk newborns means that neonatal hypoglycemia could be diagnosed in 6–19% of asymptomatic newborns with no risk factors the first 48 h of life [1]. For those neonates identified as being at higher risk, including late preterm, small for gestational age and large for gestational age term infants, and infants of diabetic mothers, the risk may be up to 50% [2]. However, the very definition of neonatal hypoglycemia is not agreed upon and therefore the threshold used influences reported incidence. What is clear is that the higher the glucose threshold and the more screening tests performed, the more cases of "neonatal hypoglycemia" will be diagnosed, leaving the clinician to make clinical judgements for asymptomatic infants. This is of great importance because "neonatal hypoglycemia" has been implicated in poor neurodevelopmental outcomes in later life but the thresholds i.e. where neuroglycopenia (deficient glucose for brain metabolism) occurs in the neonate is not known and is very difficult to study [3]. Our understanding of glucose metabolism and of neonatal transitional hypoglycemia have grown but we still don't know: "How low is too low and for how long? " [3].

2. Transitional neonatal hypoglycemia

The Pediatric Endocrine Society (PES) focused on the first 48 h of life to take a neuroendocrine approach to define a normal glucose level for neonates. They focused on the major metabolic fuel and hormonal responses to low blood glucose levels that occur during this transition. At birth the infant's blood glucose concentration is about 70% of the maternal level. It falls to a nadir by 1 h of age to a 5th or 10th percentile level as low as 20–25 mg/dl. This nadir and the lower glucose levels are prevalent in all healthy neonates and are seen in all mammalian newborns [4]. These levels are transient and begin to rise over the first hours and days of life the levels becoming similar to adult values, suggesting that neonates are physiologically predisposed to experience low plasma glucose levels.

In examining the metabolic and hormonal responses during this transition, this period appears to resemble a form of congenital hyperinsulinism causing a lowering of the plasma glucose threshold for suppression of insulin secretion [5]. The PES noted this that this "transitional hypoglycemia" was characterized by hyperinsulinemia, suppressed levels of ketones and glycemic responses to glucagon and epinephrine [6–8]. This profile is consistent with a neurogenic response at a glucose level of 55–65 mg/dl in older children and adults and therefore represented the normal glucose level for the PES since at this level the adult has a neurogenic response to stabilize glucose levels and protect the brain. A level below 50 mg/dl is where brain injury or neuroglycopenia occurs for the adult but this level is not known for the newborn.

The AAP interpreted this data differently, suggesting that "physiologic hypoglycemia" is beneficial and part of the normal adaption for postnatal life that establishes postnatal glucose homeostasis [4,9–11]. The potential benefits included stimulating physiologic processes

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required for survival including promoting glucose production through gluconeogenesis and glycogenolysis [11]. In addition the decrease in glucose concentration enhances oxidative fat metabolism and stimulates appetite and helps adapt to fast-feed cycles [11].

The PES relies on neuroendocrine data and mean values of glucose during transition for asymptomatic newborns including recommended treatment values are shown on Table 1. The AAP relies on the lower ranges, clinical condition, and risk factors for the first 24 h of life in asymptomatic late preterm and term infants including Small for Gestational Age(SGA), Large for Gestational Age (LGA) and Infants of Diabetic Mothers (IDM) shown on Table 2. A paper called Imperfect Advice -neonatal hypoglycemia made recommendations of plasma glucose > 45 mg/dl for 24–48 h of life since the AAP algorithm guidance was only for the first 24 h. The advice also suggested that after 48–72 h the glucose levels rose, consistent with PES recommendations [13].

3. Incidence of low glucose levels in neonates

A study including 514 infants > 35 weeks gestation at risk of hypoglycemia (SGA, LGA, IDM, late preterm) were screened for hypoglycemia. The incidence of plasma glucose <47 mg/dl over the first 48 h was reported for the four groups at risk [2]. They found that 51% of these patients had at least one episode of plasma glucose below the threshold chosen and 19% had a plasma glucose < 36 mg/dl [2]. Glucose oxidase methods were used for initial measurements as opposed to the less precise bedside point of care screening methods. This 51% incidence of low glucose concentrations supports the decision of the AAP to focus recommendations on these patients [12].

