Hypoglycemia

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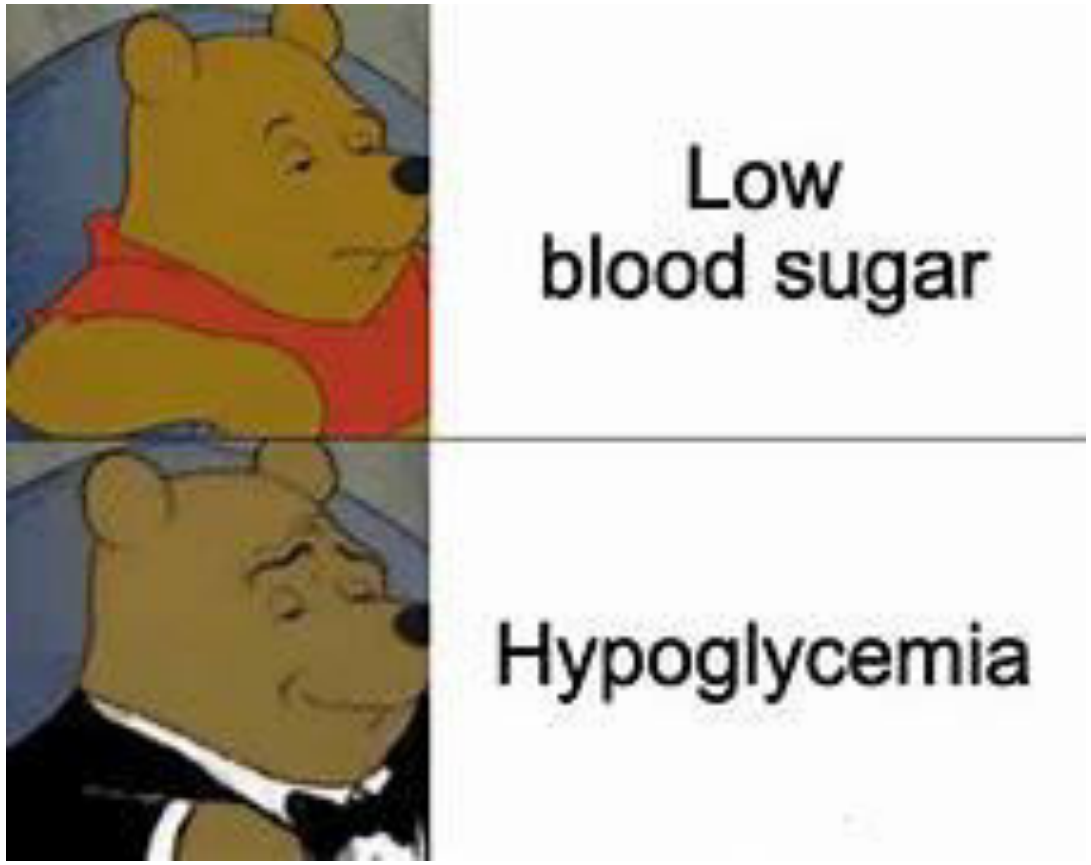


We are not talking about hypoglycemia in the context of diabetes , but rather the hypoglycemia occurs in neonates or children who do not have underlying diagnosis of diabetes.

Outlines:

- **Definition of hypoglycemia**
- **Causes**
- **Congenital hyperinsulinism**
- **Symptoms**
- **Investigations**
- **Management**

-Hypoglycemia occurs most frequently in the early neonatal period, often as a result of transient neonatal hyperinsulinemia in infants of diabetic mothers or as a result of inadequate energy stores to meet the disproportionately large metabolic needs of premature or small for gestational age newborns.

Hypoglycemia during the first few days of life in an otherwise normal newborn is less frequent and warrants concern .
After the initial 2-3 days of life, hypoglycemia is far less common and is more frequently the result of endocrine or metabolic disorders (although sepsis must always be ruled out).

-Clinical hypoglycemia is defined as a plasma glucose (PG) concentration low enough to cause symptoms and/or signs of impaired brain function.
Brain glucose utilization is reduced at a PG concentration of approximately 55-65 mg/dL.
Autonomic system (neurogenic) symptoms are perceived at a PG concentration <55mg/dL.
Cognitive function is impaired (neuroglycopenia) at a PG concentration <50mg/dL

Causes

Newborn, transient:

1-Neonatal transitional hypoglycemia

2- Transient Neonatal hypoglycemia

NEONATAL, INFANTILE, OR CHILDHOOD PERSISTENT HYPOGLYCEMIAS :

A- Hyperinsulinism

B- Counterregulatory Hormone Deficiency

- Panhypopituitarism
- Isolated growth hormone deficiency
- Adrenocorticotropic hormone deficiency
- Addison disease
- Epinephrine deficiency

