

Newborn Guideline 5

NEONATAL HYPOGLYCEMIA

1. INTRODUCTION

Hypoglycemia is the most common metabolic problem occurring in newborn infants. In the majority of cases it merely reflects a normal process of adaptation to extrauterine life:

“Hypoglycemia is not a medical condition in itself, but a feature of illness or of failure to adapt from the fetal state of continuous transplacental glucose consumption to the extrauterine pattern of intermittent nutrient supply.”¹

A normal range for neonatal blood glucose levels has not been properly defined, and there is controversy over the definition of a safe blood glucose concentration.¹ The World Health Organization now designates a blood glucose “operational threshold” ≤ 2.6 mmol/L as requiring treatment, and makes no distinction between preterm and term infants. Historically however, there have been at least four different approaches to defining hypoglycemia based on clinical manifestations, epidemiological approaches to blood glucose values, acute changes in metabolic and endocrine responses and neurologic function, and long term outcome.²

Clinically significant episodes of hypoglycemia are associated with low blood glucose resolving within minutes of re-establishing normoglycemia. The clinical manifestations, e.g. tremor, irritability, apnea, hypothermia, etc. are non-specific and occur with a variety of other neonatal conditions. Term and preterm infants with hypoglycemia *in the presence of abnormal clinical signs* have poor outcomes, whereas evidence of risk in newborns with hypoglycemia *in the absence of abnormal clinical signs* remains controversial.

With the epidemiological approach to hypoglycemia, the operational cut off for treatment was defined by blood glucose levels measured during 48-72 hours of life at two standard deviations below the mean. In term newborns, hypoglycemia was defined as blood glucose less than 2.0 mmol/L, and 1.11 mmol/L for preterm infants. Concerns with this approach arose following observations that some infants had no clinical signs, even with extremely low plasma glucose concentrations. These concerns were underscored by the suggestion that asymptomatic hypoglycemia might also lead to neurodevelopmental sequelae.³

Physiologically, hypoglycemia is present when glucose delivery is inadequate to meet glucose demand, and this can occur over a wide range of blood glucose concentrations. A fall in blood glucose concentration provokes measurable counter regulatory responses with increases in epinephrine, growth hormone, cortisol, and glucagon. Free fatty acids, glycerol, and ketone bodies are alternate metabolic substrates for the neonatal brain, and the neonatal brain is capable of using ketone bodies for oxidative metabolism. Hence, the significance of blood glucose concentration on neurodevelopmental outcome cannot be interpreted in isolation, and factors such as developmental stage of the infant, brain blood flow, availability of alternate fuels, activity metabolic processes of the various constituents of the nervous system must be considered.

2. DEFINITION

A clinically significant episode of hypoglycemia is characterized by a blood glucose concentration ≤ 2.6 associated with clinical manifestations resolving within minutes of re-establishing normoglycemia. Severe neurological sequelae may occur as a consequence of symptomatic neonatal hypoglycemia.

3. CLINICAL SIGNS

- Tremor, jitteriness, hypotonia, irritability
- Seizures
- Abnormal cry (whining or high pitched)
- Lethargy, poor feeding/sucking
- Apnea, tachypnea
- Diaphoresis, pallor
- Temperature instability
- Unexplained cyanosis
- Cardiac arrest

However these are **non-specific as similar signs occur with a variety of other important neonatal conditions such as birth asphyxia, sepsis, and metabolic dysfunctions**. It is important that clinical judgments and interventions are based on individualized assessments.

4. ADDITIONAL FINDINGS IN INFANTS OF DIABETIC MOTHERS (IDM)

Infants of diabetic mothers represent a specific group at risk of early hypoglycemia due to increased secretion of insulin persisting after delivery. These infants are often asymptomatic and at significantly higher risk for morbidity and mortality at all gestational ages. They often behave more immaturely than their gestational age would suggest. These infants may have additional findings associated with IDMs such as:

- Macrosomia
- Birth trauma
- Congenital anomalies
- Respiratory distress
- Polycythemia
- Hyperbilirubinemia
- Myocardial dysfunction
- Renal vein thrombosis

5. RISK FACTORS

Symptomatic hypoglycemia may be associated with risk of long term neurodevelopmental sequelae in both term and preterm infants. Controversy persists as to whether hypoglycemia in the absence of clinical signs causes, or is merely associated with adverse neurodevelopmental

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outcomes.¹ Risk factors associated with neonatal hypoglycemia include:

5.1 MATERNAL

- Intrapartum administration of glucose
- Drug treatment - propranolol, oral hypoglycemic agents
- Diabetes in pregnancy/infant of diabetic mother – increased secretion of insulin persists after delivery

