Hypoglycemia in the Newborn with Risk Factors:

Identification and Management Guide for Newborn Less Than 5 Days of Age

Purpose

This provincial document is intended to promote best practice in the prevention, screening, and management of hypoglycemia in at-risk infants in the newborn period. It has been developed in collaboration with the MNCY SCN, Operational Leadership, and key stakeholders, including Physicians. This document provides guidance to the entire interprofessional health care team (e.g., Pediatricians, Family Practitioners, Midwives, Neonatologists, Nurse Practitioners, Nurses, Emergency Departments, NICUs, Obstetrical Units) involved in the care of the newborn. This guidance facilitates communication between health care professionals and teams, including considerations for consult to the NICU (Neonatal Intensive Care Unit) and possible transfer.

- For newborns less than 72 hours of age - a nurse implemented protocol, supporting scope of practice will be available to provide direction to health care professionals who are working in Obstetrical Units for the identification and management of a hypoglycemic episode in the at-risk newborn, those identified with mild isolated jitters, or when directed by the most responsible health practitioner (MRHP) to follow for treatment and ongoing surveillance. Refer to AHS *Hypoglycemia Identification and Management in the Newborn less than 72 hours of age* Protocol (in draft).
- For additional clarity to health care professionals, this guideline is supported by three (3) Appendices. They are:
    - Appendix A: *Newborn at Risk for Hypoglycemia Algorithm*
    - Appendix B: *Oral Glucose Gel 40% Dose and Administration for Newborns* ≥ 34 Weeks
    - Appendix C: *Glucose Infusion Rate (GIR) Table and Calculator*

Lastly, for newborns greater than five (5) days of age:

- NICU settings may continue to use this guide at the direction of the MRHP, if appropriate to their clinical condition and response.
- Providers outside of the NICU setting should refer to the AHS *Glycemic Management: Pediatric* Policy Suite and supporting resources.

Objectives

This Guide primarily applies to newborns receiving care with their mothers and those admitted to NICU to improve continuity of care. Newborns up to five (5) days of age, who are receiving medical care in different environments, can be managed using this treatment algorithm.

These practices aim to:

- Enhance detection of both symptomatic and asymptomatic hypoglycemia in at risk newborns.

Alberta Health Services Inspiring solutions. Together.
Maternal Newborn Child & Youth Strategic Clinical Network™

June 23, 2023

- Prevent morbidity associated with hypoglycemia in newborns.
- Correct blood glucose levels in hypoglycemic newborn.
- Avoid unnecessary treatment in newborns with normal transitioning low blood glucose
- Identify newborns with serious underlying hypoglycemic disorders.

Principles

Neonatal hypoglycemia is common, occurring in up to 15% of infants born near or at term. At the time of birth, the principal source of blood glucose must shift from the placenta to the newborn's own energy stores. This is triggered by the natural blood glucose nadir that happens in the first one (1) to two (2) hours of life. In newborns with risk factors, the necessary hormonal counter regulation may not be well developed, and clinically significant hypoglycemia can occur (ACORN). The brain utilizes 95% of the body's available glucose. Long term follow-up studies of hypoglycemic infants suggest there is an association between hypoglycemia and adverse neurologic sequelae, even if asymptomatic.

Both sick and well appearing infants with risk factors are known to be susceptible to hypoglycemia.

There is lack of consensus on the optimal strategy for management of hypoglycemia, though it is known that early and frequent feeds provide nutrient substrates to support gluconeogenesis to possibly prevent hypoglycemia in at-risk infants.

There is no standard definition of minimum safe blood glucose level (BG), and neonatal hypoglycemia cannot be defined by a single value of blood glucose applicable to all clinical situations and to all infants. According to the Canadian Pediatric Society (CPS, 2019), the operational cut-off for blood glucose level in newborns less than 72 hours of age is 2.6mmol/L, even when asymptomatic. This lower limit blood glucose increases for newborns outside of the transitional period (greater than 72 hours of age) to 3.3 mmol/L.