C- Glycogenolysis and Gluconeogenesis Disorders :
(Glycogenolysis)

glucose-6-phosphatase deficiency (gsd 1a)
glucose-6-phosphate translocase deficiency (gsd 1b)
amylo-1,6-glucosidase (debranching enzyme) deficiency (gsd 3)
liver phosphorylase deficiency (gsd 6) phosphorylase kinase deficiency (gsd 9)
glycogen synthetase deficiency (gsd 0)
(Gluconeogenesis)
fructose-1,6-diphosphatase deficiency
pyruvate carboxylase deficiency

D- metabolic disorders
Galactosemia
Hereditary fructose intolerance

E- Lipolysis Disorders
fatty acid oxidation disorders

F-Inadequate substrate :
Ketotic hypoglycemia
G-Poisoning-Drugs :
salicylates ,alcohol ,oral hypoglycemic agents , insulin, propranolol

H-Liver disease

Reye syndrome, Hepatitis, Cirrhosis, and Hepatoma

I- Systemic disorders:

- **Sepsis**
- **Heart failure**
- **Malnutrition**
- **Malabsorption**
- **Antiinsulin receptor antibodies**
- **Antiinsulin antibodies**
- **Neonatal hyperviscosity**
- **Renal failure, Diarrhea, Burns, AND Shock**

>> Pseudohypoglycemia

Excessive insulin therapy of insulin- dependent diabetes mellitus.

-Factitious.

-Nissen fundoplication (dumping syndrome).

- **NEONATAL TRANSITIONAL HYPOGLYCEMIA-WITHIN FIRST FEW HOURS OF LIFE :**
- This occurs during transition from fetal to extra uterine life in normal newborns.
  - They need proper supply to meet demand and that depends on glycogen stores, gluconeogenesis precursors ,functioning hepatic enzymes and functioning endocrine system .
  - During this transition, blood glucose level falls down as they gave impaired establishment of normal glucose homeostasis which results in hypoglycemia.
  - 30% of normal neonate will experience this.
  - resolves with feeding / iv glucose.
- **TRANSIENT NEONATAL HYPOGLYCEMIA –DAYS:**

Due to :

- A)Change in maternal metabolism (transient hyperinsulinism):
- antenatal steroids exposure, labetalol use, diabetes .
- B)Neonatal problems :failure to produce or depletion of glycogen stores

SGA or LGA Preterm infant

IUGR Hypothermia

Birth asphyxia

Sepsis/Infections

Sick infants

- Higher energy needs.
- Hypoxic infants may rely on anaerobic glycolysis (inefficient-large amount of glucose used for low yield).
- Aerobic metabolism yields 38 ATP per molecule of glucose
- Anaerobic yields 2 ATP per molecule of glucose
- Therefore, rapidly deplete stores.

Preterm Infants

- Majority of glycogen stored in 3rd trimester
- Available stores rapidly depleted
- At TERM 5-8% of liver and muscle weight is glycogen storage
- Immature counter regulatory response to low glucose concentrations.
- Preterm
  - lack adipose required for ketone production
  - or unable to mobilize free fatty acids from adipose
  - Preterm-may not have enzymes required for he breakdown of glycogen into glucose (glycogenolysis)

SGA

- Low glycogen and fat stores.
- Hyperinsulinism and low glucagon may persist for weeks to months.
- May require GIR>20 or glucocorticoid.
- Chronically stressed fetus may use most of the placentally transferred glucose for growth and survival.

Infant of Diabetic Mother

- Glucose crosses placenta/insulin does not
- Fetal glucose level 70-80% of mother's
- Infant produces insulin in response to higher blood sugars
- At cord clamping, glucose supply is gone but insulin production in infant remains elevated
- The expected nadir is more rapid than non IDM infants (1-6 hours)
- May take several days to down regulate insulin production

Nour Emad Odeh

HYPERINSULINISM

TRANSIANT HYPERINSLUMIA: hours to days.

PERSISTENT HYPOGLYCEMIA: lasts more than seven days or requires continuous treatment.

HYPERINSULINISM IS THE MOST COMMON CAUSE OF PERSISTENT HYPOGLYCEMIA IN EARLY INFANCY.

IT IS AN inappropriate secretion of insulin.

infants with hyperinsulinism may be macrocosmic at birth, reflecting the anabolic ejects of insulin in utero.

The onset of symptoms is from birth to 18 mo. of age, but occasionally it only becomes evident in older children.

Insulin concentrations are inappropriately elevated at the time of documented hypoglycemia

- with nonhyperinsulinemic hypoglycemia, plasma insulin concentrations should be <5 µU/mL.
- hyperinsulinemic hypoglycemia, at the time of hypoglycemia are usually >5 µU/mL
- insulin glucose ratio > 0.4
- plasma insulin-like growth factor binding protein-1 (IGFBP-1), β-hydroxybutyrate, and FFA levels are low with hyperinsulinism

INSULINOMA

1. insulin-secreting pancreatic beta-cell tumors.
2. sporadically but they can also occur in patients with multiple endocrine neoplasias (e.g., parathyroid tumors, pituitary adenomas, gastrinomas).
3. Typical clinical features include recurrent attacks of symptomatic hypoglycemia in individuals without diabetes.
4. The diagnosis is established if serum insulin and C-peptide are elevated despite hypoglycemia, either during a spontaneous episode or during a hypoglycemic episode provoked by a 72-hour fasting test.
5. The treatment of choice is surgical enucleation of the insulinoma. In inoperable cases and patients with persistent hypoglycemic attacks, pharmacotherapy (e.g., diazoxide, somatostatin analogues) can be used to decrease insulin secretion.