5.2 NEONATAL

- Prematurity
- Small for gestational age (SGA)
- Intrauterine growth restriction (IUGR)
- Perinatal hypoxia-ischemia
- Hypothermia
- Infection
- Hyperviscosity/Polycythemia
- Hyperinsulinism
- Erythroblastosis fetalis, fetal hydrops
- Congenital cardiac malformations
- Endocrine disorders and inborn errors of metabolism
- Iatrogenic causes such as loss of intravenous in preterm or compromised term infant

6. BLOOD SUGAR INVESTIGATION

When hypoglycemia is suspected from clinical signs or when the infant has significant risk factors, the blood sugar should be measured. The most accurate method of determining the blood sugar is by using a biochemical laboratory assay and is the standard of care to confirm hypoglycemia and evaluate an infant's response to treatment. However, there are important tips to remember when taking a blood sugar:

- The blood sample should be analyzed rapidly after being taken (red cells consume glucose and this can artificially lower the blood glucose).
- Postprandial sampling is the best method of managing hypoglycemia.
- Screening for hypoglycemia using paper reagent strips has poor specificity and sensitivity.

7. CRITERIA FOR BLOOD SUGAR SCREENING

7.1 HEALTHY TERM NEWBORNS

Routine blood sugar screening is not indicated providing the infant is behaving normally and feeding appropriately. Healthy term, appropriate for gestational age breast fed infants do not develop symptomatic hypoglycemia as a result of simply underfeeding. There is no evidence that low blood glucose concentrations among healthy breast fed term babies who are feeding well are detrimental to outcome.

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7.2 INFANTS AT RISK

- Blood glucose levels should be measured by 4-6 hr of age (hypoglycemia is most likely to occur in the first 24 hours of life.).
- In symptomatic infants, blood glucose levels should be repeated after 30 minutes.

7.3 INFANTS OF DIABETIC MOTHERS (IDM)

- Immediately after birth (within 1 hour)
- ac second feeding
- If unstable, ac feedings
- If mother is insulin dependent diabetic, ac feedings until 6-12 hours of age
- Screening may be discontinued after 12 hours in an IDM with consistently normal blood glucose levels

7.4 SMALL FOR GESTATIONAL AGE INFANTS (SGA)

- Baseline screening should be continued until 36 – 48 hours of age as these infants frequently experience labile blood glucose levels.

8. TREATMENT

8.1 ENTERAL

A. At Risk Infants

- Infants at risk of hypoglycemia that are mature and strong enough to suckle should be breastfed on demand.
- Asymptomatic hypoglycemia (< 2.6 mmol/L)
 - Treat first by feeding the infant (breast, cup, bottle, or gavage)
 - Repeat blood glucose measurement within the hour
 - If blood glucose still < 2.6 mmol/L, intravenous glucose should be considered¹
 - Continue frequent feeds and preprandial glucose measurements
- Feeding milk as the provision of fat will promote ketogenesis and reduce glucose uptake into cells. Dextrose water should not be used as it exacerbates and prolongs the hypoglycemia.
- Gestational age \geq 32 weeks or birthweight > 1500 g *may* be able to breastfeed sufficiently or receive sufficient enteral nutrition to satisfy their nutritional needs and maintain normoglycemia,¹ but if there is any doubt of the infant's ability to feed effectively, milk should be administered by an alternative route.

8.2 INTRAVENOUS 10% DEXTROSE

If the blood glucose concentration is below 2.6 mmol/L, intravenous 10% dextrose should be initiated in symptomatic and asymptomatic infants not responding to enteral feeding. Where possible, it is highly desirable to provide enteral milk concurrently as this will limit the severity of the hypoglycemia.

A. Symptomatic Hypoglycemia

- Symptomatic infants should have their blood glucose measured urgently.
- If blood glucose < 2.6mmol/L, give a bolus of 2 ml/kg of 10% dextrose IV.
- Follow with a continuous infusion of dextrose 10% (commencing at 60 mL/kg/d or 4-6 mg/kg/min of glucose) to avoid rebound hypoglycemia in response to increased insulin secretion. **Note:** Bolus pushes will restore blood glucose levels rapidly, but often results in rebound hypoglycemia.

B. Asymptomatic Hypoglycemia not responding to enteral feeding adjustment

- Dextrose 10% (commencing at 80 mL/kg/d or 5-8 mg/kg/min.).

See **TREATMENT ALGORITHM FOR NEONATAL HYPOGLYCEMIA** on page 6.