As to how the clinician views the reason for transient neonatal hypoglycemia will influence their decision over whether these concentrations of glucose, especially at the lower range of "normal" are harmful. Most agree that symptomatic hypoglycemia should be treated, as should extremely or persistently low glucose concentrations. However, there is little consensus regarding the significance of transient and asymptomatic low glucose concentrations. As we will see, the value of 47 mg/dl came from a Nutrition study of very preterm infants 25 years before this study. If we applied <47 mg/dl as this study did as the level to treat, then these four groups would generate more than 550,000 neonates in the USA that would be screened and 12.5% of all newborns would be diagnosed with hypoglycemia.

Another study used the PES screening recommendations which included many more newborns to screen at a threshold level <50 mg/dl to determine the effect on well-appearing at risk newborns screened for hypoglycemia [14]. Blood glucose values were obtained at < 72 h of age. Almost 50% of babies were screened, twice as many as the AAP guideline would have. Forty three percent were diagnosed as hypoglycemic and nearly 5% required intensive care for hypoglycemia [14]. They also found a statistically significant association between using this threshold value of <50 mg/dl and reduction in exclusive breast feeding from 65% for those without "hypoglycemia" vs 22% for those with values below 50 mg/dl [14]. They concluded that the hypoglycemia risk criteria recommended by the PES result in screening a larger proportion of otherwise well newborns than the AAP four risk criteria and negatively impact rates of exclusive breastfeeding [14].

Table 1
2015 PES Neonatal Hypoglycemia Guidelines.

POSTNATAL GLUCOSE TREATMENT TARGETS: PES		
High-risk newborns without a suspected congenital hypoglycemia disorder	0-48 h	>50 mg/dL
	>48 h	>60 mg/dL
Neonates with suspected congenital hypoglycemia disorder and those requiring IV glucose to treat hypoglycemia	Any time	>70 mg/dL
The PES set the above thresholds based on the following observations about the impact of specific glucose concentrations in adults:		
55-65 mg/dL	Brain glucose utilization becomes limited.	
50-55 mg/dL	Neurogenic symptoms (palpitations, tremor, anxiety, sweat, hunger, parethesia) perceived	
<50 mg/dL	Cognitive function impaired (neuroglycopenia, characterized by confusion, seizure, coma).	

Abbreviations: IV intravenous; PES, Pediatric Endocrine Society.
From: Thornton PS, et al[2]

4. Neurodevelopmental impact of "hypoglycemia"

A neurodevelopmental approach is aimed at finding the critical threshold of plasma glucose associated with brain injury or where "neuroglycopenia" occurs in the newborn. Neuroglycopenia in the adult occurs at < 50 mg/dl. At levels between 55 and 65 mg/dl newborn infants demonstrate neuroendocrine responses similar to an adult exhibiting a neurogenic response [15].

A multicenter nutrition trial in the UK published in 1988 changed the landscape concerning neonatal hypoglycemia and suggested they had found neuroglycopenia in the neonates or the level at which there is inadequate supply of glucose for the brain [16]. The critical level of 47 mg/dl was noted to reliably predict poorer outcomes [16]. This study included 661 preterm infants <1850 g at birth, a group not included in the AAP guideline. The AAP believed that preterms with mean gestational ages of 31 weeks as in this study would already be in the NICU setting and already screened as part of their routine clinical care.

The study from the UK collected plasma glucose levels daily initially and then weekly until discharge for these preterm infants in a study looking at the relationship between early diets and cognitive outcomes some 18 months later [16]. They found that the number of days these infants experienced "moderate hypoglycemia" (<47 mg/dl) was correlated with reduced scores for mental and motor development at 18 months of age [16]. Hypoglycemia was not the focus of this project and many babies had very low blood glucose levels that were not addressed in real time as some infants had plasma glucose levels <20 mg/dl for as long as 3–7 days without intervention. At follow-up 7 years later, the authors suggested in a letter that there was "difficulty of providing causation when an observational approach is used" [17] noting that randomized controlled trials should be done. However, this value of 47 mg/dl originally examined in preterm infants, has now become the worldwide standard after 1988 and is applied even to term appropriate for gestational age as the critical threshold defining hypoglycemia and risk of brain injury.

