Hypoglycemia Guideline

Definition:

For purposes of this guideline, we define hypoglycemia as a plasma glucose value of <50 mg/dL. The precise definition of hypoglycemia in infants and children continues to be controversial. This is because normal distributions of glucose values depend on conditions of feeding and fasting, and also vary with clinical factors such as age, gestation, and/or weight. Despite this natural variation, we use a single threshold to define hypoglycemia for diagnostic purposes because the overall goal of identifying children with hypoglycemia is to protect their central nervous systems from irreparable damage.[1,2,3]

Etiology:

Hypoglycemia occurs when the rate of appearance of glucose into the plasma space is less than its rate of utilization. This can be caused by defective glucose production, increased glucose utilization, or some combination of the two.

In infants and children, important causes of hypoglycemia include:

- Hormonal: adrenal insufficiency (Addison disease, ACTH deficiency, CAH, etc.), growth hormone deficiency, hyperinsulinism (congenital hyperinsulinism, insulinoma, Beckwith-Wiedemann Syndrome, "dumping syndrome," exogenous insulin administration, etc.), hyperthyroidism, and hypopituitarism
- Metabolic: disorders of carbohydrate metabolism (disorders of glycogenolysis, gluconeogenesis, and glycosylation), disorders of amino acid metabolism (methylmalonic aciduria, etc.), and disorders of fatty acid metabolism (MCAD, etc.)
- Ketotic hypoglycemia
- Toxic ingestions: for example, oral hypoglycemic agents, salicylates, and beta-blockers
- Other conditions causing increased glucose requirements: for example, sepsis and burns
- Other conditions causing decreased glucose production: for example, liver dysfunction and Reye syndrome

Guideline Inclusion Criteria:

Blood glucose < 50 mg/dL

Guideline Exclusion Criteria:

Patients with a previously diagnosed hormonal or metabolic disorder known to cause hypoglycemia
Patients admitted to NBN or NICU
Diabetes mellitus

Diagnostic Evaluation:

- History: A thorough history is always important; however, particular attention should be paid to the timing of episode and relationship to food intake, recent illnesses, possibility of toxic ingestion, birthweight and gestational age (especially if a neonate), family history of hypoglycemia, sleeping habits, growth and developmental history, prior history of hypoglycemia, history of recurrent abdominal pain, and weight loss
- Physical examination: On examination, pay attention to evidence of hypopituitarism (micropenis, cleft lip or palate, short stature, blindness, midline defects), glycogenosis (hepatomegaly), adrenal insufficiency (hyperpigmentation, hypotension), Beckwith-Wiedemann (macrosomia, macroglossia, hemihypertrophy, and omphalocele), toxic ingestion (altered mental status not improved by glucose correction, vital sign changes, mydriasis, nystagmus, etc.), CAH (ambiguous genitalia), liver dysfunction (jaundice, hepatomegaly, ascites)
- Laboratory tests: prior to correction of hypoglycemia, a critical serum sample should be collected for diagnostic testing (refer to Practice Recommendations and Clinical Management)
- Imaging tests: not required during initial evaluation

Critical Points of Evidence

Evidence Supports

Specimens for identifying etiology of hypoglycemia should be obtained at presentation and before treatment.
Treatment should focus on maintain glucose >70 mg/dL.
Hypoglycemia should be treated with glucose; either oral or intravenously depending on circumstances.

Practice Recommendations and Clinical Management

(See Hypoglycemia Pathway's for specific management guidance.)

Laboratory Testing

Diagnostic testing (aka "critical sample") (1,4) should be collected at the time of hypoglycemia and prior to treatment. Testing aims to identify the underlying etiology of the hypoglycemic event.

