HYPOGLYCEMIA

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- No fixed cut off
- FPG lower limit is 70 mg/dl
- But lower values can also be normal

WHIPPLE'S TRIAD:

- (1) symptoms consistent with hypoglycemia,
- (2) a low plasma glucose concentration measured with a precise method (not a glucose monitor),
- (3) relief of symptoms after the plasma glucose level is raised.

SYMPTOMS

Neuroglycopenic

- behavioral changes,
- confusion,
- fatigue,
- seizure,
- loss of consciousness,
- death

Neurogenic (or autonomic)

Adrenergic symptoms

- palpitations,
- tremor,
- Anxiety

Cholinergic symptoms

- sweating,
- Hunger
- paresthesias

TABLE 420-2 PHYSIOLOGIC RESPONSES TO DECREASING PLASMA GLUCOSE CONCENTRATIONS

Response	Glycemic Threshold, mmol/L (mg/dL)	Physiologic Effects	Role in Prevention or Correction of Hypoglycemia (Glucose Counterregulation)
↓ Insulin	4.4–4.7 (80–85)	↑ R_a (↓ R_d)	Primary glucose regulatory factor/first defense against hypoglycemia
↑ Glucagon	3.6–3.9 (65–70)	↑ R_a	Primary glucose counterregulatory factor/second defense against hypoglycemia
↑ Epinephrine	3.6–3.9 (65–70)	↑ R_a, ↓ R_c	Third defense against hypoglycemia, critical when glucagon is deficient
↑ Cortisol and growth hormone	3.6–3.9 (65–70)	↑ R_a, ↓ R_c	Involved in defense against prolonged hypoglycemia; not critical
Symptoms	2.8–3.1 (50–55)	Recognition of hypoglycemia	Prompt behavioral defense against hypoglycemia (food ingestion)
↓ Cognition	<2.8 (<50)	—	Compromises behavioral defense against hypoglycemia

TABLE 420-1 CAUSES OF HYPOGLYCEMIA IN ADULTS

Ill or medicated individual

1. Drugs
   - Insulin or insulin secretagogue
   - Alcohol
   - Others
2. Critical illness
   - Hepatic, renal or cardiac failure
   - Sepsis
   - Inanition
3. Hormone deficiency
   - Cortisol
   - Glucagon and epinephrine (in insulin-deficient diabetes)
4. Non–islet cell tumor

Seemingly well Individual

5. Endogenous hyperinsulinism
    - Insulinoma
    - Functional β-cell disorders (nesidioblastosis)
        - Noninsulinoma pancreatogenous hypoglycemia
        - Post–gastric bypass hypoglycemia
    - Insulin autoimmune hypoglycemia
        - Antibody to insulin
        - Antibody to insulin receptor
    - Insulin secretagogue
    - Other
6. Accidental, surreptitious, or malicious hypoglycemia

DIABETES

- Type 1 DM

- Type 2 DM

Early and late

CAUSES

- Insulin
- Oral drugs
- Metformin/ Gliptins/SU/ Glinides/ Glitazones/ GLP -1 agonists

RISK FACTORS

- (1) insulin (or insulin secretagogue) doses are excessive, ill-timed, or of the wrong type;
- (2) the influx of exogenous glucose is reduced (e.g., during an overnight fast or after missed meals or snacks);
- (3) insulin-independent glucose utilization is increased (e.g., during exercise);
- (4) sensitivity to insulin is increased (e.g., with improved glycemic control, in the middle of the night, late after exercise, or with increased fitness or weight loss);
- (5) endogenous glucose production is reduced (e.g., after alcohol ingestion)
- (6)insulin clearance is reduced (e.g., in renal failure).

RISK FACTOR REDUCTION

- Intensive blood glucose control
- Metabolic memory
- Results of trials

OTHER CAUSES - DRUGS

- SU
- Insulin
- Alcohol
- angiotensin-converting enzyme inhibitors and angiotensin receptor antagonists,
- β-adrenergic receptor antagonists,
- quinolone antibiotics,
- indomethacin,
- quinine
- sulfonamides.

CRITICAL ILLNESS

- renal, hepatic, or cardiac failure; sepsis are second only to drugs as causes of hypoglycemia.
- renal failure -the reduced clearance of insulin and the reduced mobilization of gluconeogenic precursors in renal failure.
- Sepsis is a relatively common cause of hypoglycemia.
- Increased glucose utilization is induced by cytokine production in macrophage rich tissues such as the liver, spleen, and lung.
- starvation,

HORMONAL CAUSES

- Cortisol
- GH

NON-B-CELL TUMORS

- overproduction of an incompletely processed form of insulin-like growth factor II ("big IGF-II") that does not complex normally with circulating binding proteins and thus more readily gains access to target tissues.

ENDOGENOUS HYPERINSULINISM

- Critical diagnostic findings are a
- plasma insulin concentration ≥3 μU/mL (≥18 pmol/L),
- a plasma C-peptide concentration ≥0.6 ng/mL (≥0.2 nmol/L), and
- a plasma proinsulin concentration ≥5.0 pmol/L

- when the plasma glucose concentration is <55 mg/dL (<3.0 mmol/L) with symptoms of hypoglycemia

URGENT TREATMENT

- If the patient is able and willing, oral treatment with glucose tablets or glucose-containing fluids, candy, or food is appropriate. A
- reasonable initial dose is 20 g of glucose.
- If the patient is unable or unwilling (because of neuroglycopenia) to take carbohydrates IV administration of glucose (25 g) should be followed by a glucose infusion
- If IV therapy is not practical, SC or IM glucagon (1.0 mg in adults) can be used, particularly in patients with T1DM.
- These treatments raise plasma glucose concentrations only transiently, and patients should therefore be urged to eat as soon as is practical to replete glycogen stores.

SPECIFIC THERAPIES

- Identifying the cause