- **Whipple triad** is the clinical presentation of pancreatic insulinoma and consists of:
- fasting hypoglycemia) <50 mg/dl(
- symptoms of hypoglycemia
- immediate relief of symptoms after the administration of IV glucose

CONGENITAL HYPERINSULINISM

- Congenital hyperinsulinism is caused by mutations in genes that regulate the release of insulin, which is produced by beta cells in the pancreas.
- In these infants, hyperplasia of the pancreatic islet cells develops in the absence of excess stimulation by maternal diabetes.
- There are currently 11 genes associated with monogenic forms of hyperinsulinism as well as several syndromic genetic forms of HI (e.g., Beckwith-Wiedemann, Kabuki, and Turner syndromes).
- Mutations in the ABCC8 gene are the most common and account in approximately 40 percent of affected individuals.
- Less frequently, mutations in the KCNJ11 gene have been found in people with congenital hyperinsulinism.
- Mutations in each of the other genes associated with this condition account for only a small percentage of cases.
- In approximately half of people with congenital hyperinsulinism, the cause is unknown.

Treatment :

infusion of intravenous (iv) glucose at high rate .

- Diazoxide to suppress insulin secretion.

- If diazoxide therapy is unsuccessful, long-acting somatostatin analogs can be tried.

- Often medical therapy for persistent hyperinsulinemic hypoglycemia of the newborn is unsuccessful, therefore subtotal (90%) pancreatectomy is required to prevent long term neurologic sequelae of hypoglycemia.

BECKWITH- WIEDEMANN SYNDROME:

- **Definition**: congenital disorder of growth with a predisposition to tumor development
- **Epidemiology**
  - ~ 1/15,000 newborns in the US
  - Increased risk of **nephroblastoma**, hepatoblastoma, neuroblastoma, adrenal tumors
- **Etiology**: associated with *WT2* gene mutation on chromosome 11 (~ 80% of cases)
- **Pathophysiology**: defect in genetic imprinting → overexpression of genes
- **Clinical features**
  - Macrosomia , omphalocele (i.e., exomphalos)
  - **Macroglossia**, organ enlargement (heart, liver, kidney, etc.)
  - **Hemihypertrophy** (hemihyperplasia): One side or a part of one side of the body is larger than the other.
  - Features of neonatal hypoglycemia : irritability, intellectual disability
  - Genitourinary abnormalities
  - Facies: midface hypoplasia, infraorbital and earlobe creases
  - Cleft palate (rare)

- **Diagnosis**
  - ↓ Blood glucose, ↑ serum insulin, IGF-2 (hypoglycemia)
  - Screening options for embryonal tumors [9]
    - Abdominal ultrasound every 3 months until 8 years of age
    - Alpha-fetoprotein levels every 3 months until 4 years of age
- **Treatment**
  - Frequent feedings to maintain sufficient blood glucose levels
  - Resection of embryonal tumors

Beckwith-Wiedemann syndrome

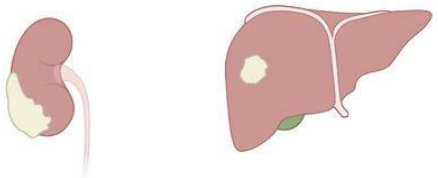
Definition
Congenital disorder of growth with a predisposition to tumor development

Etiology
WT2 gene mutation on chromosome 11 → defect in genetic imprinting

Diagnostics
Clinical diagnosis and/or genetic testing

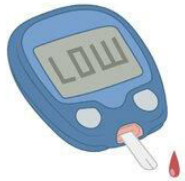
Treatment
- Treatment of manifestations (e.g., omphalocele repair)
- Regular screening for tumors and urinary tract abnormalities (e.g., abdominal ultrasound, serum AFP levels)

