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 Back to: [eMedicine Specialties](#) > [Pediatrics](#) > [Endocrinology](#)

## Hyperinsulinemia

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**Synonyms and related keywords:** hyperinsulinemia, beta -cell hyperplasia, hyperinsulinemic hypoglycemia, nesidioblastosis

### AUTHOR INFORMATION

Section 1 of 11

[Author Information](#) [Introduction](#) [Clinical Differentials](#) [Workup](#) [Treatment](#) [Medication](#) [Follow-up](#) [Miscellaneous](#) [Pictures](#) [Bibliography](#)

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### INTRODUCTION

Section 2 of 11 [Back](#) [Top](#)
[Author Information](#) [Introduction](#) [Clinical Differentials](#) [Workup](#) [Treatment](#) [Medication](#) [Follow-up](#) [Miscellaneous](#) [Pictures](#) [Bibliography](#)

**Background:** Primary hyperinsulinism is a rare but important cause of hypoglycemia in infants and children. It is the most common cause of neonatal hypoglycemia following the first few hours of life.

The clinical presentation varies with the age of the child. Early diagnosis and treatment are essential to prevent seizures and neurologic sequelae. Persistent hypoglycemia and inappropriately high concentrations of insulin are diagnostic findings. The concentrations of free fatty acids and ketones are low.

(ie, beta-hydroxybutyrate, acetoacetate) are low. Several genetic causes of persistent hyperinsulinism recently have been identified.

**Pathophysiology:** The differential diagnosis of hypoglycemia is extensive, and determining the underlying cause often is difficult. An understanding of glucose homeostasis can help narrow the differential diagnosis. In the fasting state, glucose is provided through glycogenolysis in the liver. After a few hours of fasting, insulin levels fall, and increased lipolysis creates free fatty acids and glycerol. Fatty acids do not cross the blood brain barrier and, therefore, are not used by the brain. However, fatty acids are used by the heart and muscle. Increased free fatty acids result in production of ketones, and the brain is able to metabolize ketones as an alternative source of fuel.

Disorders that result from defective glycogenolysis in the liver lead to hypoglycemia within a few hours of fasting. This hypoglycemia occurs in the setting of low insulin levels.

Disorders of fat metabolism result in the unavailability of free fatty acids and ketones as alternative fuels. Hypoglycemia occurs after several hours of fasting. Circulating insulin levels also are low.

Growth hormone deficiency and hypocortisolemia also can cause hypoglycemia associated with low insulin levels, possibly by unopposed insulin action and decreased ketogenesis.

Hypoglycemia associated with elevated insulin levels makes defects in glucose, free fatty acid, and ketone metabolism, growth hormone, and cortisol deficiency unlikely. Conversely, hypoglycemia associated with ketonuria makes hyperinsulinism less likely. Ketonuria does not rule out hyperinsulinemia.

Glucose and several amino acids stimulate insulin secretion under physiologic conditions, and the sequence of events leading to insulin secretion is well delineated. The rate of insulin secretion is dependent on the ATP/ADP ratio in the beta cell. The rate of glucose entry into the beta cell is facilitated by a glucose transporter and exceeds its rate of oxidation.

The first step in glycolysis (ie, conversion of glucose to glucose-6-phosphate by glucokinase) is the rate-limiting step in glucose metabolism; thus, it regulates the rate of glucose oxidation and subsequent insulin secretion. An increase in the intracellular ATP/ADP ratio activates ATP-sensitive potassium dependent channels (KATPs) in the cell membrane. KATP consists of 2 subunits, the sulfonylurea receptor (*SUR-1*) and the potassium inward rectifier (*Kir6.2*). Activation leads to closure of the potassium channel and depolarization of the cell membrane. Opening of a voltage-gated calcium channel allows influx of calcium and results in insulin secretion.

Transient hyperinsulinism usually results from environmental factors such as maternal diabetes or birth asphyxia. However, children with persistent hyperinsulinism may have a genetic defect that results in inappropriate secretion of insulin.

### Frequency:

- **In the US:** Hyperinsulinemia is estimated to occur in 1 out of every 50,000 live births.
- **Internationally:** Autosomal recessive forms of hyperinsulinemic hypoglycemia are more common in inbred populations of Saudi Arabia and among Ashkenazi Jews.

**Mortality/Morbidity:** Glucose is the primary substrate used by the CNS. Free fatty acids do not cross the blood-brain barrier; however, the brain can metabolize ketones. Unrecognized or poorly controlled hypoglycemia may lead to persistent severe neurological damage. Patients with hyperinsulinism are at high risk of developing seizures, mental retardation, and permanent brain damage.

