Consensus Clinical Guidelines for Screening & Management of Hypoglycemia in Late Preterm and Term Infants (≥ 34 weeks GA) 
UCSF NC² (Northern CA Neonatology Consortium)

PART I: Background
• Risk factors for neonatal hypoglycemia
  o Inadequate glycogen stores
    ▪ Small for gestational age (SGA)
    ▪ Intrauterine growth restriction (IUGR)
    ▪ Prematurity (<37 weeks gestational age)
    ▪ Post-term gestation (≥42 weeks gestational age)
  o Increased glucose utilization
    ▪ Large for gestational age (LGA)
    ▪ Infant of a diabetic mother (IDM)
      • Includes mothers with pre-existing diabetes (DM1 or 2) or gestational diabetes (GDMA1 = diet-controlled or GDMA2 = medication-controlled)
    ▪ Conditions which increase metabolic demand: sepsis, encephalopathy, HIE, perinatal stroke, seizures, hypothermia, prematurity, polycythemia, hemolytic disease, metabolic disease, respiratory distress, endocrine abnormalities, congenital heart disease, maternal substance use
  o Hyperinsulinemia
    ▪ LGA
    ▪ IUGR
    ▪ IDM
    ▪ Certain genetic/metabolic conditions (e.g. Beckwith-Weideman Syndrome)
• Sequelae of neonatal hypoglycemia
  o Neurodevelopmental Sequelae
    ▪ Association with worse cognitive and motor performance on developmental testing at 18 months, 3 years, 5 years; lower school achievement in children at 4th grade children
    ▪ NOTE: recurrent episodes of hypoglycemia are more predictive of long-term sequelae
    ▪ CAVEAT: causality has not been determined for these associations, nor effectiveness / safety of screening and intervention to raise glucose levels

PART II: Definition of hypoglycemia
• Definition of hypoglycemia
  o “Plasma glucose concentration below which normal brain function cannot occur”
  o Published thresholds for diagnosing hypoglycemia:
    ▪ NOTE: difficult to define a single blood glucose concentration that warrants intervention in every neonate. Published literature and guidelines primarily rely on normative values since defining hypoglycemia based on presence/absence of sequelae or performing prospective clinical trials is impossible.
    ▪ NOTE: units for all glucose values are in mg/dL
- Alkalay, et al. (2006) - estimate of 5<sup>th</sup> percentile (breast and formula fed infants):
  - 1-2hrs: 27
  - 3-23hrs: 40
  - 24-47hrs: 41
  - 48-72hrs: 48
- Cornblath & Ichord (2000) - formula fed infants:
  - All infants <20-25
  - First 24hrs <30-35 (sick <45-50)
  - >24hrs <40-50
- Canadian Pediatric Society (2004):
  - <32 2hrs post-feed
  - <36 post-subsequent feed
  - Birth-4hrs <25 (target >40)
  - 4-24hrs <35 (target >45)
- Academy of Breastfeeding Medicine (ABM) (2014):
  - <20-25 requires intervention (goal >40)

- UCSF NC<sup>2</sup> consensus thresholds for hypoglycemia:
  - Target/goal neonatal glucose:
    - ≥ 45 prior to routine feeds @ 0-24 hours after birth
    - ≥ 50 prior to routine feeds @ >24 hours after birth
  - Intervention thresholds for hypoglycemia in asymptomatic infants:
    - NOTE: see PARTS III, & IV below for specifics regarding timing of screening and management of hypoglycemia
    - Initial screening (~1 hour, after initial feeding):
      - <25 → re-feed (breast or formula)
    - 1-4 hours screening:
      - <25 → IV treatment
      - 25-40 → oral treatment
    - 4-24 hours screening:
      - <35 → IV treatment
      - 35-45 → oral treatment
  - Intervention threshold for hypoglycemia in symptomatic infants
    - NOTE: See PART V below for specifics regarding assessment and management of symptomatic infants
    - <35 (regardless of age) → IV treatment
    - 35-45 → consider oral treatment

PART III: Screening of asymptomatic, at risk infants
- Screening criteria for asymptomatic, well-appearing, at risk infants
  - IDM (pre-existing maternal diabetes, GDMA1, GDMA2)
  - SGA or LGA (defined by average of male & female weights on AAP 2010 intrauterine growth curves):
    - SGA (<5<sup>th</sup>%)
• LGA (>97.5th%)
• NOTE: use of a strict birthweight criteria for all term infants is no longer recommended (e.g. <2500, >4000)

<table>
<thead>
<tr>
<th></th>
<th>37 wks</th>
<th>38 wks</th>
<th>39 wks</th>
<th>40 wks</th>
<th>41 wks</th>
</tr>
</thead>
<tbody>
<tr>
<td>SGA (&lt;5th%)</td>
<td>2100</td>
<td>2400</td>
<td>2600</td>
<td>2700</td>
<td>2800</td>
</tr>
<tr>
<td>LGA (&gt;97.5th%)</td>
<td>4100</td>
<td>4300</td>
<td>4400</td>
<td>4500</td>
<td>4600</td>
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- Late preterm (34-37 weeks)
- Post term (≥42 weeks)
- Additional consideration: neonates with conditions known to be associated with secondary hypoglycemia (i.e. polycythemia, sepsis) should also be considered for hypoglycemia screening.