Prevention of hypoglycemia

- Clinically well, late preterm and term newborns should be offered their first attempt at feeding as soon as possible, ideally within the first hour of life. A supplemental feed is not required unless otherwise indicated.

- Newborns admitted to intensive care that are unable to feed or are receiving less than the expected target volume of feeds for their postnatal age should have an intravenous glucose solution started within 30 minutes of receiving a patient care order to do so.

Risk Factors

Early guided screening of at-risk newborns is necessary due to asymptomatic hypoglycemia. At-risk infants include the following:

- Preterm (less than 37 weeks);
- Infants of diabetic moms (Type 1, 2 or gestational)
- Small for gestational age (SGA) – defined as less than the 10th percentile for gestational age or evidence of intrauterine growth restriction (IUGR) (low birth weight for length and head circumference or known IUGR on antenatal scans);
- Large for gestational age (LGA) – defined as greater that the 90th percentile for gestational age;
- Infants will be plotted on the Fenton Growth Chart (Form 19438) as a one-time plot with birth weight to determine the 10th and 90th percentiles for their gestational age. Fenton growth charts should not be used for ongoing growth monitoring of term infants;
- Perinatal stress (evident by cord gases [pH<7.0 or BE < -12 mM]) suspected sepsis or significant cold stress;
- Maternal beta-blockers, valproic acid or chronic oral or parenteral corticosteroids;
- Can consider screening with a family history of metabolic or genetic disorders associated with hypoglycemia such as CPT-1 deficiency in Inuit families; and
- All newborns with symptoms of an acute illness.

Symptoms

Many newborns may be asymptomatic, or symptoms may be vague. All newborns who are clinically unwell should be screened for hypoglycemia. Symptoms may include:

- Jitters or tremors;
- Low temperature;
- Seizures; or
- Can be concomitant with any central nervous system or cardiorespiratory symptoms.

If the newborn is symptomatic and there are concerns for possible hypoglycemia, they should immediately be tested with a point of care (POCT) meter, irrespective of feeds or timing from birth.

Babies without identified risk factors for hypoglycemia, who present with symptoms suggestive of hypoglycemia (such as jitteriness), should have a blood glucose level checked. If the blood glucose level is within normal limits, continue with management as per MRHP, if blood glucose is less than 2.6mmol/L then follow algorithm (See Appendix A).

Screening

- Screening glucose measurement may be obtained from an AHS approved point of care (POCT) meter, blood gas analyzer, or as ordered from rapid laboratory testing. Blood glucose measurement should only be performed using a meter that has been correctly validated according to POCT Quality Assurance program standard.

For **asymptomatic** newborns with identified risk factors, blood glucose screening should proceed as follows:

- First POCT check should be at two (2) hours of life, irrespective of having fed;
- Screening should then continue every two (2) to three (3) hours, before feeds. Once two (2) consecutive pre-feed values equal to or greater than 2.6mmol/L have been achieved. screening can continue every three (3) to six (6) hours pre-feed, following infant feeding cues, until minimum screening requirements have been met;
- SGA and preterm newborns should have ongoing POCT checks for a minimum of 24 hours;
- Newborns with all other risk factors should be screened for a minimum of 12 hours.
- If blood glucose levels are below 2.6mol/L, follow screening and treatment algorithm (See Appendix A) and continue checks until two (2) consecutive pre-feed levels equal to or greater than 2.6 mmol/L are achieved;
- If the blood glucose level is less than 2.6 mmol/L, recheck level 30 minutes after the intervention (oral glucose gel and feed) is complete or maximum 60 minutes after the initial low blood glucose level; and
- **The target of equal to or greater than 2.6mmol/L is appropriate for the first 72 hours of life to allow for physiologic transitioning. After 72 hours, a target of 3.3mmol/L should be used.**

Feeding and Management

- Encourage early breastfeeding, starting within the first hour of life, and skin to skin care.
- Expressed breast milk, human donor milk if available or infant formula are alternative feed options.
- In asymptomatic infants with hypoglycemia, follow algorithm (Appendix A). Offer oral glucose gel with breastfeeding or supplemental feeds of 5-10mL/kg (offer supplement in addition to breastfeed and oral glucose gel if blood glucose still low on second check).