**Age:** Transient hyperinsulinism is relatively common in neonates. An infant of a diabetic mother, an infant who is small or large for gestational age, or any infant who has experienced severe stress may have high insulin concentrations. In contrast, congenital hyperinsulinism is rare.

	<b>CLINICAL</b>	Section 3 of 11 <a href="#">Back</a> <a href="#">Top</a>
<a href="#">Author Information</a> <a href="#">Introduction</a> <a href="#">Clinical Differentials</a> <a href="#">Workup</a> <a href="#">Treatment</a> <a href="#">Medication</a> <a href="#">Follow-up</a> <a href="#">Miscellaneous</a> <a href="#">Pictures</a> <a href="#">Bibliography</a>		

### History:

- Pregnancy and birth history may reveal risk factors that could predispose an infant to hyperinsulinism. Maternal diabetes, poor fetal growth, and birth asphyxia all can lead to excessive insulin release.
- Signs and symptoms associated with hyperinsulinemic hypoglycemia result from 2 physiologic processes. Hypoglycemia triggers autonomic nervous system activation and epinephrine release. Central nervous system hypoglycemia also leads to neurologic manifestations.
  - Infants may present with cyanosis, respiratory distress, apnea, lethargy, sweating, hypothermia, jitteriness, irritability, poor feeding, seizures, tachycardia, and vomiting.
  - Older children may present with sweating, shakiness, anxiety, hunger and increased appetite, staring or strabismus, lethargy, nausea and vomiting, headache, behavior changes, mental status changes, inattention, loss of consciousness, tachycardia, hypothermia, and seizures.

### Physical:

- Macrosomia reflects the anabolic effects of prolonged hyperinsulinemia in utero in infants; they are large for their gestational age and in infants of diabetic mothers.
- Microsomia can occur in infants who are small for their gestational age (particularly those who have experienced maternal toxemia). Infants with microsomia may require high rates of glucose infusion initially to maintain euglycemia.
- Some neonates have physical signs consistent with Beckwith-Wiedemann syndrome. Signs may include fetal overgrowth, omphalocele, macroglossia, visceromegaly, and creases on the ear lobe.

### Causes:

- Classification of hyperinsulinism of infancy is based on the following:
  - Transient

- Infant of the diabetic mother
- Small for gestational age infant
- Perinatal stress/asphyxia
- Erythroblastosis fetalis
- Sepsis
- Beckwith-Wiedemann syndrome
- Drug-induced hyperinsulinism
  1. Surreptitious insulin administration
  2. Oral hypoglycemic ingestion
  3. Blood transfusion
- Umbilical artery catheter placement
- Persistent
  - Adenoma
  - Focal islet cell hyperplasia
  - Generalized beta-cell hyperplasia
- Classification of hyperinsulinism of childhood is based on the following:
  - Adenoma
  - Islet cell hyperplasia
- Transient causes
  - Infants of diabetic mothers: During gestation, glucose is transferred freely across the placenta. Prolonged hyperglycemia in poorly controlled maternal diabetes results in fetal hyperglycemia. Fetal hyperglycemia induces fetal pancreatic beta-cell hyperplasia resultant hyperinsulinemia and macrosomia. Withdrawal of transplacental supply of glucose after birth leads to a precipitous drop in the concentration of glucose. When neonates present with signs and symptoms of hypoglycemia, many require infusion of large quantities of glucose to maintain normal blood glucose levels. Hyperinsulinism typically resolves within 1-2 days following birth. For a full discussion, see [chapter 1 of Diabetic Mother](#).