(Strong recommendation, high-quality evidence)

The following blood tests are recommended (priority level provided in case not enough blood collected):

- Highest priority: BMP, beta-hydroxybutyrate, and lactate
- Medium priority: free fatty acids, insulin level, C-peptide, cortisol, growth hormone, ammonia, and acetoacetate
- Lowest priority: free carnitine, acylcarnitine profile, IGFBP-1, serum amino acids, and pyruvate
- Consider serum toxicology screen for ethanol and salicylates if indicated

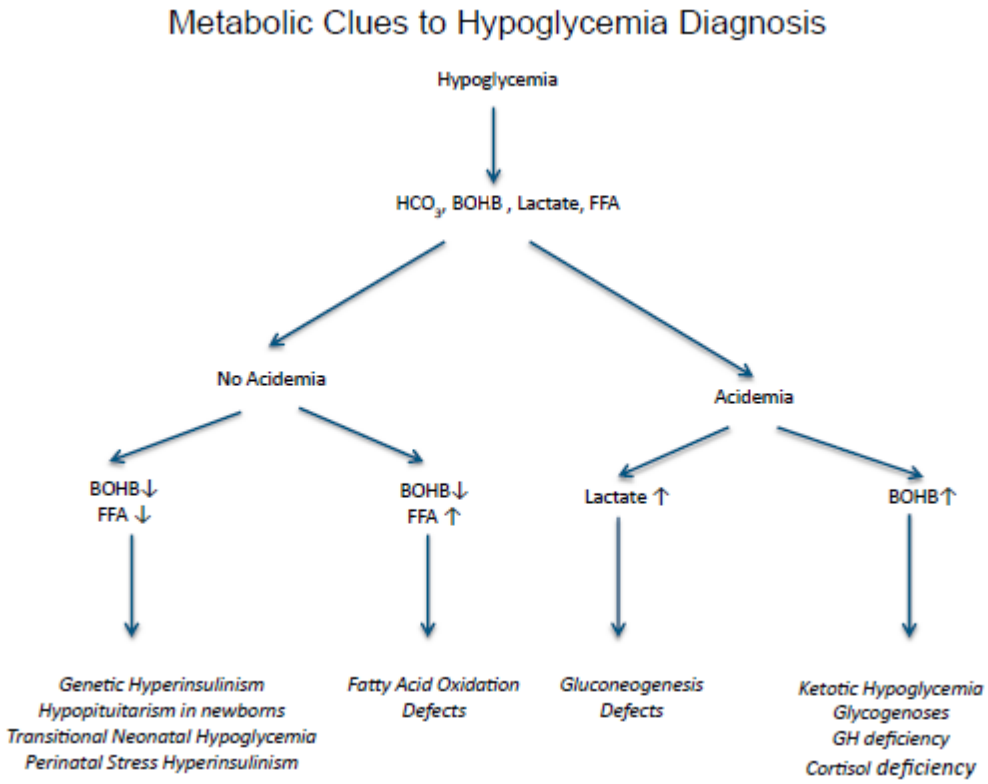

Figure 1. Thornton PS, et al. Recommendations from the pediatric Endocrine Society for Evaluation and Management of Persistent Hypoglycemia in Neonates, Infants, and Children. J Pediatr. 2016 Aug;167(2):238-45

Blood glucose should be monitored every 15 minutes until > 70 mg/dL then every 30 minutes.

(Strong recommendation, low-quality evidence)

Monitoring

In the emergency department setting, patients should be placed on a cardiac monitor, continuous pulse oximetry, and telemetry. Vital signs should be monitored every 5 minutes until stable and then every 15 minutes for one additional hour. Neurologic checks should be assessed every 15 minutes for one hour or until patient is deemed stable.

(Strong recommendation, low-quality evidence)

In the inpatient setting, patients should be placed on continuous pulse oximetry. Vital signs and neurologic checks should be monitored every 15 minutes until patient is stabilized.