Oral Glucose Gel

- Intrabuccal 0.5mL/kg of 40% oral glucose gel (provides 200mg/kg of glucose that is equivalent to an IV bolus of 2mL/kg of D10W).

Table 1	
Oral glucose Gel Dosing (Dose is 0.5mL/kg (200mg/kg)	
Dosing Weight	**Suggested Dose**
Less than or equal to 2 kg	1 mL (400 mg)
2.1 to 3 kg	1.5 mL (600 mg)
3.1 to 4 kg	2 mL (800 mg)
4.1 to 5 kg	2.5 mL (1000 mg)
5.1 to 6 kg	3 mL (1200 mg)

- Used primarily for treating asymptomatic hypoglycemia less than 2.6 mmol/L.
- Should not be confused with oral sucrose 24%

- Administer in conjunction with enteral supplementation (breastfeeding or bottle).
- Can be administered a maximum of two times per episode of blood glucose less than 2.6 mmol/L and can be repeated if there is a recurrent value less than 2.6mmol/L for a total maximum of four (4) doses in a 48-hour period. (See Appendix B).
- If the blood glucose level is less than 2.6mmol/L on three consecutive checks, contact MRHP.
- For infants admitted to NICU, may be used as a temporizing measure while establishing IV access.

Referral Criteria

- MRHP must be contacted immediately for any newborn with symptomatic hypoglycemia and/or any blood glucose level less than 1.8mmol/L irrespective of symptoms.
- Strongly consider NICU admission for:
    - blood glucose level less than 1.8mmol/L at any time;
    - symptomatic (excluding mild isolated jitters) hypoglycemia (less than 2.6mmol/L);
    - blood glucose less than 2.6mmol/L after two consecutive doses of oral glucose gel and feeding;
    - a rebound blood glucose level less than 2.6 mmol/L after achieving serial normal values; and,
    - any blood glucose level less than 3.3mmol/L after 72 hours of life.

Care of the newborn presenting to ED or another medical environment.

- This guidance will be applied for infants up to five (5) days of age who are presenting to medical care and are found to have hypoglycemia (blood glucose less than 2.6mmol/L in the first 72 hours of life or less than 3.3mmol/L after 72 hours of life).
- The newborn should enter the treatment algorithm (See Appendix A). Depending on the clinical condition of the baby (if they are able to feed) and on the blood glucose measurement, they should be treated with oral glucose gel and oral feed or with IV dextrose.

Care of Newborn admitted to the NICU

The guidance in this document applies to newborns recently admitted to the NICU. It also applies to infants in the NICU who become hypoglycemic in the context of a new illness or clinical deterioration. After 72 hours of life, the higher threshold of 3.3mmol/L will be used for determining need for intervention.

Screening

Screening should be initiated in unwell infants:

- 30 minutes after intravenous fluid is initiated;
- 30 minutes after change in glucose management after a low glucose level;
- With parenteral nutrition bloodwork; or
- As ordered.

For asymptomatic newborns that meet the criteria for BG screening based on risk factors, consider following screening timelines as previously specified (See Appendix A)

- Frequency of blood glucose monitoring is based on previous values, clinical assessment, and patient care orders.

Infants in NICU should have a point-of-care (POC) glucose checked with any of the following:

- Any symptoms that may be associated with hypoglycemia;
- An acute change in clinical condition;
- Switched from full feeds to NPO or less than 50% previous feed volume without IV dextrose support;
- During and following an exchange transfusion or packed cell transfusion;
- Cessation of IV fluids for greater than 30 minutes and at less than 50% volume feeds; or
- Any other ordered bloodwork.