- Prolonged hyperinsulinism in infants who are small for gestational age (SGA) and asphyxiated newborns: Infants who are SGA, experience maternal toxemia, or have asphyxia are at increased risk for developing hypoglycemia. These infants have high rates of glucose metabolism and may require dextrose infusions as high as 20 mg/kg/min to maintain euglycemia. Some evidence suggests that this may be due to hyperinsulinism, although the exact mechanisms are still unclear. These patients may have prolonged hypoglycemia for as long as 2-4 weeks following birth. Afterwards, the hypoglycemia appears to resolve completely.
- Erythroblastosis fetalis: Neonates with severe Rh isoimmunization have islet cell hyperplasia and hyperinsulinism. The cause of hyperinsulinism is unknown. Research hypothesizes that elevated levels of glutathione from massive hemolysis may serve as a stimulus for insulin release.
- Drug-induced hyperinsulinism
  - Surreptitious insulin administration: This phenomenon is rare but may occur in the setting of Munchausen syndrome by proxy. The timing of hypoglycemia is unpredictable and occurs when the offender has access to the patient. Laboratory evaluation reveals elevated insulin levels and a low serum C-peptide level.
  - Ingestion of oral hypoglycemic agents: Toddlers may accidentally ingest drugs prescribed for adult diabetics (eg, sulfonylureas). Depending on the half-life of the preparation ingested, the duration of hypoglycemia varies. Glucose infusion (to maintain normoglycemia) is the treatment of choice. On rare occasions, diazoxide may be needed to suppress insulin secretion.
  - Blood transfusion: Certain preparations of blood products (eg, citrated blood) contain large amounts of dextrose. During transfusion, the high glucose load triggers insulin secretion. Problems arise when the transfusion is completed. Elevated insulin could lead to a precipitous drop in blood glucose levels. This fall typically occurs about 2 hours posttransfusion.
- Umbilical artery catheter placement: Malposition of the umbilical artery catheter in neonates may be associated with hypoglycemia and hyperinsulinemia. Repositioning of the catheter usually resolves the hypoglycemia and hyperinsulinemia. Theoretically, this problem may be caused by a high glucose load administered to the celiac axis. Localized hyperglycemia may induce insulin secretion and result in hypoglycemia in the systemic circulation.
- Congenital causes
  - Beckwith-Wiedemann syndrome includes signs of omphalocele, macroglossia, and visceromegaly.
  - These infants have generalized islet cell hyperplasia.
  - Hyperinsulinemic hypoglycemia may be difficult to control. These patients require large quantities of glucose. Treatment with diazoxide often is needed to control hyperinsulinemia. Hyperinsulinism usually resolves spontaneously when the infant

several weeks or months.

- Focal causes
  - Islet adenomatosis and beta-cell adenoma: Few cases have been reported of patients with congenital hyperinsulinism who demonstrate histologic finding of islet adenomatosis or beta-cell adenoma. Patients older than 1-2 years who present with hyperinsulinemic hypoglycemia are more likely to have a focal cause of hyperinsulinism. A recent study employing preoperative pancreatic catheterization and intraoperative histologic studies suggests that as many as half of all neonates presenting with congenital hyperinsulinism have focal islet-cell hyperplasia. Focal causes of hyperinsulinism can be treated with partial pancreatectomy.
  - Patients with genetic defects of beta-cell regulation have a condition known as persistent hyperinsulinemic hypoglycemia of infancy (PHHI). Other terms used but have fallen out of favor include leucine sensitive hypoglycemia, islet cell dysmaturity syndrome, and nesidioblastosis.
- At least 6 genetic forms of congenital hyperinsulinism exist.
  - Autosomal recessive
    - Recessive mutations on chromosome 11 lead to alterations in the potassium channel on the plasma membrane of pancreatic beta cells. Two adjacent genes encode *SUR* and *Kir6.2*. Mutations in these genes create a nonfunctional potassium channel with membrane depolarization and unchecked insulin secretion. Mutations of the *SUR* gene are more common than mutations of the *Kir6.2* gene. *SUR* mutations have been found more frequently in less heterogeneous populations in Saudi Arabia and in Ashkenazi Jews.
    - These patients present with high birth weights from the anabolic effects of insulin in utero. These disorders cannot be controlled with diazoxide, which acts to block the *SUR* gene to suppress insulin secretion. Near-total pancreatectomy often is required.
  - Autosomal dominant: Mutations of the glucokinase gene and the glutamate dehydrogenase gene transmitted in an autosomal dominant inheritance can lead to hyperinsulinemia. The molecular defects in other autosomal dominant inherited forms of hyperinsulinism are yet to be elucidated. These infants tend to have less severe hypoglycemia and respond more favorably to diazoxide.
  - Mutation of the glucokinase gene: A mutation of the glucokinase gene has been associated with hyperinsulinism. This mutation increases the affinity of glucokinase for glucose. Accelerated rates of glycolysis result in increased ATP/ADP ratio and insulin secretion. These patients have a milder form of hyperinsulinism compared to those with potassium channel defects. These patients also respond well to diazoxide treatment. In some patients, treatment can be discontinued after several years.
  - Hyperinsulinism and hyperammonemia: Several infants have been reported to have

hyperinsulinism and hyperammonemia. They presented with hypoglycemic seizure few months of age.

- Mutation of the glutamate dehydrogenase gene: Molecular studies have revealed a mutation of the glutamate dehydrogenase (*GDH*) gene. Two metabolic pathways use GDH. Leucine GDH-mediated oxidation in beta cells leads to ATP production and its release. GDH also prevents formation of glutamate in liver cells, which could prevent conversion of ammonium to urea. Excessive activity of GDH increases the rate of its release and impairs the detoxification of ammonia. Patients with a *GDH* gene mutation present with low blood glucose levels and persistent mild elevations of serum ammonia 100-200 mol/L.