In 2012, 25 years later, a prospective trial was done including infants <32 weeks who had blood glucose levels measured daily for the first 10 days of life [18]. Forty seven of 566 (8%) had a blood glucose level < 47 mg/dl on at least three of the first 10 days of life (18). All were matched with hypoglycemia free controls. No differences were found in developmental progress or physical disability at 2 years of age. Incredibly, 81% of the original cohort were matched again at 15 years of age and they were almost identical in full scale IQ [18]. The inclusion of children who had a level <47 mg/dl for > 4 days and another group with blood glucose < 37 mg/dl on three different days did not alter these results. The authors concluded that they found no evidence that recurrent low blood glucose levels (<47 mg/dl) in the first 10 days of life pose a hazard to preterm infants. Clearly the study did not imply that low blood glucose levels cannot be damaging in the preterm infant even in the absence of clinical signs. However, the data did suggest that the danger threshold or where neuroglycopenia might occur must be lower than many were suggesting [18].

Current literature does not, in my opinion, support 47 mg/dl of plasma glucose as a critical threshold for the newborn. A recent study provides a literature review evaluating whether <47 mg/dl portends a

Table 2
Screening and management of postnatal glucose homeostasis in late preterm and term SGA, IDM/LGA Infants [(LPT) Infants 34 – 36 6/7 weeks and SGA (screen 0-24 hrs); IDM and LGA > 34 weeks (screen 0 -12 hrs)] Modified from ref [12].

Symptomatic and <40mg/dl ⟶ IV Glucose			
ASYMPTOMATIC			
Birth to 4 hours of age		**4 – 24 hours of Age**	
INITIAL FEED WITHIN 1 Hour Screen glucose 30 minutes after 1st feed		Continue feeds q2-3 hours Screen Glucose prior to each feed	
Initial Screen <25mg/dl		Screen <35mg/dl	
Feed and check in 1 hour		Feed and check in 1 hour	
<25mg/dl ↓ IV Glucose*	25 – 40mg/dl ↓ Refeed/IV Glucose* as needed	<35mg/dl ↓ IV Glucose*	35 – 45m/dl ↓ Refeed/IV Glucose* as needed
Target Glucose screen ≥45mg/dl prior to routine feeds			
*Glucose dose = 200mg/kg (dextrose 10% at 2ml/kg) and/or IV infusion at 5 – 8mg/kg/min (80 – 100ml/kg/d) Achieve plasma glucose 40 – 50mg/dl.			
Symptoms of Hypoglycemia include: Irritability, tremors, jitteriness, exaggerated moro reflex, high-pitched cry, seizures, lethargy, floppiness, cyanosis, apnea, poor feeding.			

quantifiable risk for future neurologic impairment [19]. This review emphasizes that studies do not control for other factors known to impact neurodevelopmental outcomes, such as maternal education or socio-economic status. A unique study from the state of Arkansas evaluated 1400 infants at 10 years of age who had a single glucose level during transition or the first hours of life <45 mg/dl [1]. On the basis of fourth grade school examinations from across the state, they found that a single episode of hypoglycemia that resolved by 3 h of age was associated with a 50% reduction in the odds of achieving proficiency in literacy and numeracy [1]. This group of patients represented every single birth during a calendar year at the University of Arkansas, so they were mostly made up of late preterm and term infants. The low glucose levels were followed by a second value above the cut-off of <30, <40, and <45 mg/dl, respectively. It is not clear if the exposure group had only the one episode below the cut off values since no levels were reported after the second value.

Current guidelines recommend screening only for newborns that are symptomatic or at risk of developing hypoglycemia. The Arkansas study suggests that transient newborn hypoglycemia may be associated with poorer academic achievement at age 10 years. Should we now consider universal glucose screening of all neonates? The brief period of "hypoglycemia" was diagnosed at 90 min of age but the actual result was available 30 min after that. The second measurements showing resolution above the threshold came 70 min later or at 3 h of age. It is unlikely that any intervention after the results were known could shorten the exposure to this brief period of transitional hypoglycemia [3].