• Method of screening
  - Glucometer
    - NOTE: accuracy in low range depends on make/model of glucometer; newer meters are more accurate in low range
    - NOTE: sample should be drawn from warmed heel stick
  - Confirm low values with iSTAT if available or stat blood sample sent to laboratory
  - NOTE: Consider initiating treatment for hypoglycemia prior to confirmatory testing if waiting for laboratory result will delay treatment excessively

• Timing of screening
  - General principles:
    - Initial screen after first (breast)feeding (by ~1 hour after birth)
    - More frequent screening in first 2-4 hours of life, then pre-prandial screening that is roughly linked to feeding schedule
    - Stop screening at 12 hours for LGA, IDM infants (very low risk of late hypoglycemia)
    - Continue screening until 24 hours for SGA, late preterm infants (greater risk of late hypoglycemia)
    - Consider 36 hour screening for SGA, late preterm infants if glucose consistently <45 in first 24 hours after birth
  - Time points for Glucose Screening: ~1, 2, 4, 6, 9, 12, 24 hours
  - “Early exit”: consider discontinuing glucose screening prior to completion of all time points in asymptomatic infants with “stable”, “normal” glucose in the first 24 hours after birth:
    - Glucoses >45 on 3 occasions
    - Repeat one pre-prandial glucose measurement at 24 hours after birth for SGA, late L infants
    - NOTE: these recommendations are consensus-based; no specific evidence is currently available to support these recommendations

PART IV: Management of asymptomatic infants
- See APPENDIX 2 for summary clinical pathway / decision tree (ASYMPTOMATIC)
- Intervention thresholds (see PART II above for details):
  - NOTE: treatment thresholds vary at 0-4 hours and 4-24 hours after birth to reflect changing physiology / normal values during transition to postnatal life
- Treatment:
o Oral feeding (breast or formula):
  ▪ Indications:
    • Initial screen: <25
    • 1-4 hours: 25-40
    • 4-24 hours: 35-45
  ▪ Method:
    • Breastfeeding
      o Re-check glucose 1 hour after *initiation* of feeding
      o Repeat breastfeeding if glucose remains below threshold; if glucose remains below threshold after >2 breastfeeding attempts, then consider oral formula supplementation
      o Oral administration of expressed maternal breastmilk (MBM) is also an acceptable form of treatment
    • Formula
      o Use protein hydrolysate formula (i.e. Alimentum, Nutramigen, Pregestimil) preferentially if available to reduce exposure to cow milk protein
        ▪ 1-4 hours → 10-20 mL
        ▪ 4-24 hours → 15-30 mL
      o Re-check glucose 1 hour after *initiation* of feeding
      o If glucose remains below threshold after >2 oral feedings, then consider IV treatment
  o IV treatment:
    ▪ Indications:
      • 1-4 hours:
        o <25
        o Consider if recurrent 25-40 despite oral feeding
      • 4-24 hours:
        o <35 after one attempt at oral feeding
        o Consider if recurrent 35-45 despite oral feeding
    ▪ Method:
      • D10W 2-3 ml/kg IV bolus, followed by:
      • D10W @ 80 ml/kg/day (3.5 ml/kg/hr)
        o Glucose infusion rate (GIR) 5.5 mg/kg/min
        o Increase D10W in increments of 20 ml/kg/day (0.8 ml/kg/hr) if needed for persistent hypoglycemia
        o *NOTE:* If total fluid administration exceeds 150 ml/kg/day (6.25 ml/kg/hr), consider increasing dextrose concentration to D12.5 rather than IV rate to avoid fluid overload
      • Continue IV treatment until glucose levels are stable >50, then wean IV gradually
      • *NOTE:* For any infant with persistent hypoglycemia, consider further evaluation for underlying etiology in parallel with treatment