<b>DIFFERENTIALS</b>	Section 4 of 11 <a href="#">Back</a> <a href="#">Top</a>
<a href="#">Author Information</a> <a href="#">Introduction</a> <a href="#">Clinical Differentials</a> <a href="#">Workup</a> <a href="#">Treatment</a> <a href="#">Medication</a> <a href="#">Follow-up</a> <a href="#">Miscellaneous</a> <a href="#">Pictures</a> <a href="#">Bibliography</a>	

### [Beckwith-Wiedemann Syndrome](#) [Infant of Diabetic Mother](#)

#### **Other Problems to be Considered:**

Patients with hyperinsulinism usually have elevated levels of insulin for their glucose concentration (ie, even if they do not have hypoglycemia, their insulin level is inappropriately high for their glucose levels). In contrast, patients with the following disorders have an appropriate concentration of insulin for the simultaneous glucose concentration:

- Adrenal insufficiency
- Disorders of branched-chain amino acids
- Enzymatic block in the Cori and alanine cycles
- Fatty acid release/oxidation disorders
- Ketone utilization disorders
- Fructosemia
- Galactosemia
- Glycerokinase deficiency
- Glycogen storage disease type Ia and type Ib (von Gierke disease, glucose-6-phosphatase deficiency)
- Glycogen storage disease type III (Cori disease; amylo-1, 6-glucosidase deficiency)
- Glycogen storage disease type VI (Hers disease, phosphorylase deficiency)

- Growth hormone deficiency

	<b>WORKUP</b>	Se
<a href="#">Author Information</a> <a href="#">Introduction</a> <a href="#">Clinical Differentials</a> <a href="#">Workup</a> <a href="#">Treatment</a> <a href="#">Medication</a> <a href="#">Follow-up</a> <a href="#">Miscellaneous</a> <a href="#">Pictures</a> <a href="#">Bibliography</a>		

### Lab Studies:

- All patients suspected of having hyperinsulinism should have blood drawn for measurement of glucose, insulin, growth hormone, cortisol, free fatty acids, and beta-hydroxybutyrate. It is also important to measure arterial blood gas, lactate, pyruvate, and alanine levels. These studies should be performed during hypoglycemic.
  - Glucose and insulin
    - A plasma insulin level higher than 13  $\mu\text{U}/\text{mL}$  in the face of a serum glucose  $< 40$  mg/dL is diagnostic of hyperinsulinism.
    - Infants with hyperinsulinism require unusually high rates of glucose infusion (glucose levels higher than 40 mg/dL).
    - A glucose-to-insulin ratio of less than 3 and low concentrations of free fatty acids during hypoglycemia are highly suggestive of hyperinsulinism.
  - Low levels of beta-hydroxybutyrate ( $< 1$  mmol/L) in conjunction with low levels of free fatty acids during hypoglycemia may indicate hyperinsulinism.
  - Finding low levels of insulinlike growth factor-binding protein-1 (IGFBP-1) may be useful. IGFBP-1 secretion is normally elevated in the fasting or hypoglycemic child. IGFBP-1 is not secreted in the presence of hyperinsulinism.
  - C-peptide levels should be elevated proportionately with insulin levels. A low C-peptide may indicate surreptitious insulin administration.
  - If ingestion of oral hypoglycemic medications is suspected, a drug screen may be helpful.

### Imaging Studies:

- Imaging studies (eg, pancreatic ultrasonography, CT scan, MRI) generally are not very useful. Angiography and pancreatic venous sampling have successfully been used in selective cases of focal causes of hyperinsulinism. Also, spiral CT scan has been used for the localization of focal lesions in adults.

### Other Tests:

- A glycemic response of more than 30 mg/dL after administration of glucagon indicates a true hyperinsulinemic state and usually is observed in patients with hyperinsulinism.

- *L*-leucine stimulates the secretion of insulin. Leucine sensitive hypoglycemia is no longer diagnostic entity. Determination of insulin concentration in response to leucine administration for hyperinsulinemia. This test has limited diagnostic value and can result in severe hypoglycemia.
- Because pancreatic adenomas are often very small and have the same density as the normal pancreas, studies such as ultrasound, CT scan, and MRI are often of limited value. Pancreatic arteriography has been useful in delineating an adenoma, even in infants and young children. Transhepatic sampling also has been used to elucidate the extent of pancreatic involvement. Open pancreatotomy at the time of surgery may be helpful in locating a pancreatic insulin-secreting adenoma.