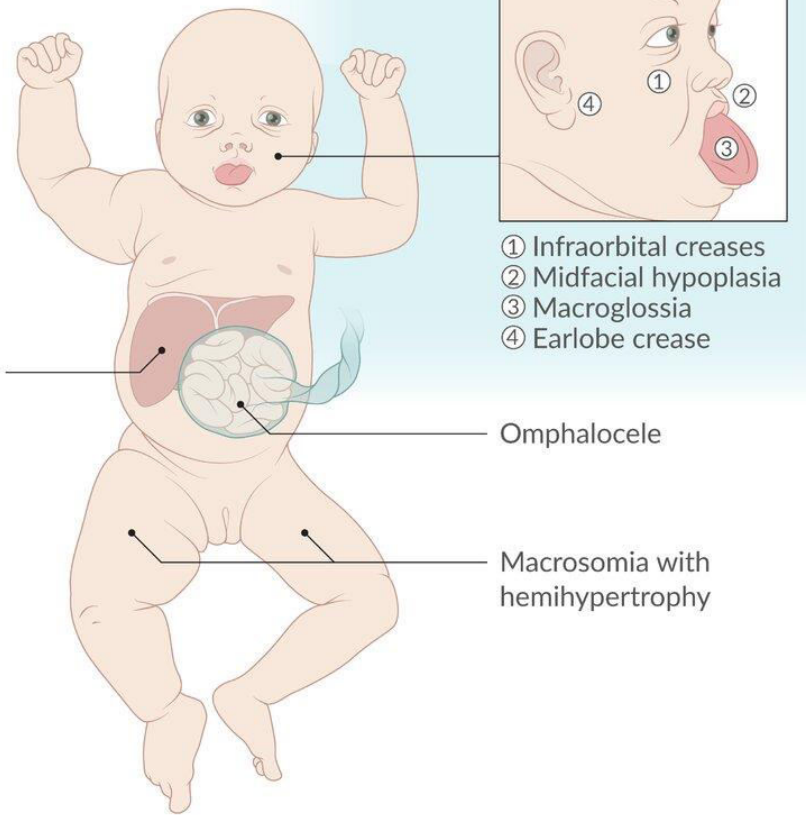
Most common tumors



Nephroblastoma Hepatoblastoma

Neonatal hypoglycemia (due to hyperinsulinism)





Characteristic facies

① Infraorbital creases
② Midfacial hypoplasia
③ Macroglossia
④ Earlobe crease

Organomegaly (e.g., hepatomegaly)

Omphalocele

Macrosomia with hemihypertrophy

FACTITIOUS HYPERINSULINEMIA

- **In rare cases insulin or a hypoglycemic medication is administered by a parent or caregiver to a child as a form of child abuse, which is a condition referred to as Munchausen syndrome by proxy.**
- **This diagnosis should be suspected if :**
- **extremely high insulin concentrations are detected(>100 µU/Ml).**

C-peptide concentrations are low or undetectable, which confirms that the insulin is from an exogenous source.

DEFECTS IN COUNTER-REGULATORY HORMONES

- Abnormalities in the secretion of counter-regulatory hormones that produce hypoglycemia usually involve GH, cortisol, or both.

- GH and cortisol deficiency occur as a result of hypopituitarism. Hypopituitarism results from congenital hypoplasia or aplasia of the pituitary or, more commonly, from deficiency of hypothalamic releasing factors.

- Deficiencies in glucagon and epinephrine secretion are rare.

- Deficient cortisol secretion also can occur in primary adrenal insufficiency, resulting from a variety of causes. In infants it often results from congenital adrenal hyperplasia, most frequently as a result of 21-hydroxylase deficiency. In older children, primary adrenal insufficiency is seen most frequently in Addison disease and other disorders

- Clues to this diagnosis in infants include the presence of hypoglycemia in association with midline facial or neurological defects (e.g., cleft lip and palate or absence of the corpus callosum),
- pendular (roving) nystagmus (indicating visual impairment from possible abnormalities in the development of the optic nerves, which can occur in optic nerve hypoplasia),
- and the presence of microphallus and cryptorchidism in boys (indicating abnormalities in gonadotropin secretion).
- Jaundice and hepatomegaly also can occur, simulating neonatal hepatitis.
- Despite the presence of GH deficiency, these infants are usually of normal size at birth.

Diagnosis:

Confirmation of GH or cortisol deficiency as the cause of hypoglycemia requires :

the detection of low serum GH and cortisol concentrations during an episode of hypoglycemia or after other stimulatory testing.

In contrast to hyperinsulinism, serum and urine ketones are positive at the time of hypoglycemia and FFAs are elevated.

Treatment:

involves supplementation of the deficient hormones in physiological doses.

D- IDIOPATHIC KETOTIC HYPOGLYCEMIA

- *Patients have symptoms of hypoglycemia after decrease oral intake due to prolonged fasting or gastrointestinal illness with vomiting.*
- *A common cause of new-onset hypoglycemia.*
- *Usually seen in children between 18 months and 6 years of age.*
- This illness causes a low blood sugar and bulid-up of ketones in the body's
- These patients my be small and thin for their age
- no specific diagnostic tests for this disorder, so its diagnosed after exclusion of various metabolic disease.

