Chapter 16

NEONATAL HYPOGLYCEMIA

"The definition of clinically significant hypoglycemia remains one of the most confused and contentious issues in contemporary neonatology"

I. Cornblath, Pediatrics 2000

True Hypoglycemia

- Not a single blood sugar value

- Whipple's Triad:
  - Presence of clinical symptoms
  - A reliable significantly low blood glucose
  - Prompt response to adequate therapy

Clinical Manifestations

- Change in level of consciousness
  - Irritability
  - Lethargy
  - Coma
- Hypotonia – floppiness
- Feeding poorly after feeding well
- Tremors – jitteriness
- Apnea
- Seizures

Evaluation of Hypoglycemia

- Age of onset
- Transient or persistent
- Symptomatic or asymptomatic

Causes of Neonatal Hypoglycemia

- Transient
  - Failure to adapt to transition
    - Intrapartum administration of glucose

- Maternal drug treatment
- Infant of diabetic mother
- Growth restriction

♦ Related to neonatal problems

- Asphyxia
- Hypothermia
- Hydrops fetalis
- Congenital anomalies
- Iatrogenic causes
- Sepsis

▪ Persistent

♦ Hyperinsulinism

♦ Inborn error of metabolism

- Carbohydrate
- Amino acid
- Fatty acid

♦ Endocrine disorders

- Pituitary, adrenal
- Glucagon deficiency

What happens at birth?

▪ Steady decline of blood glucose reaching a steady state by 2-3 hours after birth – associated with a hepatic release of glucose of 4-6 mg/kg/min.

▪ Breastfed term infants have lower concentrations of blood glucose, but higher concentrations of ketone bodies (alternate fuel) than formula fed babies.

This suggests that the provision of alternate fuels is a normal adaptive response to transiently low nutrient intake during the establishment of breastfeeding.

These infants may well tolerate lower levels of blood glucose without symptoms or sequelae.

Factors that put babies at risk and why?

▪ Prematurity
▪ Growth restriction
▪ Maternal diabetes

The common link is that these babies cannot mount an appropriate or adequate response to the sudden cessation of nutrient delivery from their mother.

What newborns should be screened?

- Infants of diabetic mothers
- Small/Preterm Infant < 37 weeks gestation, < 2500 grams, physiologic instability
- Large/Hyperinsulin Risk Infant > 4250 grams, 37+0 to 39+6 and > 4000 grams (because of the concern that these babies are, in fact, macrosomic due to undiagnosed maternal diabetes)
- Ill babies, eg.
    - Poor transition/respiratory distress
    - Asphyxia
    - Sepsis
- Babies with a family history of specific endocrine/metabolic disorders
- Any baby with symptoms that could reflect hypoglycemia
- Infant of a woman on beta blockers or hypoglycemic medications

The routine monitoring of glucose concentration in the term healthy infant is not indicated and may be counterproductive, as it may interfere with bonding and establishment of breastfeeding.

Measuring Glucose Concentrations

- Reagent strips are not reliable at lower blood glucose levels, regardless of whether measured by eye or meter's
- Bedside quantitative techniques are more reliable
- All low "screening" results require validation in the lab (handling of sample and prompt analysis is important)
- At least one reliable lab value that is significantly low should be obtained before a definitive diagnosis can be made

Management Goals

- Remember that glucose screening is only for symptomatic babies, or those who are at high risk for both low sugars AND an insufficient ability to mobilize other fuel
- Screening at risk babies and aiming for a glucose of ≥ 2.6 is a reasonable goal
- In "at risk" babies, values below this level should trigger feeds and close monitoring
    - Persistent values below this level despite feeds should be treated with intravenous glucose therapy

- **Glucose screening immediately after birth is of little value and may be falsely reassuring (ie. before the nadir).**

A practical approach

- Encourage immediate and uninterrupted skin to skin contact
- Identify babies at risk and aim for a glucose of at least 2.6 mmol/L
- Initiate feeds within 1-2 hours of birth and ensure baby feeds every 2-3 hours
- If supplementation is necessary then supplement with colostrum and/or formula (72 ml/kg/day) start slowly.
- Glucose screening prior to feeds (starting with second feed) for 1st 6-12 hours (up to 24 hours for IDMs and IUGR)
- If glucose $\leq$ 2.6***** (by PCX) or infant that is symptomatic
    - ♦ Lab glucose to confirm
    - ♦ Feed and repeat in 1 hour
- If glucose $\leq$ 2.6 again*****
    - ♦ Confirm, feed and repeat in 1 hour
- If glucose remains $\leq$ 2.6, institute IV therapy
- Symptomatic babies with glucose $\leq$ 2.6 require immediate action to raise blood glucose level (IV therapy)

*****consider instituting IV therapy sooner, if baby unable to feed adequately, or glucose extremely low

See Appendix A for ACoRN algorithm

What to feed?