### Procedures:

- Perioperative pancreatic catheterization may provide vital information for determining the extent of disease.

**Histologic Findings:** Histologic examination of pancreatic tissue samples (frozen section) also provides information for determining the extent of surgery. Histological examination may reveal focal islet cell hyperplasia (which requires partial pancreatectomy) or diffuse lesions (which indicates the need for near-total pancreatectomy).

<b>TREATMENT</b>	See
<a href="#">Author Information</a> <a href="#">Introduction</a> <a href="#">Clinical Differentials</a> <a href="#">Workup</a> <a href="#">Treatment</a> <a href="#">Medication</a> <a href="#">Follow-up</a> <a href="#">Miscellaneous</a> <a href="#">Pictures</a> <a href="#">Bibliography</a>	

### Medical Care:

- Maintaining normoglycemia is essential to prevent neurologic sequelae. Infants with hyperinsulinism have a higher incidence of neurologic sequelae than infants with hypoglycemia from other causes. Because insulin stimulates ketogenesis, hyperinsulinism results in the paucity of alternate fuel used by the brain.
- The glucose output from the liver is 2-3 mg/kg/min in adults. Infants and children have a glucose output estimated at 5-7 mg/kg/min. Patients with hyperinsulinism may require very high glucose infusion rates (20-30 mg/kg/min) to maintain normoglycemia. Attempts should be made to keep blood glucose levels at 70 mg/dL or higher.
- Neonates and infants should be able to fast for 6 hours without hypoglycemia.
- Medications should be administered to suppress insulin secretion or stimulate glucose release.

### Surgical Care:

- Gastrostomy tube placement may be indicated in extreme cases to administer food if the patient cannot meet the increased glucose requirements.
- Partial or near-total pancreatectomy
  - This procedure is reserved for infants who fail to establish adequate control on medical therapy.
  - Most current practices involve initially removing 95% of the pancreas.
  - Follow-up laboratory studies are conducted to test for normoglycemia. If hypoglycemia recurs, further surgery may be indicated.

therapy should be reattempted. If medical therapy is unsuccessful, near-total pancreatectomy should be performed.

- Partial pancreatectomy is indicated for patients who are found to have focal islet-cell hyperplasia.
- Complications include pancreatic exocrine insufficiency, diabetes mellitus, and injury to the remaining pancreas.

**Consultations:**

- Endocrinology
- Surgery
- Neonatology
- Genetics (if family history present or suspected)

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	<b>MEDICATION</b>	
Se		
<a href="#">Author Information</a> <a href="#">Introduction</a> <a href="#">Clinical Differentials</a> <a href="#">Workup</a> <a href="#">Treatment</a> <a href="#">Medication</a> <a href="#">Follow-up</a> <a href="#">Miscellaneous</a> <a href="#">Pictures</a> <a href="#">Bibliography</a>		

Medical therapy is the treatment of choice. Patients with hyperinsulinism often require multiple doses of insulin to maintain normoglycemia. Patients with severe hyperinsulinism may be refractory to medical therapy and require partial or the entire pancreas. In general, maintenance of normoglycemia should be attempted and surgery should be contemplated. At the same time, because hypoglycemia can result in irreversible brain damage, treatment should not be delayed in patients with severe hypoglycemia.

**Drug Category:** *Insulin secretion inhibiting agents* -- Insulin secretion may be altered by diazoxide which inhibits pancreatic secretion of insulin, stimulates glucose release from the liver, and increases insulin release, which elevates blood glucose levels. Octreotide is a peptide with pharmacologic action on the endocrine system.

which inhibits insulin secretion. KATPs (composed of SUR and Kir6.2) are believed to function nesidioblastosis. These channels initiate depolarization of the beta-cell membrane and opening resultant increase in intracellular calcium triggers insulin secretion. Calcium channel blockers block calcium channels, decreasing insulin secretion. Nifedipine is the only calcium channel blocker treatment of hyperinsulinism in humans.