TREATMENT of IKH:

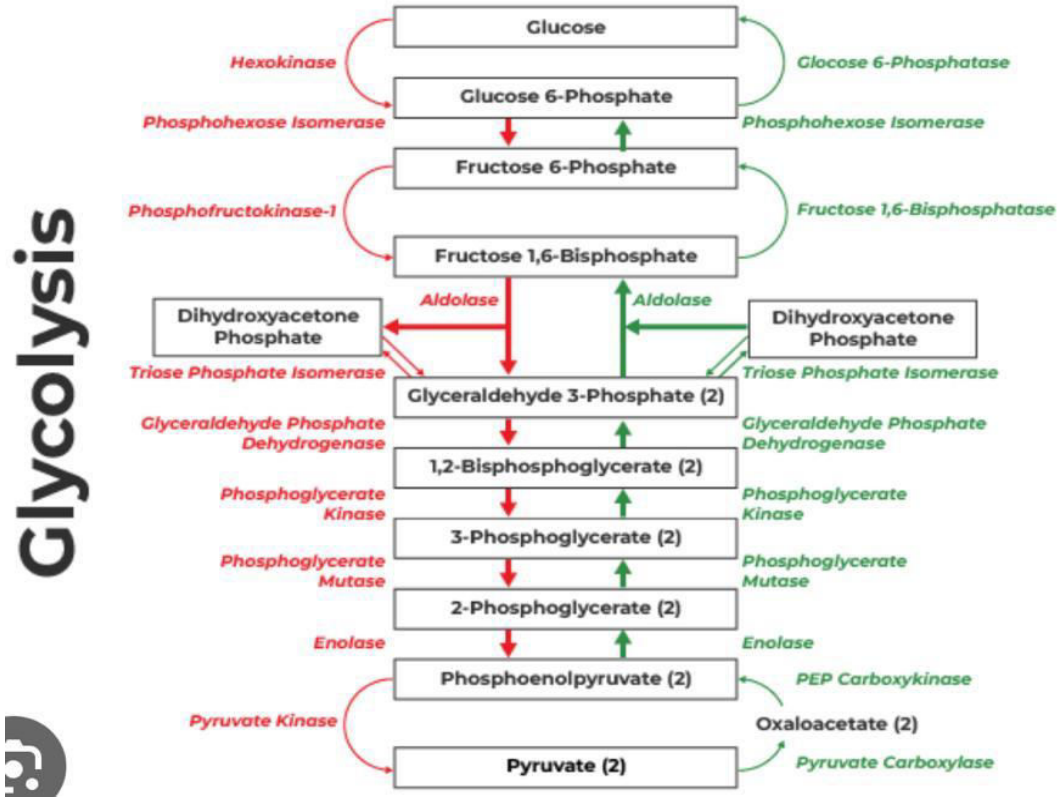
1. No specific treatment.
2. Avoidance of prolonged fasting with close monitoring of oral intake.
3. Increase frequency of feedings.
4. *May need Hospitalization for IV glucose infusion if they cannot maintain adequate oral intake during a period of illness.*

- usually resolves spontaneously by 7 to 8 years of age.

E- DISRUPTED METABOLIC RESPONSE PATHWAY

- Maintenance of normal serum glucose concentrations in the fasting state requires glucose production via:

1. glycogenolysis.
2. Gluconeogenesis
3. The production of alternative energy sources (FFAs and ketones) via lipolysis and fatty acid oxidation.



1. glycogenolysis.

- The most common subtype of glycogen storage disease that cause hypoglycemia is **glucose-6-phosphatase deficiency.**
- which is characterized by:

1. severe hypoglycemia.
2. massive hepatomegaly.
3. growth retardation.

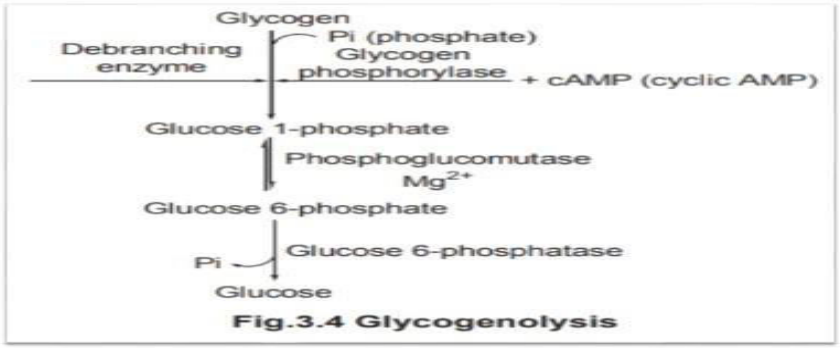


Fig.3.4 Glycogenolysis

- The diagnosis of glycogen storage disease can by finding hepatomegaly without splenomegaly.
- To confirmation the diagnosis we require a liver biopsy.

- Treatment:

✓ Increase frequency of high-carbohydrate feeding during the day.

✓ Continuous NG tube feeding at night.