Management

Clinically well newborns 33 weeks gestational age and greater may attempt to manage hypoglycemia with enteral feeds if there are no other contraindications.

- Start feeds at 60mL/kg/day with breastfeeding/EBM/DHM/formula as indicated according to clinical indication, patient preference and unit practice.
- If repeat measurement continues to be less than 2.6mmol/L, consider increasing feed volume by 20mL/kg/day.
- Consider feeding at every two (2) hour interval.
- In a well appearing infant, who is able to feed but continues to have blood glucose levels 1.8-2.5 mmol/L, consider starting IV fluid at 30mL/kg/day and increasing as needed.

Asymptomatic newborns 34 weeks and greater gestational age with blood glucose level less than 2.6 mmol/L may be managed with 40% oral glucose gel (See Appendix B) in addition to enteral feeds. (Refer to Table 1 above).

Newborns who are unwell, unable to feed or less than 33 weeks should initiate IV fluid within 30 minutes of admission to the NICU.

- Start D10W or parenteral nutrition at 60 mL/kg/day.
- Check BG level 30 minutes after initiating IV fluid.
- If BG level is less than 2.6 mmol/L, increase IV fluid by 20mL/kg/day or increase dextrose concentration.
- If BG level is less than 1.8mmol/L and symptomatic consider giving a D10W bolus of 2mL/kg IV. A POCT reading of “low” should be treated immediately. In infants 34 weeks and greater, consider the use of oral glucose gel as a temporizing measure while establishing IV access.
- Previous guidance has suggested that central venous access be used if administering dextrose concentrations greater than D12.5W. A new study suggests that recommendation may be obsolete, and higher concentrations can be administered through a peripheral vein. However, it is necessary to consider overall patient stability,

ease of IV access, maximum flow rates and stability of central line when deciding on placing a central line. If requiring a GIR of 10mg/kg/min or greater, consider obtaining central access (See Appendix C).
- Patients requiring higher than usual total fluid intake (TFI) of IV fluid to manage hypoglycemia need close monitoring of serum electrolytes and fluid balance.

Weaning IV fluid in newborns with hypoglycemia
- Consider starting to wean IV fluid and transition to full enteral feeds once three consecutive normal blood glucose measurements have been obtained.
- There is not evidence to support a specific weaning pattern, however one suggestion is to wean IV rate by 1mL/hr every 3 hours if blood glucose is equal to or greater than 3mmol/L (in the first 72 hours of life) or equal to or greater than 3.5mmol/L (after 72 hours of life) while increasing enteral feeds.
- Can consider use of fortified feeds in more mature babies if needed, when attempting to wean IV support.

Management of refractory or late onset hypoglycemia.
- Refractory hypoglycemia is ill-defined, but for the purposes of this document is considered to be hypoglycemia requiring treatment with GIR of 10mg/kg/min to achieve BG levels above target, or if unable to achieve normoglycemia.
- Late onset hypoglycemia occurs after an established period of normoglycemia, persists beyond one single measurement and is not due to interruption in feeds or oral glucose administration. Newborns with refractory hypoglycemia may require a slower wean of IV dextrose.
- Consider transferring newborns with refractory hypoglycemia despite administering a GIR greater than 10-12mg/kg/min and/or administration of additional medications, to a level 3 NICU.

Investigations
- A critical sample should be sent for babies with refractory hypoglycemia. In the first 72 hours of life, a cut off of 2.6mmol/L should be used. After 72 hours of life, a critical sample should be sent with a blood glucose of 2.8mmol/L or less.
- A critical sample includes insulin, cortisol, glucose, blood gas, lactate, beta-hydroxybutyrate, free fatty acids, carnitine and acylcarnitine profile.
- Further work up should be conducted in consultation with subspecialists from endocrinology and/or metabolics.