(Strong recommendation, low-quality evidence)

Following treatment of hypoglycemia, capillary blood glucose should be monitored via point-of-care testing every 15 minutes until > 70 mg/dL and then every 30 minutes. Blood glucose monitoring can be further spaced or discontinued based on patient's response to treatment.
(Strong recommendation, low-quality evidence)

Management
Symptomatic hypoglycemia in non-diabetes mellitus patients should be rapidly corrected with IV dextrose infusion.
(Strong recommendation, moderate-quality evidence)

IV dextrose (**~0.2-0.5 g/kg/dose**) should be administered at varying concentrations based on patient's age and fluid availability:

- Infants/Children up to 12 years old: D10W 2 - 5 ml/kg/dose
  (This dosing can be used for older children on the inpatient unit, where D25W and D50W may be unavailable)
- Adolescents: D25W 1 - 2 ml/kg/dose | MAX = 100 ml/dose
- Adolescents/Adults: D50W 0.5 - 1 ml/kg/dose | MAX = 1 amp (50 mL/dose)

Based on ability to tolerated oral fluids and complex carbohydrate snacks, patients may require initiation of dextrose-containing maintenance fluids to stabilize blood glucoses. Rate of dextrose-containing IV fluids may need to be further adjusted based on blood glucose measurements. [5]
(Strong recommendation, moderate-quality evidence)

Consults/Referrals:
Consider consultation with an endocrinologist or metabolic specialist

Admission Criteria
No strict admission criteria exist, and provider discretion is indicated; however, the following criteria can serve as a guide in the emergency department setting:

- Patient unable to maintain blood glucose > 70 mg/dL without the need for continued IV dextrose administration
- Inability to tolerate oral fluids and complex carbohydrates
- No clear etiology apparent on initial evaluation or lab work inconsistent with ketotic hypoglycemia
- Age < 1 year
- No close follow-up care available

Discharge Criteria

- Patient able to maintain blood glucose > 70 mg/dL without the need for IV dextrose for > 2 hours
- Tolerating oral fluids and complex carbohydrates
- Close follow-up ensured
- Patient's history and exam are not concerning for an underlying hormonal or metabolic etiology of hypoglycemia, unless work-up and treatment with subspecialist has already been initiated

Follow-Up Care
Follow-up with a primary care provider within 1-2 days of discharge; however, ongoing follow-up will be required as some laboratory testing may take days or weeks for results
Follow-up with endocrinology and metabolics as indicated

Outcome Measures
Emergency Department & Inpatient Length of Stay
Readmissions to the Emergency Department & Hospital
New-onset hypoglycemia patients with critical samples obtained

Emergency Department Hypoglycemia Pathway

Evidence Based Outcome Center

EXCLUSION CRITERIA

- Patients with a previously diagnosed hormonal or metabolic disorder known to cause hypoglycemia
- Patients admitted to NBN or NICU
- Diabetes mellitus

Inclusion Criteria
Blood glucose < 50 mg/dL

! ALERT
Glucose < 50 mg/dL
OR
Declining Mental Status
Notify Provider

Place peripheral IV
- AND -
Initiate patient monitoring ❶

1 Patient monitoring:
- Place on cardiac monitor, pulse oximetry, and telemetry
- Monitor vital signs q5 min until stable, then q15 min x 4
- Perform neurologic checks q15 min x 4

2 Lactate: Use grey tube
Ammonia: Use green tube
Samples must be placed on ice

3 Discharge is at the discretion of provider;
Criteria to consider:
- Maintains POC glucose > 70 x 2 hours without need for IV dextrose
- Age > 1 year
- Tolerating po
- Consistent with ketotic hypoglycemia (presence of ketones with history of prolonged fasting, normal growth parameters, and no hepatomegaly)
- Has PCP who can review pending labs

Seizing OR Apnea
YES
NO

Initial Diagnostic Labs:
Collect Critical Sample Prior to Treatment:

High Priority:
BMP
Beta Hydroxybutyrate
Lactate❷

Tier 2 priority labs (if enough blood):

Free fatty acids	Cortisol
Insulin	Growth hormone
C-peptide	Ammonia❷
Acetoacetic acid	

Tier 3 priority labs (with remaining blood):

Free carnitine	Serum amino acids
Acylcarnitine profile	Pyruvate
IGFBP-1	
Save Serum Tube (-70 C | spin and hold)	