<b>Drug Name</b>	Diazoxide (Proglycem) -- First-line treatment. Oral diazoxide (Proglycem) opens KATP channels and inhibits insulin secretion. The IV preparation (Hyperstat) is not used in hyperinsulinism.
<b>Adult Dose</b>	3-5 mg/kg/d PO divided q8h; titrate to effect
<b>Pediatric Dose</b>	5-20 mg/kg/d PO divided q8h; titrate to effect
<b>Contraindications</b>	Documented hypersensitivity; diabetes mellitus
<b>Interactions</b>	Diazoxide is highly bound to serum protein and displaces other protein-bound substances such as bilirubin or coumarin, increasing their serum levels; may decrease serum hydantoins, possibly resulting in decreased anticonvulsant effects; thiazide diuretics, may potentiate hyperuricemic effects of diazoxide
<b>Pregnancy</b>	C - Safety for use during pregnancy has not been established.
<b>Precautions</b>	Adverse effects of oral diazoxide include fluid retention, hypertension, hyperglycemia, hyperuricemia, hypertrichosis, facial changes, leukopenia (rare), and thrombocytopenia (rare); caution in patients hypersensitive to other thiazides or sulfonamide derived drugs because cross-reactivity may occur; closely monitor blood glucose levels during use because severe hyperglycemia may occur; half-life may be prolonged in patients with renal impairment; causes sodium and water retention (caution in CHF or poor cardiac reserve)
<b>Drug Name</b>	Octreotide (Sandostatin)- -- Somatostatin analog, activates G-protein K channel. Hyperpolarization of beta cell results in inhibition of calcium influx and insulin release. Octreotide also used for acromegaly, carcinoid tumors, and VIPomas.
<b>Adult Dose</b>	50 mcg SC q12-24h initially; may gradually titrate upward while monitoring blood glucose; alternatively may administer daily dose as a continuous SC infusion
<b>Pediatric Dose</b>	5-40 mcg/kg/d SC divided q4-6h; alternatively, daily dose may be administered as a continuous SC infusion; titrate to effect
<b>Contraindications</b>	Documented hypersensitivity
<b>Interactions</b>	May decrease absorption of orally administered drugs; may decrease blood levels of cyclosporine; patients may require dose adjustments of insulin, beta-blockers, calcium channel blockers, or agents to control fluid and electrolyte balances while on this drug
<b>Pregnancy</b>	B - Usually safe but benefits must outweigh the risks.
	May cause GI toxicity (eg, steatorrhea, diarrhea, vomiting,

<b>Precautions</b>	abdominal distention, biliary sludge); cholelithiasis may occur; hyperglycemia; hypothyroidism; bradycardia, cardiac conduction abnormalities, and arrhythmias have been reported; caution in renal impairment (decrease dose)
<b>Drug Name</b>	Nifedipine (Adalat, Procardia) -- Blocks calcium channels and insulin release. Also used to treat hypertension and angina.
<b>Adult Dose</b>	10 mg PO tid initial; may gradually titrate upward to 80 mg PO tid as determined by blood glucose
<b>Pediatric Dose</b>	0.25-0.7 mg/kg/d PO divided q8h
<b>Contraindications</b>	Documented hypersensitivity
<b>Interactions</b>	Caution with coadministration of any agent that can lower BP, including beta-blockers and opioids; H2 blockers (eg, cimetidine) may increase toxicity; may increase serum levels of digoxin or quinidine; nifedipine levels may be affected by CYP3A4 inhibitors (eg, erythromycin, itraconazole) or inducers (eg, carbamazepine, rifampin)
<b>Pregnancy</b>	C - Safety for use during pregnancy has not been established.
<b>Precautions</b>	May cause lower extremity edema or hypotension; allergic hepatitis has occurred but is rare

**Drug Category:** *Dextrose and glucose release stimulators* -- Emergent blood glucose dextrose. Glucagon enhances release of hepatic glycogen as glucose.

<b>Drug Name</b>	Dextrose (D-glucose) -- IV glucose is used to elevate serum glucose promptly. Oral glucose absorbed from intestine and stored or used by the tissues. Parenterally injected dextrose used in patients unable to sustain adequate oral intake. Direct oral absorption results in a rapid increase in blood glucose concentrations. Dextrose is effective in small doses and no evidence that it may cause toxicity exists. Concentrated dextrose infusions provide higher amounts of glucose in a small volume of fluid.
<b>Adult Dose</b>	10-25 g IV bolus; may follow with continuous IV infusion according to patient requirements
<b>Pediatric Dose</b>	250-500 mg/kg IV (1-2 mL of 25% dextrose per kg); may follow with continuous IV infusion of 10% dextrose according to patient requirements
<b>Contraindications</b>	There are no contraindications to the judicious use of IV glucose in hypoglycemic patients. Oral glucose is contraindicated in patients with glucose-galactose malabsorption.
<b>Interactions</b>	Caution with coadministration with drugs that may increase blood glucose
<b>Pregnancy</b>	C - Safety for use during pregnancy has not been established.
	May cause nausea, which also may occur with hypoglycemia; IV dextrose solutions may result in dilution of serum electrolyte