Studies from the Children with Hypoglycemia and their later development (CHYLD) have added a lot of information about the effects of low plasma glucose (<47 mg/dl) and developmental outcomes including follow up of infants treated with dextrose gel [20,21]. The investigators reported on over 600 late preterm and term infants at risk for hypoglycemia. Studies also included continuous glucose monitoring done with interstitial sensors recording a glucose level every 5 min. Infants were screened and treated aggressively to maintain plasma glucose above 47 mg/dl. There were long and undetected periods of glucose levels below their threshold detected only with continuous monitoring and missed on intermittent blood sampling [20]. More than half of the infants at risk were diagnosed with hypoglycemia. Almost 25% had undetected hypoglycemia with intermittent sampling and 25% of these episodes only detected with continuous glucose monitoring lasted greater than 5 h [20].

Follow-up at age 2 years was reported among five groupings, including a reference group who never had hypoglycemia, any episode of hypoglycemia, > 3 days of hypoglycemia, or severe hypoglycemia <36 mg/dl. There was no association between neonatal hypoglycemia and neurodevelopmental outcome at 2 years of age [20]. Even those with undetected episodes of hypoglycemia showed no differences in neurosensory impairment or processing difficulty relative to controls. However, at 4.5 years of age, the follow-up demonstrated executive function difficulties in those infants suffering more than one episode of hypoglycemia, found only with continuous glucose monitoring [21].

A recent multicenter study compared outcomes balancing treatment without risking adverse consequences while at the same time avoiding overutilization of health care resources. This study challenges the required treatment at glucose <47 mg/dl vs < 36 mg/dl [22]. This was a prospective multicenter randomized noninferiority study including 689 otherwise healthy newborns born at > 35 weeks and identified as being at risk for hypoglycemia. Study allowed for <0.5 standard deviation below the mean, as a threshold for noninferiority. One standard deviation from the mean is considered normal. Cognitive and motor outcome scores were found to be similar in the two groups including a follow up of 85% of the study patients. The prespecified inferiority limit was not crossed. The mean glucose concentration was 57 mg/dl in the lower threshold group and 61 mg/dl in the traditional-threshold group [22]. Fewer and less severe hypoglycemic episodes occurred in the traditional threshold group, but that group had more invasive diagnostic and treatment interventions. The authors concluded that in otherwise healthy newborns with asymptomatic moderate hypoglycemia, a lower glucose treatment threshold (36 mg/dl) was noninferior to a traditional threshold (47 mg/dl) with regards to psychomotor development at 18 months [22].

It must be noted that there was no defined protocol for how to treat hypoglycemia as it was left to provider discretion despite wide practice variation. Like most studies the longer the follow up the better. Follow up at 18 months of age is likely too soon to detect differences in neurodevelopment outcomes. The CHYLD studies found no difference in

neurodevelopmental outcomes between those with glucose <47 mg/dl and those without at 24 months of age but did find differences at 4.5 years of age [20,21].

5. Let it glow

The Glucose in Well babies (GLOW) study determined postnatal changes in plasma and interstitial glucose concentrations (continuous glucose monitoring) of 67 healthy infants. All were AGA and over the first 5 days of life. These infants received current recommended care and the incidence of observed low glucose concentration with recommended thresholds for treatment of at risk infants were compared [23]. Mean glucose concentrations were noted to increase over the first 18 h, remained stable to 48 h (~60 mg/dl) before increasing to a new plateau by the fourth day of (~90 mg/dl). Plasma glucose concentrations of 47 mg/dl approximated the 10th percentile in the first 48 h, and 39% of infants had ≥1 episode below this threshold [23].