2. Gluconeogenesis

- Uncommon
- include **fructose-1,6-diphosphatase deficiency** and **phosphoenolpyruvate carboxykinase deficiency.**
- patients exhibit:

1. Hypoglycemia.
2. Hepatomegaly.
3. lactic acidosis.
4. Hyperuricemia.

- Treatment:

✓ Increase frequency of high-carbohydrate feeding and low protein.

3. FATTY ACID OXIDATION:

- Fatty acid oxidation disorders include:
  - **Acyl-coenzyme A dehydrogenase deficiencies.**
  - **Long chain, medium chain, short chain acyl-coA dehydrogenase deficiencies.**
  - **Hereditary carnitine deficiency .**
- medium-chain acyl-CoA dehydrogenase deficiency is the most common.
- The first episode of hypoglycemia may the patient have at 2 years old or older.
- Episodes of hypoglycemia usually occur with prolonged fasting or during episodes of intercurrent illness.

- The patient may present with:

1. Mild hepatomegaly.
2. mild hyperammonemia.
3. Hyperuricemia.

- Treatment :

✓ Avoidance of fasting.

✓ High carbohydrate diet.

Medicines That Decrease Blood Sugar:

- Antibiotics (Bactrim/Septra)
- Alcohol (acute excess amounts)
- Aspirin and other salicylates in larger doses
- Heart and blood pressure medications (ACE inhibitors, beta blockers, Quinidine)
- Quinine
- Tylenol (acetaminophen-especially in larger doses)

Sign and symptoms :

Symptoms of hypoglycemia can be divided into neurogenic and neuroglycopenic symptoms:

1- Neurogenic (autonomic) symptoms are caused by the sympathetic nervous system's response to hypoglycemia and appear when the plasma glucose is less than 55 to 60 mg/dL. Manifestations are sweating, tremor, palpitations, tachycardia, and hunger.

2-Neuroglycopenic symptoms result from insufficient supply of glucose to the brain, leading to brain dysfunction. They include lethargy, confusion, irritability, loss of consciousness, and seizure. Neuroglycopenic symptoms typically occur when the plasma glucose falls below 50 mg/dL.

3-"hypoglycemia unawareness"

- **Older children and adults**

Hypoglycemia in these age groups typically demonstrates the Whipple triad:

- **Symptoms and signs consistent with hypoglycemia**
- **A documented low plasma glucose concentration**
- **Resolution of the symptoms with normalization of the glucose concentration**

- **Infants and toddlers**

Symptoms in these age groups are frequently nonspecific and include irritability, lethargy, poor feeding, cyanosis, and tremor or jitteriness. Commonly, infants manifest no symptoms of hypoglycemia until they present with a hypoglycemic seizure.

History

1- Age at presentation

Although there is considerable overlap, age at presentation suggests diagnostic categories:

Neonatal period and early infancy – Hyperinsulinism, disorders of gluconeogenesis,most inborn errors of metabolism and panhypopituitarism

First two years of life – Glycogen storage disorders, growth hormone or cortisol deficiencies

Toddlers and young children – Ingestion, idiopathic ketotic hypoglycemia, glycogen
storage disorders

School-aged children and adolescents – Insulinoma, factitious hypoglycemia, other ingestions

2- Symptoms : mentioned above

3- Triggers:

a- Duration of fasting

Details should be obtained on how long the child fasted prior to the acute event, as well as how long the child fasts on a routine basis.

A short duration of fasting (several hours) before onset of symptoms suggests hyperinsulinism or glycogen storage disorder.

A longer duration of fasting (overnight) suggests a different glycogen storage disorder, a hormone deficiency, a disorder of gluconeogenesis, or idiopathic ketotic hypoglycemia.

b- Specific foods

Determine whether specific foods and nutrients may have triggered the hypoglycemic episode. Symptoms after ingestion of milk products or fructose may indicate galactosemia or hereditary fructose intolerance, respectively.

c-Concurrent illness

In children with unrecognized hypoglycemic disorders, the episodes are often triggered by illnesses that interrupt normal feeding. Thus, further evaluation is indicated for a child presenting with hypoglycemia during a noncritical, intercurrent illness . The misperception that hypoglycemia is a common and normal result of routine childhood illnesses leads to delays in diagnosis and increased risk of neurologic damage. Hypoglycemia occurring during common childhood illnesses may be a clue to an underlying hypoglycemia disorder.

d-Ingestion

The clinician must inquire about possible exposure to substances that cause hypoglycemia, such as oral hypoglycemic agents (sulfonylureas or meglitinides), ethanol, or beta blockers.

4-Past medical history:

a-Perinatal history

A thorough perinatal history is crucial and should include the birthweight, gestational age, and whether the child had hypoglycemia at birth or in theneonatal period, including what type of treatment was necessary. A history of being born large for gestational age suggests congenital hyperinsulinism or Beckwith-Wiedemann syndrome. Intrauterine growth restriction or born small for gestationalage can result in the perinatal stress-induced form of hyperinsulinism

b-Prior events

It is important to explore the child's past medical history and to review available medical records to determine whether the child had other episodes suggestive of hypoglycemia that may have been missed or diagnosed as another condition (eg, seizure disorder).

