**Pediatric Hypoglycemia**

* **Definition:** Hypoglycemia diagnosis is based on plasma glucose (PG) values and never by point of care (POC) values
	+ Common in the newborn period (premature, IUGR, sepsis/asphyxia, high basal needs)
	+ Transitional hypoglycemia – 30% healthy infants with PG <50 mg/dL in first 24 hours of life
		- >24 hours of life, PG should be >50 mg/dL
	+ Beyond 48 hours of life, normal PG concentrations are the same as older children/adults
		- In general, PG >60-70 mg/dL is normal, <50 mg/dL is hypoglycemia
* **Normal Physiology**:
	+ Brain needs continuous supply of glucose (prevents long-term neurologic sequelae, psychomotor retardation, seizures)
	+ If glucose unavailable, brain uses ketones (β-hydroxybutyrate, acetoacetate) from fatty acid oxidation as fuel
	+ To maintain normal plasma glucose during fasting requires 3 things:



* **Clinical Manifestations of Hypoglycemia**
	+ Autonomic
		- Sweating, hunger, paresthesias, tremors, pallor, anxiety, nausea, palpitations
	+ Neuroglycopenic (varies according to age)
		- Warmth, fatigue, weakness, dizziness, headache, inability to concentrate, blurred speech, difficulty speaking, confusion, bizarre behavior, lack of coordination, difficulty walking, coma, seizures
* **Differential diagnosis**:
	+ Are ketones present in response to hypoglycemia?

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| Hypoglycemia without ketosis | Hypoglycemia with ketosis |
| Hyperinsulinism (e.g. IDM, congenital hyperinsulinism, transient hyperinsulinism, Beckwith-Wiedemann syndrome, factitious) | Cortisol/ACTH deficiency |
| Defects in fatty acid oxidation / ketone synthesis | Growth hormone deficiency / hypopituitarism |
|  | Disorders of carbohydrate metabolism (e.g. Glycogen storage diseases, Disorders of gluconeogenesis) |
| Disorders of protein metabolism |
| Ingestions (ethanol, salicylates, beta-blockers, quinine, sulfonylureas) |
| Prolonged starvation |
| Increased glucose consumption (sepsis, organ failure) |
| Reactive hypoglycemia (mismatch of insulin secretion to carbohydrate consumption) |
| Ketotic hypoglycemia (otherwise healthy children with repeated AM hypoglycemia and ketosis) |
| Low glycogen stores - Small for gestational age (SGA), prematurity |

* **Evaluation**:
	+ History
		- Birth details (weight, GA, maternal health/meds), symptoms of hypoglycemia, age of onset of symptoms, jaundice, association with feeding, potential drug exposures, unusual odors, recurrent “pneumonia” (metabolic acidosis)
	+ Physical Exam
		- Stature, microphallus, midline defects, liver size, skin pigmentation, macrosomia, odor, hyperventilation, heart gallop or cardiomyopathy
	+ **Critical labs** (drawn when any glucose <50 mg/dL, and prior to treatment with dextrose)
		- Repeat *plasma* glucose (confirm hypoglycemia). Insulin, c-peptide, pro-insulin.
		- Ketones (β-hydroxybutyrate in plasma, urinalysis). Growth hormone. Cortisol.
		- Metabolic work-up guided by metabolic experts.
	+ Glucagon challenge
		- During hypoglycemia, injection of 1 mg glucagon IV followed by large increase in plasma glucose suggests hyperinsulinism as cause of hypoglycemia.
	+ Clues towards hyperinsulinism:
		- Hyperinsulinemia (plasma insulin >2 uU/mL when PG < 50 mg/dL) if sensitive insulin assay.
		- Otherwise, look for evidence of inappropriate insulin effects - hypoketonemia, glycemic response to glucagon challenge, hypo-free fatty acidemia.
* **References**:
1. Sperling, Mark A. Pediatric Endocrinology 4th Edition.
2. Pediatric Endocrinology, Fifth Edition Volume 2. Lifshitz.