Continuous monitoring showed that half of the babies were "hypoglycemic" at some point [23]. If you compare these results from this study with recommendations for thresholds for treatment over the first days of life with four society recommendations (British Association of Perinatal Medicine, World Health Organization, PES and AAP), the majority of healthy newborn infants with no risk factors at all will have levels defined as abnormal and would be treated (see Table 3) [24]. The data thus show that many healthy infants have glucose concentrations below the international recommended thresholds for treatment of at risk infants [23] and that apparently healthy term infants born at < 40 weeks gestation were more likely to have episodes of low glucose concentrations (Table 4). Similar to late preterms who are identified as a risk category, the data suggest that healthy early term infants are more likely to have low plasma glucose concentrations than more mature infants [23].

Is hypoglycemia more dangerous for the at-risk infants? Risk groups are considered to be more likely to develop low blood sugars but no evidence that they are more likely to have long lasting sequelae [24]. A letter to the Editor from the PES in response to the GLOW study argues comparing glucose thresholds for at risk babies with glucose concentrations in normal healthy babies is inappropriate [25]. The intentions of the GLOW study was not to suggest a change in the care of the at-risk infants but to show that low glucose concentrations are common in healthy newborns. At this they clearly state they are unable to determine if low glucose concentrations in healthy babies may be associated with impairments in later childhood [23].

6. Conclusion

The optimal strategy for managing asymptomatic infants with low plasma glucose levels enhanced with use of continuous glucose monitoring in babies at risk or no risk still remains elusive and more confusing than ever. Recommendations from various organizations and experts are educated "guesses" and only long term randomized controlled trials will take us closer to finding neuroglycopenia in the neonate. I am afraid it is not as simple as a number.

Practice Points.

- No guideline is perfect
- Individual patient characteristics and exam are important and clinical judgement is important
- Neuroglycopenia cannot be defined by a single numerical value and a low glucose concentration is not a diagnosis
- Take extra care before discharge for those treated for hypoglycemia or who had low values followed over the first 24–48 h to make sure that there is not the possibility of a Persistent Hypoglycemic syndrome.

Research Gaps.

Table 3
Numbers of healthy no risk infants with glucose levels below recommended thresholds for treatment. CGM continuous glucose monitoring Modified from ref [23]

Glucose levels using plasma or CGM PLASMA/CGM Percentages that would require treatment for that organization					
	0–4 (%)	4–24 (%)	24–48 (%)	48–72 (%)	72–120 h (%)
AAP	O/0,	3/11,	1/5,	1/2,	0/0
BAPM	5/7	4/16	2/5	3/2	0/0
WHO	18/38	24/63	13/33	10/30	1/9
PES	25/50	40/73	22/58	46/73	6/55

Table 4
″At-risk infants have a marginally increased chance of a glucose below the thresholds vs perfectly healthy "not-at-risk". Modified ref [24].

Number of healthy and at-risk infants with episodes of low glucose concentrations				
Thresholds, mg/dL [mmol/L]	Plasma glucose		Interstitial glucose	
	Healthy Infants	At-risk infants	Healthy Infants	At-risk infants
<47 [2.6]	26/67 (39%)	159/326 (49%)	37/51 (68%)	33/44 (75%)
<26 [2.0]	7/67 (10%)	48/326 (15%)	12/51 (23%)	14/44 (32%)
<27 [1.5]	0/67 (0%)	9/326 (3%)	0/51 (2%)	3/44 (3%)

- Can an exact diagnosis of hypoglycemia ever be based on a single level of glucose?
- Why are the clinical signs of neonatal hypoglycemia so variable?
- What are the long-term effects of repeated asymptomatic hypoglycemia?
- How should we treat asymptomatic hypoglycemia in high-risk infants?
- What is the neurocognitive performance at school age of infants who have had the diagnosis of hypoglycemia and does executive function at 4.5 years predict academic outcomes?