Medications
- Pharmacologic therapy should be considered for use in refractory hypoglycemia when GIR is 10-12mg/kg/min.
- Glucagon is the more commonly used medication when treating refractory hypoglycemia in the newborn. Other medications may be considered such as hydrocortisone, diazoxide or octreotide.

- Strongly consider consultation with endocrinology if requiring treatment with multiple medications.
- Please refer directly to medication monographs for details.

References

David H. Adamkin, Committee on Fetus and Newborn; Postnatal Glucose Homeostasis in Late-Preterm and Term Infants. *Pediatrics* March 2011; 127 (3): 575–579. 10.1542/peds.2010-3851

Boulton, J., Coughlin, K., O'Flaherty, D., & Solimano, A. (Eds.), ACoRN: Acute Care of at-Risk Newborns: A Resource and Learning Tool for Health Care Professionals. Oxford, UK: Oxford University Press. 2021

Hammer, Denise DNP, RNC-NIC; Pohl, Carla DNP, APRN, CNM; Jacobs, Peggy J. DNP, APRN, CNM, RNC-OB; Kaufman, Susan MS, RNC-MNN; Drury, Brenda MSN, RNC-MNN Innovations and Challenges of Implementing a Glucose Gel Toolkit for Neonatal Hypoglycemia, Advances in Neonatal Care: October 2018 - Volume 18 - Issue 5 - p 378-385 doi: 10.1097/ANC.0000000000000527

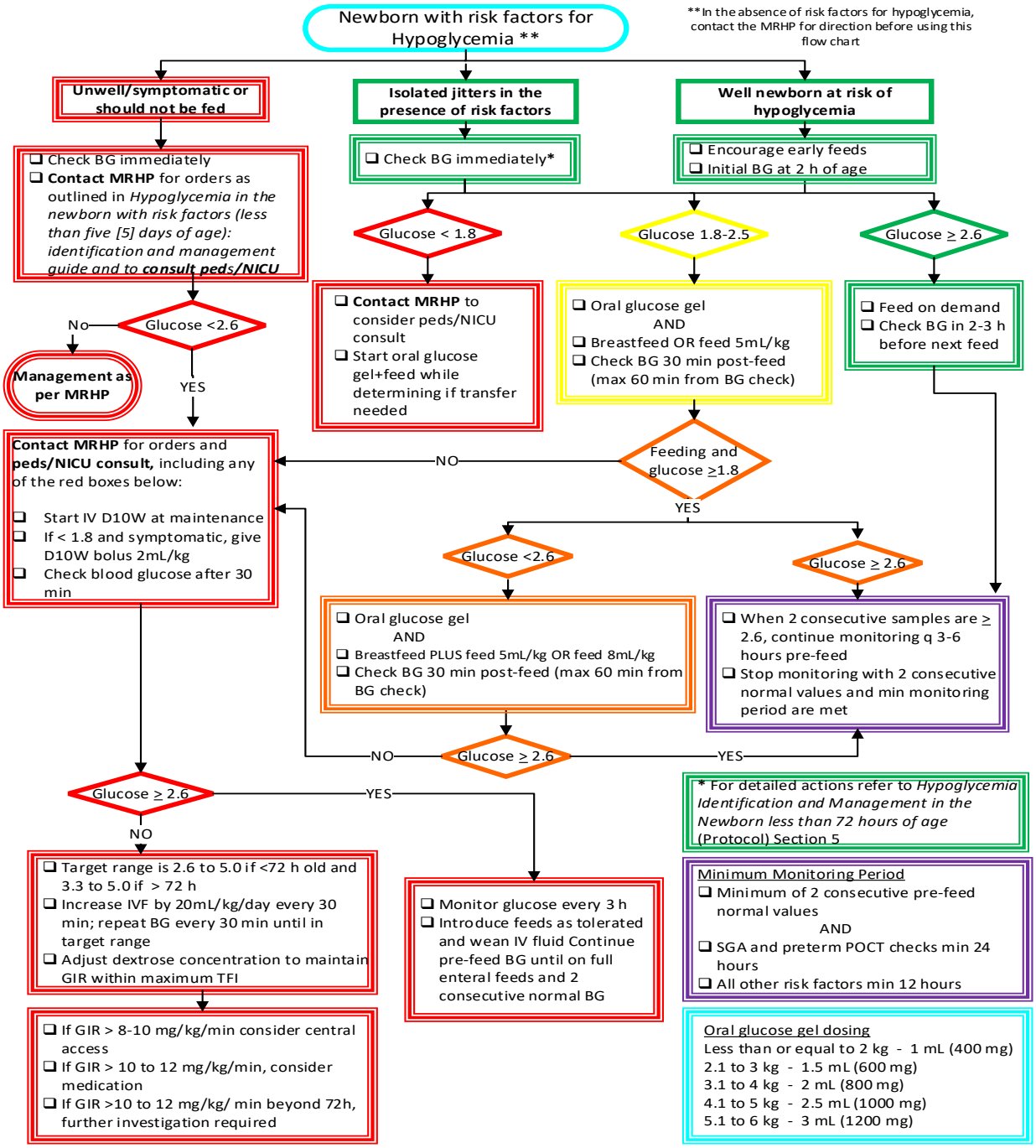
Narvey MR, Marks SD. The screening and management of newborns at risk for low blood glucose. Paediatr Child Health. 2019 Dec;24(8):536-554. doi: 10.1093/pch/pxz134. Epub 2019 Dec 9. PMID: 31844395; PMCID: PMC6901164.
study