- The energy content of milk is 70% higher than that of 10% dextrose
- Enteral milk feeds promote ketogenesis and gut maturation
- Breast milk is more ketogenic (alternate fuel) than formula

Ongoing Management

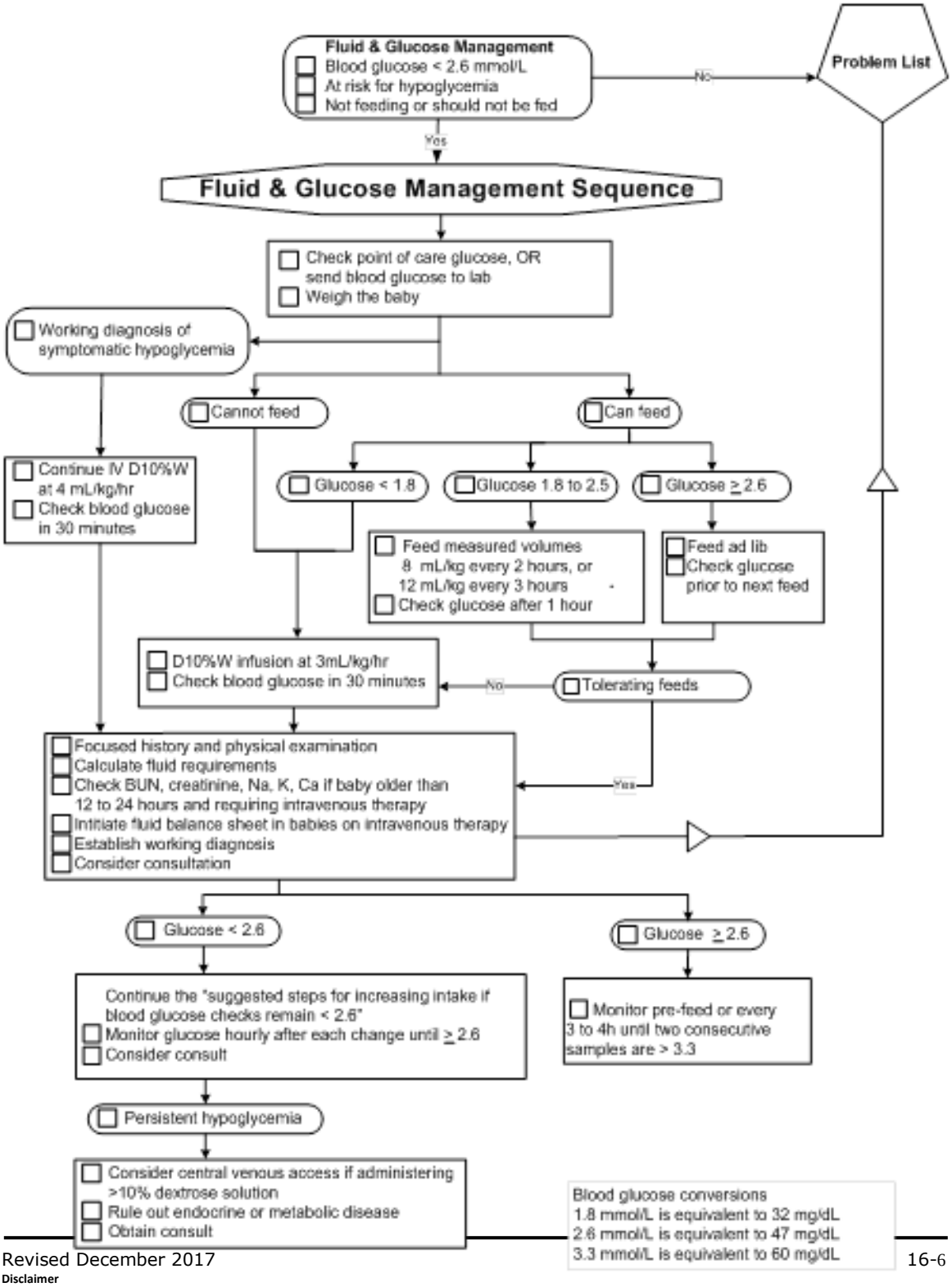
- Provision of intravenous glucose starting at 5 mg/kg/min (normal consumption)
    - ♦ D10W at 3 ml/kg/hr - Do Not use D25 or D50
- Avoid boluses - if given to raise a very low value acutely, should not exceed 2 ml/kg of D10W (200 mcg glucose)
- Transition from intravenous to enteral intake, as tolerated
- Monitoring of blood glucose until steady state is achieved
- Consider endocrine and metabolic abnormalities if hypoglycemia persists

- Baseline bloodwork during a hypoglycemic episode (BG<2.0) should be drawn for analysis of insulin, glucagon, cortisol, growth hormone and free fatty acids. The urine should be tested for ketones.

Refractory Hypoglycemia

- Hypoglycemia refractory to IV glucose therapy requires assessment/care at tertiary level
- Therapeutic options include administration of glucagon, steroids, or diazoxide, depending on etiology
- Increased intravenous glucose to a MAXIMUM of 12 mg/kg/min
- Concentration of IV glucose can be increased to D12.5W safely through a peripheral IV. Intravenous glucose delivery should not exceed 12 mg/kg/min (≈7 ml/kg/hr of D10W – too much fluid for 1st few days of life), or (≈ 6ml/kg/hr of D12.5W – still a lot of fluid). Central venous access (eg. UVC) should be used for glucose concentration greater than D12.5W.

Appendix A



Suggested Reading

1. The ACoRN Editorial Board, *ACoRN, Acute Care of At-Risk Newborns*, Vancouver, BC, 2012.

2. Evans, R. J., Evans, M. K., Brown, Y. M. R., & Orshan, S. A. (2014). Canadian Maternity, Newborn, & Women's Health Nursing. (2nd Ed.). Philadelphia, PA: Lippincott.

3. K Aziz, P Dancey; Canadian Paediatric Society Fetus and Newborn Committee. Screening guidelines for newborns at risk for low blood glucose. Paediatr Child Health 2004;9(10):723-9, Posted: Dec 1 2004 Reaffirmed: Feb 1 2016