5-Family history

Physical examination

Anthropometrics – The child's weight and length or height should be measured and plotted on an appropriate growth chart

Short stature or poor linear growth may indicate growth hormone deficiency or a glycogen storage disorder.

Tall stature is associated with an overgrowth syndrome, such as Beckwith-Wiedemann syndrome

Poor weight gain suggests a glycogen storage disease or a disorder of gluconeogenesis. Poor weight gain also may be caused by hypopituitarism and adrenocorticotropic hormone (ACTH) deficiency or primary adrenal insufficiency.

Midline defects (eg, a single central incisor, optic nerve hypoplasia, cleft lip or palate, umbilical hernia) and microphallus or undescended testicles in boys may indicate hypopituitarism and/or growth hormone deficiency.

•**Hepatomegaly** is common feature of the glycogen storage disorders.

•**Macroglossia, abdominal wall defects, or hemihypertrophy** may indicate Beckwith-Wiedemann syndrome .

•**Hyperventilation** may be a clue to metabolic acidosis from an inborn error of metabolism or ingestion.

•**Hyperpigmentation** suggests primary adrenal insufficiency

Investigation

●**Blood** – When hypoglycemia is suspected based on symptoms , the condition should be confirmed via venous plasma glucose. Additionally, a sample should be obtained to measure major metabolic fuels and counter-regulatory hormones when the plasma glucose is <50 mg/dL (2.8 mmol/L) because this is the crucial step to establishing a specific etiology.

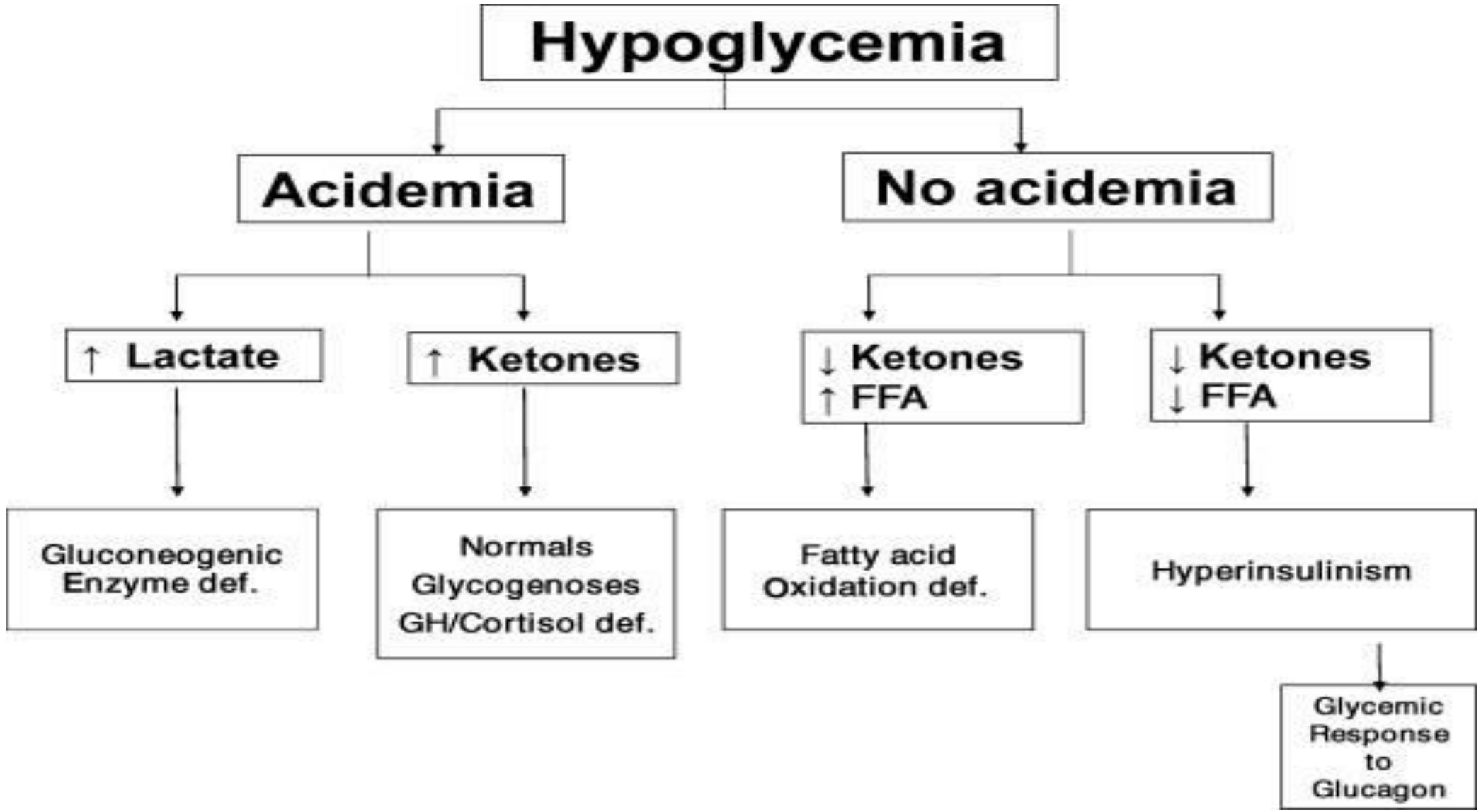
- **ABG, Bicarbonate**
- **Lactate**
- **insulin level, C-peptide**
- **growth hormone, and cortisol levels**
- **FFAs, Beta-hydroxybutarate.**
- **total and free carnitine, acylcarnitines**
- **ammonia**
- **LFT**