<b>Precautions</b>	concentrations, or overhydration when there is fluid overload; caution in patients with congestion or pulmonary edema; hypertonic dextrose given peripherally may cause thrombosis (administer through central venous catheter instead); rapid administration associated with increased risk of inducing significant hyperglycemia or hyperosmolar syndrome, especially in patients with chronic uremia; concentrated solutions should not be administered SC or IM; rates of dextrose infusion higher than 0.5 g/kg/h may produce glycosuria; at infusion rates of 0.8 g/kg/h, incidence of glycosuria is 5%; closely monitor fluid balance, electrolyte concentrations and acid-base balance; dextrose administration may produce vitamin B-complex deficiency
<b>Drug Name</b>	Glucagon -- Stimulates hepatic glycogenolysis and gluconeogenesis.
<b>Adult Dose</b>	1 mg (1 unit) IV/IM/SC
<b>Pediatric Dose</b>	2-10 mcg/kg/h IV; alternatively, 0.2 mg/kg IV/IM/SC bolus; not to exceed 1 mg/dose
<b>Contraindications</b>	Documented hypersensitivity; pheochromocytoma
<b>Interactions</b>	Effects of anticoagulants may be enhanced by glucagon (although onset may be delayed); monitor prothrombin activity and for signs of bleeding in patients receiving anticoagulants; adjust dose accordingly
<b>Pregnancy</b>	B - Usually safe but benefits must outweigh the risks.
<b>Precautions</b>	Useful only if liver glycogen stores are adequate; may lead to elevated blood pressure from stimulation of catecholamine release; may result in nausea and vomiting

**Drug Category:** *Drugs inhibiting insulin effect* -- In refractory cases, cortisol and growth hormone with variable rates of success to inhibit insulin effects. Both diminish the hypoglycemic effects and enhance ketogenesis and increase the availability of alternate fuels.

<b>Drug Name</b>	Hydrocortisone (Hydrocortone, Cortef, Solu-Cortef) -- Possesses glucocorticoid activity and weak mineralocorticoid effects. Causes peripheral insulin resistance, gluconeogenesis, and, with prolonged therapy, increased pancreatic release of glucagon (which promotes glycogenolysis).
<b>Adult Dose</b>	25-50 mg/m <sup>2</sup> /d PO divided q8h; alternatively, administer daily dose as a continuous IV infusion
<b>Pediatric Dose</b>	Administer as in adults
<b>Contraindications</b>	Documented hypersensitivity; severe bacterial, viral, fungal, or tubercular infections
<b>Interactions</b>	May increase digitalis toxicity secondary to hypokalemia
<b>Pregnancy</b>	C - Safety for use during pregnancy has not been established.
<b>Precautions</b>	Caution in infections and other severe disorders; may exacerbate hypertension; may cause fluid retention and weight

	gain	
<b>Drug Name</b>	Growth hormone, human (Genotropin, Humatrope, Nutropin) -- Some patients demonstrate reduced glucose requirement and improved glycemic control. Stimulates growth of linear bone, skeletal muscle, and organs. Stimulates erythropoietin which increases red blood cell mass.	
<b>Pediatric Dose</b>	0.05-0.06 mg/kg/d SC	
<b>Contraindications</b>	Documented hypersensitivity; actively growing intracranial tumor	
<b>Interactions</b>	Glucocorticoids may decrease growth promoting effects	
<b>Pregnancy</b>	C - Safety for use during pregnancy has not been established.	
<b>Precautions</b>	Reconstitute with sterile water for injection if administering to newborns	
<b>FOLLOW-UP</b>		Se
<a href="#">Author Information</a> <a href="#">Introduction</a> <a href="#">Clinical Differentials</a> <a href="#">Workup</a> <a href="#">Treatment</a> <a href="#">Medication</a> <a href="#">Follow-up</a> <a href="#">Miscellaneous</a> <a href="#">Pictures</a> <a href="#">Bibliography</a>		

### Further Inpatient Care:

- Admit patients for stabilization of blood glucose, further testing, and medical or surgical c

### Further Outpatient Care:

- Monitor medication dosages and side effects carefully, with frequent glucose determinati
- Monitor for symptoms and signs of hypoglycemia.

### In/Out Patient Meds:

- Medications include diazoxide, octreotide, nifedipine, glucagon, growth hormone, and glu medications varies with etiology and severity of hypoglycemia.

### Transfer:

- Transfer to a tertiary care facility is required to provide prompt diagnosis and medical tre: intervention.