Urine organic acids
Urine reducing substances
Consider urine toxicology

IV dextrose (**0.2-0.5 g/kg/dose**) should be administered at varying concentrations based on patient's age and fluid availability:
- Infants/Children up to 12 years old: D10W 2 - 5 ml/kg/dose
- Adolescents: D25W 1 - 2 ml/kg/dose | MAX = 100 ml/dose
- Adolescents/Adults: D50W 0.5 - 1 ml/kg/dose | MAX = 1 amp (50 mL/dose)

Tolerating po?
Yes
No

- Provide sugary beverages @ maintenance fluid rate
- Provide complex carbohydrate snacks

- Start D5 NS, D5 ½ NS **or** D10 NS @ maintenance fluid rate
- Offer po as tolerated

- Monitor POC glucose q15 min until >70 mg/dL, then q30 min
- For glucose < 50 mg/dL, repeat IV dextrose bolus (weight-based as per above), obtain any critical labs not previously done, and return to q15 min POC glucose checks until >70 mg/dL then q30 min
- Initiate, adjust, or discontinue dextrose-containing IVF as needed based on glucose levels and po intake

Disposition ❸

Discharge home
(Family should continue to provide snacks with complex carbs at home)

ADMIT to hospital

dell children's medical center of central texas
A member of the Seton Family of Hospitals

For questions concerning this pathway,
Click Here
Last Reviewed May 2020

Inpatient Hypoglycemia Pathway
Evidence Based Outcome Center

EXCLUSION CRITERIA

- Patients with a previously diagnosed hormonal or metabolic disorder known to cause hypoglycemia
- Patients admitted to NBN or NICU
- Diabetes mellitus

Inclusion Criteria
Blood glucose < 50 mg/dL

! ALERT
Glucose < 50 mg/dL
OR
Declining Mental Status
Notify Provider

Place peripheral IV
- AND -
Initiate patient monitoring ❶
(If not previously done)

1 Patient monitoring:
- Place on pulse oximetry monitor
- Monitor vital signs and neurologic checks q15 min until glucose stabilized

2 Lactate: Use grey tube
Ammonia: Use green tube
Samples must be placed on ice

Initial Diagnostic Labs:
Collect Critical Sample Prior to Treatment:

High Priority:
BMP
Beta Hydroxybutyrate
Lactate❷

Tier 2 priority labs (if enough blood):
Free fatty acids
Insulin
C-peptide
Acetoacetic acid
Cortisol
Growth hormone
Ammonia❷

Tier 3 priority labs (with remaining blood):
Free carnitine
Acylcarnitine profile
IGFBP-1
Save Serum Tube (-70 C | spin and hold)
Serum amino acids
Pyruvate

Urine organic acids
Urine reducing substances
Consider urine toxicology

Administer IV Dextrose (0.2 g/kg/dose):
- D10W at 2 ml/kg/dose

ED Admit for hypoglycemia

Tolerating po?

Yes:
- Provide sugary beverages @ maintenance fluid rate
- Provide complex carbohydrate snacks

No:
- Start D5 or D10 NS with or without KCl @ maintenance fluid rate
- Offer po as tolerated

- Monitor POC glucose q15 min until >70 mg/dL, then q30 min x 2
- For glucose < 50 mg/dL, repeat IV dextrose bolus (weight-based as per above), obtain any critical labs not previously done, and return to q15 min POC glucose checks until >70 mg/dL then q30 min. Consider calling for critical response team (CRT) to obtain additional nursing resources. Consider transfer to higher-level of care if unable to stabilize glucose.
- Initiate, adjust, or discontinue dextrose-containing IVF as needed based on glucose levels and po intake
- Consider consult with endocrinology for further instruction

- If glucose remains > 70 mg/dL, space checks to q2hrs x 2 and then q4hrs
- If applicable, wean IVF as able
- Continue to offer complex carbohydrates po

Discontinue pathway at provider's discretion

dell children's medical center of central texas
A member of the Seton Family of Hospitals

