Hypoglycemia

Hypoglycemia is diagnosed when blood glucose levels fall to abnormally low levels. Under normal conditions, the body maintains a very narrow range of blood glucose levels despite wide variations in food intake and energy expenditure (Braunwald DE et al 2001).

This careful balance is partly regulated by two hormones, insulin and glucagon, which have opposite effects. Both are produced in the pancreas in small clusters of cells called the islets of Langerhans. High blood levels of glucose stimulate the secretion of insulin, which results in the cellular uptake of glucose and lowering of blood glucose.

Low blood levels of glucose stimulate the secretion of glucagon from the liver. Glucagon stimulates a rise in blood glucose through two processes. First, glycogen (the animal version of starch) in the liver is metabolized into glucose. The normal liver stores only a relatively small amount of glucose as glycogen, so the glycogen store can be depleted fairly rapidly. Most people's glycogen stores are virtually gone within 24 hours of no caloric intake. When glycogen levels are low, or when energy needs are high, fatty acids and amino acids are converted into glucose in the liver and kidneys through the process of gluconeogenesis. The adrenal glands also play a role in increasing blood glucose. The hormone epinephrine stimulates glycogen breakdown, and cortisol promotes gluconeogenesis.

Hypoglycemia is a result of any disorder that causes abnormal restrictions in the production of glucose by the liver or kidneys or that causes abnormal increases in glucose uptake by the cells (Barzilai N 1999). Hypoglycemia can be divided broadly into three categories: reactive, drug induced, and fasting.

Reactive hypoglycemia occurs within four hours after eating if glucose levels rise too rapidly after a meal because of underlying conditions, such as the increased absorption of glucose from the small intestine. In response, the body overexcretes insulin, which drives the glucose from the blood, and hypoglycemia results. It may be caused by the following factors (Kasper DL et al 2005):

- Increased sensitivity to counterregulating hormones such as epinephrine
- Deficiency in glucagon release
- Polycystic ovary syndrome
- Rare enzyme deficiencies, such as hereditary fructose intolerance and galactosemia

Drugs used in the treatment of diabetes (e.g., insulin and sulfonylurea) are the most common cause of drug-induced hypoglycemia. These drugs are used to lower blood glucose levels. When these drugs are used in excess, blood glucose levels drop rapidly and markedly, leading to hypoglycemia (Kasper DL et al 2005). Alcohol-induced hypoglycemia can result from alcohol ingestion after fasting long enough to exhaust glycogen stores, making liver glucose output dependent on gluconeogenesis. Hypoglycemia can be induced by blood alcohol levels well below the legal driving limits (Barzilai N 1999).

Fasting hypoglycemia occurs after strenuous exercise or during an extended period between meals. It is relatively uncommon among healthy people but can occur in people who drink heavily or have liver disease or in children who have genetic enzyme abnormalities that cause problems with the way the body metabolizes sugar (Kasper DL et al 2005).

Hypoglycemia may also be caused by other factors (Kasper DL et al 2005):

- Certain types of tumors secrete insulin-like growth factor, which acts in a manner similar to insulin.
- Autoimmune disorders may cause abnormal insulin secretion.
- Addison's disease, which affects the pituitary and adrenal glands, and chronic illnesses such as hepatic, renal, or cardiac failure or sepsis, which cause inadequate glucose to be delivered to the body's cells, may also cause hypoglycemia.

DIAGNOSIS OF HYPOGLYCEMIA

The symptoms of hypoglycemia can be divided into two categories (Kasper DL et al 2005):

- Neurogenic symptoms, which include sweating, shakiness, tachycardia, and anxiety due to the secretion of adrenal hormones (mainly epinephrine). These are the earliest signs of hypoglycemia.
- Neuroglycopenic symptoms; these include weakness, tiredness, or dizziness; difficulty with concentration; confusion; blurred vision; fatigue; seizure; loss of consciousness; and in extreme cases, coma and death.

If hypoglycemia is suspected, the diagnosis will be made by measuring glucose levels in the blood. If glucose levels are too low (usually below 60 mg/dL), the person is hypoglycemic. To test for reactive hypoglycemia, blood glucose should be measured while symptoms are present. A blood glucose level below 70 mg/dL at the time of symptoms, followed by relief after eating, will confirm the diagnosis.

In standard tests for measuring blood glucose in the context of hypoglycemia, the patient undergoes a supervised fast lasting 48 to 72 hours. Patients are usually hospitalized for this test to ensure their safety. During that time, measurements of blood glucose, insulin, glucagon, cortisol, and other components of the glucose control system are measured. The pattern of results can help physicians diagnose the underlying cause of hypoglycemia. For example, persistently high insulin levels might suggest an insulin-secreting pancreatic tumor, while low glucose with low insulin levels and normal levels of ketones (markers of fatty acid breakdown) might suggest a disorder in lipid metabolism. Many other patterns may occur during such a fast, and each provides another clue to help the physician determine the cause of an individual's hypoglycemia.