**PART V: Management of symptomatic infants**
• See APPENDIX 3 for summary clinical pathway / decision tree (SYMPTOMATIC)
• Symptoms of hypoglycemia may include:
o General symptoms:
  ▪ Abnormal cry, poor feeding, hypothermia, diaphoresis
o Neurologic symptoms:
  ▪ Tremors, jitteriness, hypotonia, irritability, high-pitched cry, lethargy, seizures
o Cardiorespiratory disturbances:
  ▪ Cyanosis, pallor, tachypnea, apnea, cardiac arrest
• Differentiation of “concerning” (“definite”) versus “possible” symptoms of hypoglycemia:
  o “CONCERNING”: seizure, lethargy, hypotonia, apnea, cyanosis
  o “POSSIBLE”: jitteriness, tremors, irritability, exaggerated Moro reflex, high-pitched cry, poor feeding
• Thresholds for intervention & treatment:
  o “CONCERNING” (regardless of age)
    ▪ <45 → IV treatment
    ▪ Use IV treatment method from PART IV above
    ▪ If symptoms do not resolve after glucose >50, pursue work-up of other potential causes of symptoms
  o “POSSIBLE” (regardless of age)
    ▪ 35-45 → oral treatment (breastfeeding or formula)
    ▪ <35 → IV treatment after one attempt at oral feeding
    ▪ Use IV or oral treatment method from PART IV above
    ▪ If symptoms do not resolve after glucose >50, pursue work-up of other potential causes of symptoms
• NOTE: For any infant with persistent hypoglycemia, consider further evaluation for underlying etiology in parallel with treatment

PART VI: NICU and Special Care / Transitional Care Nursery
• Treatment thresholds and treatment methods are different for infants in these higher level care settings; consult neonatology for recommendations
References


FEMALES

Birth Weight ______ g

Gestational Age, weeks


BIRTH SIZE ASSESSMENT

Date of birth: / / ( wks GA) Select one
Large-for-gestational age (LGA) >90th percentile □
Appropriate-for-gestational age (AGA) 10-90th percentile □
Small-for-gestational age (SGA) <10th percentile □

* 3rd and 97th percentiles on all curves for 23 weeks should be interpreted cautiously given the small sample size.
Intrauterine Growth Curves

Name
Record #

MALES

Birth Weight ______ g

Birth Size Assessment:

<table>
<thead>
<tr>
<th>Date of birth:  /  /  (wks GA)</th>
<th>Select one</th>
</tr>
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<tbody>
<tr>
<td>Large-for-gestational age (LGA) &gt;90th percentile</td>
<td>□</td>
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APPENDIX 2: Screening & Management of Neonatal Hypoglycemia in ASYMPTOMATIC infants ≥ 34wks GA

- CRITERIA:
  - IDM (DM1 or 2, GDMA1 or A2)
  - Late preterm (34-37wks) or Post-term (≥42wks)
  - SGA or LGA (see table)

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- TIMING:
  - Screen after initial feeding @ 1 hr, then @ 2, 4, 6, 9, 12 hrs (prior to feedings)
  - Screen SGA & late preterm infants @ 24 hrs (prior to feedings)
  - If glucose >45 x 3 → stop screening + re-check @ 24 hrs if SGA or late preterm

Target glucose ≥ 45 prior to routine feeds

Birth - 4 Hours
- Initial feed within 1 hour
- Screen glucose 30 minutes after 1st feed

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<thead>
<tr>
<th>&lt; 25</th>
<th>&gt; 25</th>
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<tbody>
<tr>
<td>Feed &amp; re-check in 1 hour</td>
<td>Routine care</td>
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</tbody>
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Continue glucose screening @ 2, 4 hours (before feeds)

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<tr>
<th>&lt; 25</th>
<th>25 - 40</th>
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<tbody>
<tr>
<td>IV treatment</td>
<td>Oral treatment (IV treatment PRN)</td>
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</table>

4 - 24 Hours
- Screen @ 6, 9, 12 hours + Screen @ 24 hours if SGA/ Preterm (before feeds)

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If persistent glucose < 45, Consider evaluation for underlying etiology
APPENDIX 3: Screening & Management of Neonatal Hypoglycemia in SYMPTOMATIC infants ≥ 34wks GA

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<th>“CONCERNING” symptoms</th>
<th>“POSSIBLE” symptoms</th>
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<td>• Seizure</td>
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<tr>
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<tr>
<td>• Hypotonia</td>
<td>• Exaggerated Moro reflex</td>
</tr>
<tr>
<td>• Apnea</td>
<td>• High-pitched cry</td>
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<tr>
<td>• Cyanosis</td>
<td>• Poor feeding</td>
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Target glucose ≥ 45 prior to routine feeds

"Concerning" Symptoms
- Check glucose
  - < 45
    - IV treatment
  - ≥ 45
    - Evaluate for other cause of symptoms
  - If glucose > 50 & persistent symptoms, Evaluate for other cause of symptoms

"Possible" Symptoms
- Check glucose
  - <45
    - Feed & re-check in 1 hour
  - < 35
    - IV treatment
  - 35 - 45
    - Oral treatment (IV treatment PRN)

If persistent glucose < 45, Consider evaluation for underlying etiology