### Deterrence/Prevention:

- Avoid prolonged fasting.
- Have source of glucose and glucagon emergency kit readily available if hypoglycemic sy

### Complications:

- Seizures

- Permanent brain damage
- Death

### Prognosis:

- Multiple factors affect prognosis, such as the severity of the disease at presentation, duration, etiology of hyperinsulinism, and presence of neurologic complications.
- Improving diagnostic techniques make earlier and more appropriate surgical intervention (near-total pancreatectomy) possible.
- Patients who have had near-total pancreatectomy are at risk for developing exocrine pancreatic diabetes mellitus. Diabetes mellitus is caused by the loss of islet cells surgically removed and remaining beta cells.

### Patient Education:

- Counsel the patient, family members, and school personnel how to recognize the symptoms and how to administer glucose in the event of a hypoglycemic episode.
- Families should be equipped with glucagon and instructed in its use in case hypoglycemia occurs.

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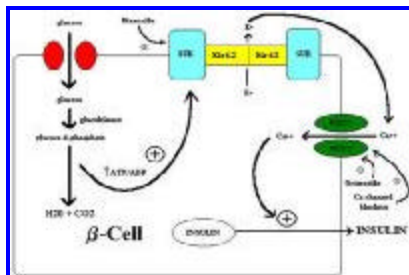
### Medical/Legal Pitfalls:

- Failure to recognize and treat hypoglycemia
- Failure to recognize the cause of hypoglycemia
- Failure to counsel family to recognize signs and symptoms of hypoglycemia and how/when to administer glucagon
- Failure to recognize associated conditions, such as cardiomyopathy in infants of diabetic mothers or problems with asphyxia

### Special Concerns:

- Some children with a known history of hypoglycemia may not be symptomatic. A high index of suspicion is required for early detection and therapy.

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**Caption:** Picture 1. Schematic representation of mechanism of insulin secretion.
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[eMedicine Zoom View \(Interactive!\)](#)
**Picture Type:** Graph

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- Craver RD, Hill CB: Cure of hypoglycemic hyperinsulinism by enucleation of a focal islet hyperplasia. J Pediatr Surg 1997 Oct; 32(10): 1526-7[[Medline](#)].
- de Lonlay-Debeney P, Poggi-Travert F, Fournet JC, et al: Clinical features of 52 neonate Engl J Med 1999 Apr 15; 340(15): 1169-75[[Medline](#)].
- Dunne MJ, Kane C, Shepherd RM, et al: Familial persistent hyperinsulinemic hypoglycemia in the sulfonylurea receptor. N Engl J Med 1997 Mar 6; 336(10): 703-6[[Medline](#)].
- Glaser B, Kesavan P, Heyman M, et al: Familial hyperinsulinism caused by an activating Engl J Med 1998 Jan 22; 338(4): 226-30[[Medline](#)].
- Lovvorn HN III, Nance ML, Ferry RJ Jr, et al: Congenital hyperinsulinism and the surgeon years. J Pediatr Surg 1999 May; 34(5): 786-92; discussion 792-3[[Medline](#)].
- Lteif AN, Schwenk WF: Hypoglycemia in infants and children. Endocrinol Metab Clin Nor 46, vii[[Medline](#)].
- Schwitzgebel VM, Gitelman SE: Neonatal hyperinsulinism. Clin Perinatol 1998 Dec; 25(4)
- Stanley CA, Lieu YK, Hsu BY, et al: Hyperinsulinism and hyperammonemia in infants with glutamate dehydrogenase gene. N Engl J Med 1998 May 7; 338(19): 1352-7[[Medline](#)].
- Stanley CA, Baker L: The causes of neonatal hypoglycemia. N Engl J Med 1999 Apr 15;
- Stanley CA: Hyperinsulinism in infants and children. Pediatr Clin North Am 1997 Apr; 44
- Thomas PM: Genetic mutations as a cause of hyperinsulinemic hypoglycemia in children North Am 1999 Sep; 28(3): 647-56, viii[[Medline](#)].
- Thomas PM, Cote GJ, Wohlk N, et al: Mutations in the sulfonylurea receptor gene in familial hyperinsulinemic hypoglycemia of infancy. Science 1995 Apr 21; 268(5209): 426-9[[Medl](#)

**NOTE:**

Medicine is a constantly changing science and not all therapies are clearly established. New research changes drug and treatment therapies daily. The journal have used their best efforts to provide information that is up-to-date and accurate and is generally accepted within medical standards at the time of publication. However, because science is constantly changing and **human error is always possible**, the authors, editors, and publisher or any other party involved with the publication of this information in this article is accurate or complete, nor are they responsible for omissions or errors in the article or for the results of using this information in this article from other sources prior to use. In particular, all drug doses, indications, and contraindications should be confirmed in the product literature.

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