Sen S, Cherkerzian S, Turner D, Monthé-Drèze C, Abdulhayoglu E, Zupancic JAF. A Graded Approach to Intravenous Oral glucose for Neonatal Hypoglycemia Decreases Blood Glucose Variability, Time in the Neonatal Intensive Care Unit, and Cost of Stay. J Pediatr. 2021 Apr;231:74-80. doi: 10.1016/j.jpeds.2020.12.025. Epub 2020 Dec 15. PMID: 33338495.

Vanhatalo T, Tammela O. Glucose infusions into peripheral veins in the management of neonatal hypoglycemia—20% instead of 15%? Acta Paediatr 2010;99(3):350–3

APPENDIX A

Newborn At-Risk for Hypoglycemia Algorithm



Based on Figure 1, in: Narvey MR, Marks SD; Canadian Paediatric Society, Fetus and Newborn Committee. The screening and management of newborns at risk for low blood glucose. Paediatr Child Health 2019 24(8):536-544. Adapted with permission.

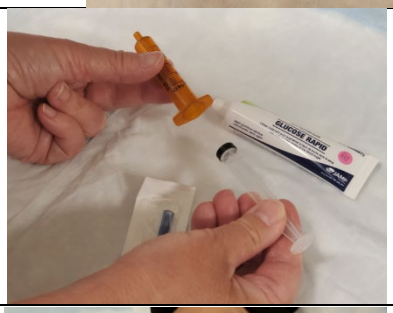
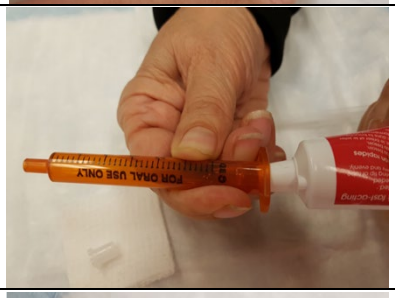
APPENDIX B

Oral glucose Gel 40% Dose and Administration (for newborns ≥ 34 weeks)