Sample	Test	Interpretation
Blood	Glucose	<2.6 mmol/L - hypoglycaemia
	Ketones (Beta hydroxybutyrate)	↓ in: • Fatty acid oxidation defect • Hyperinsulinaemia
	Lactate	↑ in: • Metabolic liver disease • Glycogen storage disorders • Sepsis • Prolonged convulsion
	Free fatty acids	Fatty acid oxidation defect
	Carnitine / acylcarnitine	Fatty acid oxidation defect
	Ammonia	↑ in: • Organic acidaemias • Tyrosinaemia • Liver dysfunction • Hyperinsulinism-Hyperammonaemia Syndrome
	Cortisol	↓ in: • Hypoadrenalism • Hypopituitarism • ACTH deficiency

Insulin & C-peptide	**Any detectable insulin in the presence of a BGL <2.6 mmol/L is inappropriate**
Growth hormone	↓ in: • GH deficiency • Panhypopituitarism
Amino acids	Amino acid disorders
Electrolytes	Adrenal disorders
Liver function tests	Sepsis Liver disease Metabolic defects

- ●**Urine** – The first urine voided during or immediately after the hypoglycemic event should be collected and tested for ketones (if blood ketones cannot be measured) and urine organic acids.
- **Diagnostic fast** — If a critical sample is not obtained during a spontaneous episode of hypoglycemia, a diagnostic fasting test should be performed to determine the cause of the hypoglycemia .
- For safety, the possibility of a fatty acid oxidation disorder should be excluded **prior** to performing the diagnostic fast. Patients with fatty acid oxidation disorders may develop potentially life-threatening complications with prolonged fasting

Urine	Glucose	
	Ketones	↓ in • Fatty acid oxidation defect • Hyperinsulinaemia
	Reducing substances	Galactosaemia Fructosaemia


Hypoglycemia
Acidemia
No acidemia
↑ Lactate
↑ Ketones
↓ Ketones
↑ FFA
↓ Ketones
↓ FFA
Gluconeogenic
Enzyme def.
Normals
Glycogenoses
GH/Cortisol def.
Fatty acid
Oxidation def.
Hyperinsulinism
Glycemic
Response
to
Glucagon

Management

- The aim of treatment is to return BGL to within the normal range (>3.9 mmol/L
- ●**Immediate management** – Patients with confirmed or suspected hypoglycemia should be treated promptly by administering glucose. A sample of blood should be taken for diagnostic testing **before** administering the glucose
- •**Oral therapy** – If the patient is fully conscious and able to drink and swallow safely, a rapidly absorbed carbohydrate (juice, glucose tablets, glucose gel) should be given by mouth. If the hypoglycemia does not improve within 10 to 15 minutes, parenteral glucose must be administered.
- •**Intravenous therapy** – If the child is unconscious , intravenous dextrose should be administered. An initial bolus of 2 mL/kg of dextrose 10% (ie, 0.2 g dextrose/kg body weight) should be given. After the initial bolus, a dextrose infusion should be started to prevent recurrent hypoglycemia
- •Glucagon – In the child with altered mental status and without intravenous access, glucagon can be used to acutely increase the plasma glucose if insulin-mediated hypoglycemia is suspected.

- After episodes of hypoglycaemia, blood glucose should be monitored every 1-2 hours until patient is alert and capable to induce oral intake.

- Treat the underlying cause if identified

- **Transient neonatal hypoglycemia** if patient asymptomatic early feeding will be useful , if he symptomatic he will need glucose infusion
- **Hyperinsulinism** : Diazoxide is effective in some variant ,other will not be effective so we try long acting somastatin analouge if it fail we heads to pncreatectomy

- **Defects in hormones** : replace them

- **Metabolic defect** :
- **fatty acid oxidation defect : ** avoid fasting for long period of time
- **gluconeogenesis** : frequent high-carbohydrate feedings and low protein .
- **glycogenolysis :** frequent high-carbohydrate feedings during the day and continuous feedings at night.
- **Adrenal insufficiency** : glucocorticoid should be administered
- **Idiopathic ketotic hypoglycemia :** avoid fasting , frequent feeding of high protein & carbohydrate