References

[1] Kaiser JR, Bai S, Gibson N, et al. Association between transient newborn hypoglycemia and fourth grade achievement test proficiency: a population study. JAMA Pediatr 2015;169:913–21.
[2] Harris DL, Weston P, Harding JE. Incidence of neonatal hypoglycemia in babies identified as at risk. J Pediatr 2012;161:787–91.
[3] Adamkin DH. Neonatal hypoglycemia. Semin Fetal Neonatal Med 2017;22(1):36–41.
[4] Srinvasan G, Pildes RS, Cattamanchi G. Plasma glucose levels in normal neonates: a new look. J Pediatr 1986;109:114–7.
[5] Adamkin DH. Metabolic screening and postnatal glucose homeostasis in the newborn. Pediatr Clin 2015;62:385–409.
[6] Hawdon JM, Ward Platt MP, Aynsley -Green A. Patterns of metabolic adaptation for preterm and term infants in the first neonatal week. Arch Dis Child 1992;67:357–65.
[7] Desmond MM, Hild JR, Gast JH. The glycemic response of the newborn infant to epinephrine administration: a preliminary report. J Pediatr 1950;37:341–50.
[8] Stanley CA, Anday EK, Baker L, Delivoria-Papadopolous M. Metabolic fuel and hormone responses to fasting in newborn infants. Pediatrics 1979;64:613–9.
[9] Heck LJ, Erenberg A. Serum glucose levels in term neonates during the first 48h of life. J Pediatr 1987;110:119–22.
[10] Hay Jr WW, Adamkin DH, Harding JE, Hawdon J. The postnatal glucose concentration nadir is not abnormal and does not need to Be treated. Neonatology 2018;114(2):163.
[11] Adamkin DH. Update on neonatal hypoglycemia. Arch Perinat Med 2005;11:13–5.
[12] Committee on Fetus and Newborn, Adamkin DH. Postnatal glucose homeostasis in late preterm and term infants. Pediatrics 2011;127:575–9.
[13] Adamkin DH, Polin RA. Imperfect advice: neonatal hypoglycemia. J Pediatr 2016;176:195–6.
[14] Mukhopadhyay S, Wade KC, Dhudasia MB, et al. Clinical impact of neonatal hypoglycemia screening in the well-baby care. J Perinatol 2020;40(9):1331–8.

[15] Stanley C, Rozance P, Thornton, et al. Re-evaluating transitional neonatal hypoglycemia: mechanism and implications for management. J Pediatr 2015:1–6.
[16] Lucas A, Morley R, Cole TJ. Adverse neurodevelopmental outcome of moderate neonatal hypoglycemia. Br Med J 1988;297:1304–8.
[17] Lucas A, Morley R. Outcome of neonatal hypoglycemia (letter). BMJ 1999;318 (7177):195.
[18] Tin W, Brunskill G, Kelly T, Fritz S. 5 year follow up of recurrent hypoglycemia in preterm infants. Pediatrics 2012;130:1497–503.
[19] Palmaccio SJ, Rodriquez AL, Drago MJ, Mercurio M. An evidence based ethical approach to parental refusal of screening tests: the case of asymptomatic neonatal hypoglycemia. Pediatrics 2010;(21):311.
[20] McKinley CJ, Alsweiler JM, Anstice NS, Chase JG, Gamble GD, et al. Neonatal glycemia and neurodevelopmental outcomes at 2 years. NEJM 2015;373:1507–18.
[21] Harris DL, Alsweiler JM, Ansell JM, Gamble GD, et al. Outcomes after two years after dextrose gel treatment for neonatal hypoglycemia; follow up of a randomized controlled trial. J Pediatr 2016;170:54–9.
[22] Van Kempen AAMN, Eskes DHGM, Nuytmans JH, et al. Lower versus traditional treatment threshold for neonatal hypoglycemia. NEJM 2020;382:534–44.
[23] Harris DL, Weston PJ, Gamble GD, Harding JE. Glucose profiles in healthy term infants in the first 5 days: the Glucose in Well Babies (GLOW) Study. J Pediatr 2020;223:34–41.
[24] Barrington K. Let it Glow. Normal blood sugar profiles in newborn infants. Neonatal Research. 6 May 2020. p. 1–6. Available from: https://neonatalresearch.org/2020/05/06/let-it-glow-normal-blood-sugar-profiles-in-newborn-infants/. [Accessed 25 January 2021].
[25] Thornton PS, Rozance PJ, Sperling MA. The GLOW Study does not light up the true Pediatric Endocrine Society recommendations for management of hypoglycemia in newborns. J Pediatr 2020;225:279.