For questions concerning this pathway,
Click Here
Last Reviewed May 2020

Hypoglycemia Critical Sample Laboratory Tests

Evidence Based Outcome Center

Laboratory test	Sunquest menumonic	Special instructions	Acceptable tubes	Minimum amount of blood (ml)
High Priority Labs				
BMP	BMPNL		MINT GREEN	**0.5 ml**
BHOB (beta hydroxybuturate)	BHOB		MINT GREEN	**0.5 ml**
Lactic Acid	LACT	Keep on ice once collected	GREY	**1 ml**
Total blood needed for High Priority labs:				**2 ml**
Tier 2 priority testing (order if enough blood is collected after high priority labs)				
MISC: Free fatty acids MAYO 8280	MISCB: FREE FATTY ACIDS	Lab-spin w/in 45min of draw	GOLD	**1 ml**
Insulin	INS		GOLD	**1 ml**
MISC: Acetoacetate to MAYO	MISCB: ACETOACETATE		PURPLE	**2.4 ml**
c-peptide	CPEP		MINT GREEN	**1.5 ml**
Cortisol	CORT		MINT GREEN	**1 ml**
Growth Hormone	GRHM		MINT GREEN	**1 ml**
Ammonia	AMON	Keep on ice once collected	MINT GREEN	**1 ml**
Total blood needed for High Priority & Tier 2 labs:				**10.9 ml**
Tier 3 priority testing (order with remaining blood after higher priority)				
IGFBP-1	SMM		GOLD	**1 ml**
Pryuvic Acid	PACID	Lab use pyruvic acid tube in ref STAT	MINT GREEN	**1 ml**
Free & total carnitine (not in acylcarnitine profile) profile	carntf		MINT GREEN	**0.5 ml**
Acyl-carnitine profile- order as MISC until pathnet go-live	misc - ACYLM		MINT GREEN	**0.5 ml**
Amino acids, plasma	AAP	LAB ONCE CENTIFUGED-CRITICAL FROZ	MINT GREEN	**1 ml**
Total blood needed for all Citical Sample Labs (High priority, Tier 2, & 3)				**14.9 ml**

Blood Tube	Minimum blood volume (ml)
GOLD	3 ml
MINT GREEN	8.5 ml
PURPLE	2.4 ml
GREY	1 ml
Total blood needed for Critical Sample	14.9 ml

References

1. Trang T Ly, et al. ISPAD Clinical Practice Consensus Guidelines – Hypoglycemia: Assessment and management of hypoglycemia in children and adolescents with diabetes. Pediatric Diabetes 2014: 15(Suppl.20): 180-192
2. Jones TW, et al. Independent effects of youth and poor diabetes control on responses to hypoglycemia in children. Diabetes 1991: 40:358-363
3. Cryer PE. Mechanisms of hypoglycemia-associated autonomic failure and its component syndromes in diabetes. Diabetes 2005: 54:3592-3601
4. Thornton PS, et al. Recommendations from the pediatric Endocrine Society for Evaluation and Management of Persistent Hypoglycemia in Neonates, Infants, and Children. J Pediatr. 2016 Aug;167(2):238-45
5. Brodows RG, et al. Treatment of insulin reactions in diabetics. JAMA 1984: 252: 3378-3381

EBOC Project Owner: Mark Tabarrok, MD

Approved by the Hypoglycemia Guideline Evidence-Based Outcomes Center Team

Revision History

Date Approved: February 9, 2015
Last Review Date: May 2020

Hypoglycemia Guideline Development EBOC Team: 2015
Mark Tabarrok, MD
Joshua Smith, MD
Melissa Cossey, MD
Harris Hayley, DO
Patrick Boswell

EBOC Leadership Committee:
Sarmistha Hauger, MD
Levy Moise, MD
Sujit Iyer, MD
Tory Meyer, MD
Meena Iyer, MD
Lynn Thoreson, MD
Teresa Stanley, DNP, RN

Hypoglycemia Guideline Review EBOC Team: 2020
Mark Tabarrok, MD
Tania Eid, MD
Melissa Cossey, MD
Shona Rabon, MD
Carmen Garudo, PM