9. PERSISTENT HYPOGLYCEMIA

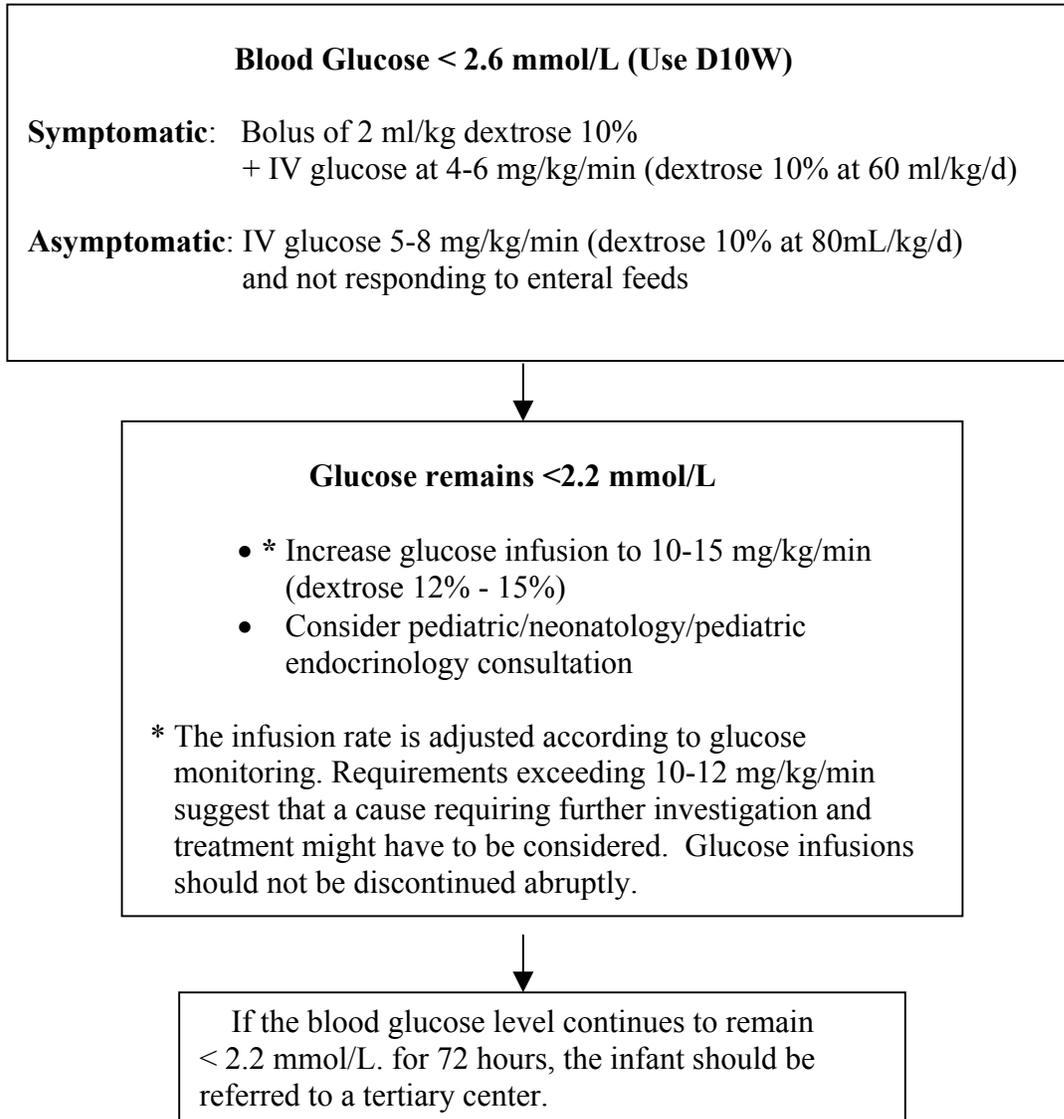
By two to three hours of life a steady-state glucose concentration is reached and levels will continue to increase over the first 24 to 48 hours of life in response to initiation of feeding and gluconeogenesis. Where hypoglycemia persists or recurs intermittently for more than 72 hours and is associated with unusually high glucose intakes, further investigations may be needed and pediatric subspecialty consultation should be seriously considered.

The etiology may be iatrogenic such as failure to screen and manage the infant's blood glucose levels, endocrine disorders, or inborn errors of metabolism. A comprehensive list of causes of persistent neonatal hypoglycemia has been previously published.⁴

It is recommended to **maintain blood glucose levels > 3.3 mmol/L in infants treated for recurrent or persistent hypoglycemia**. The treatment strategy used to achieve this goal will depend on the clinical condition and the suspected etiology of the hypoglycemia, and should be managed by an appropriate pediatric subspecialist.

TREATMENT ALGORITHM FOR NEONATAL HYPOGLYCEMIA

Commencing at these levels adjust IV according to response.



REFERENCES

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Karen Schafer RN BSN IBCLC	Educator, Newborn Care Program Children's & Women's Health Center of BC
Paul Thiessen, MD, FRCPC	Pediatrician, Children's & Women's Health Centre of BC