Instructions for Oral Glucose Gel Preparation and Administration

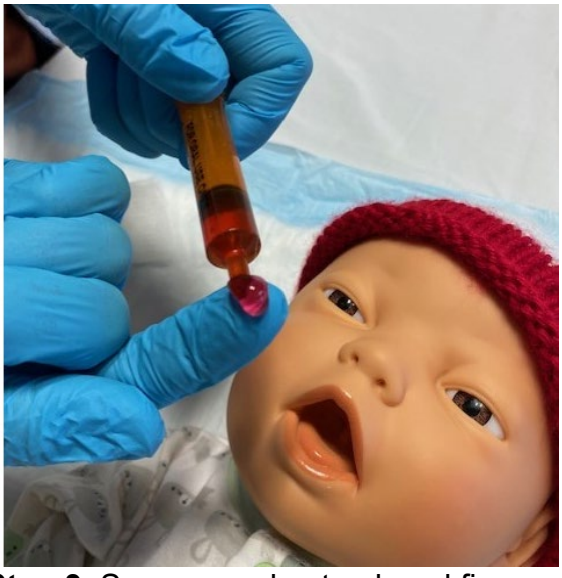
Materials Required:

1. Glucose Oral Gel (Instaglucose, Glucose Rapid or product supplied)
2. One 5 mL Oral Feeding Syringe with cap

	Remove plunger from syringe
	Insert gel into syringe at base
	Reinsert plunger and apply stopper, check medication dose, and place a patient label on the syringe.

Step 1: Gather supplies: correct dose of oral glucose gel, gauze, and gloves

Step 2: Dry the inside of the buccal mucosa with gauze (repeat on other side)



Step 3: Squeeze gel onto gloved finger

Step 4: Massage gel into buccal mucosa, repeat on other side. Try to give approximately ½ dose of gel on each side

Oral glucose Gel Dosing (Dose is 0.5mL/kg (200mg/kg))	
Dosing Weight	**Suggested Dose**
Less than or equal to 2 kg	1 mL (400 mg)
2.1 to 3 kg	1.5 mL (600 mg)
3.1 to 4 kg	2 mL (800 mg)
4.1 to 5 kg	2.5 mL (1000 mg)
5.1 to 6 kg	3 mL (1200 mg)

If oral glucose gel is unavailable, oral D50W administration has been proposed by some authors (*Solimano A, Osiovich H, Kwan E, Metzger DL, Everett R. Are there alternatives to over-the-counter diabetes-care glucose-gels for transitional neonatal hypoglycemia?. Paediatr Child Health. 2020;26(1):4-7. Published 2020 Mar 17. doi:10.1093/pch/pxaa002*).

No comparative studies using oral D50W for treatment of neonatal hypoglycemia have been published to date. An approximate equivalent dose would be 0.4mL/kg.

APPENDIX C

Glucose Infusion Rate (GIR) Table and Calculator

Table 4. Effect of fluid adjustments and dextrose concentration on glucose infusion rates

	GIR: mg/kg/min					
TFI: mL/kg/day (mL/kg/h)	D 5	D 7.5	D 10	D 12.5	D 15	D 20
60 (2.5)	2	3.1	4.1	5.2	6.3	8.4
80 (3.3)	2.8	4.1	5.5	6.9	8.3	11.0
100 (4.1)	3.4	5.1	6.6	8.6	10.3	13.1
120 (5.0)	4.2	6.3	8.4	10.4	12.5	16.7
140 (5.8)	4.8	7.3	9.7	12.1	14.5	19.4
160 (6.6)	5.5	8.3	11.0	13.2	16.5	22.0
180 (7.5)	6.3	9.4	12.5	15.7	18.8	25.0
200 (8.3)	6.9	10.4	13.9	17.3	20.8	27.7

Light grey boxes – Typical infusion starts for newborns.
Darker grey boxes – GIRs >10 mg/kg/min should prompt further investigation.
D dextrose %; GIR Glucose infusion rate; TFI Total fluid intake.

CPS The screening and management of newborns at risk for low blood glucose. Nov 2019

$$\text{GIR (mg/kg/min)} = \frac{\text{dextrose concentration (\%)} \times \text{infusion rate (mL/kg/hr)}}{6}$$