CONVENTIONAL TREATMENT

The treatment of hypoglycemia depends on the underlying cause; no single drug is used. The goal is to uncover the underlying cause and treat it, if possible.

In the case of reactive hypoglycemia, treatment usually focuses on dietary changes. For instance, people who suffer from hypoglycemic episodes after eating should eat small meals and snacks about every three hours, exercise regularly, eat a wide variety of foods, limit sugar, and eat plenty of high-fiber foods. These changes will help keep blood glucose levels stable throughout the day.

A few of the medications that might be used to treat hypoglycemia include the following:

Diazoxide . The usual treatment of hypoglycemia caused by overdose of insulin or sulfonylurea drugs is the oral consumption of glucose or sucrose. However, several studies (Johnson SF et al 1977; Pfeifer MA et al 1978) have shown that diazoxide together with glucose is more effective in correcting hypoglycemia than glucose alone and also reduces the amount of glucose needed. Diazoxide acts by inhibiting release of insulin, making this medication useful in the treatment of conditions such as insulin-secreting tumors, in which too much insulin from internal sources is present.

Glucagon. Since glucagon acts in a contrary fashion to insulin, it is used to treat severe hypoglycemic reactions due to insulin, particularly when oral consumption of glucose or sucrose is not possible. Glucagon treatment is not effective in patients who have been fasting or have been hypoglycemic for a prolonged period; glucagon can act only by releasing glucose from glycogen stores, and if these are depleted by prolonged fasting, there is nothing to release (Winegrad A 1992).

NUTRIENT AND SUPPLEMENTAL THERAPY

Acute hypoglycemia therapy focuses on immediately raising the blood sugar level. Any substance containing carbohydrates, such as saltine crackers, fruit juice, or hard candy, if taken at the beginning of a hypoglycemic episode, will help raise blood sugar quickly and ease the severity of an attack. A severe hypoglycemic attack is therefore a good time to consume rapidly absorbed simple sugars. Fruit juice, glucose syrup, or sugary soft drinks can be lifesaving. Milder attacks can be managed with foods that contain complex carbohydrates, which are less rapidly absorbed. However, these should not be used by a person having a severe attack (i.e., a diabetic with an insulin reaction).

The following nutrients have been shown to help normalize blood glucose levels:

Chromium. Chromium is widely recognized as an essential trace element. It has multiple effects on insulin levels. Chromium has been widely studied in the context of type 2 diabetes for its ability to lower blood sugar levels at higher doses by increasing insulin sensitivity (Racek J 2003). However, studies have also shown that chromium can help enhance glucagon secretion (McCarty MF 1996).

Amino acids. Glutamine is the most abundant amino acid in the human body and is involved in more metabolic processes than any other amino acid (Stumvoll M et al 1999). Few clinical trials have been conducted to determine if glutamine supplementation can increase glucose levels. Amino acid infusions, however, are known to raise glucagon levels, which in otherwise healthy individuals produces an increase in glucose (Nair KS et al 1990). Hypoglycemia was induced by insulin infusions in diabetic and nondiabetic subjects in two studies. The participants then received amino acid mixtures. The results indicated a sharp rise in glucagon secretion in normal participants and a modest rise in diabetic participants (Caprio C et al 1993).

A study in an animal model demonstrated that the liver's ability to produce glucose from certain amino acids was increased during hypoglycemia induced by insulin. Glucose levels increased in animals given the amino acid infusion but not in control animals given

only a saline infusion (de Souza HM et al 2001).

N-acetylcysteine. N-acetylcysteine (NAC) is a protein amino acid that has antioxidant properties. It has been shown to alleviate hypoglycemia in rodents exposed to toxic chemicals by preventing the rapid loss of glucose. For example, in one study of rats exposed to a toxin that causes hypoglycemia, administration of 200 mg/kg NAC prevented depletion of glucose (Sprague CL et al 2005). In another study of rats exposed to arsenic, which is known to cause hypoglycemia, administration of 163.2 mg/kg of NAC daily prevented hypoglycemia (Pal S et al 2004).

LIFESTYLE CHANGES FOR HYPOGLYCEMICS

A well-balanced diet will help normalize blood sugar levels. Usually a regimen moderate in protein, unrefined carbohydrates (such as whole-grain products and vegetables, which are slow to be absorbed), and fats is recommended. Foods high in rapidly absorbed sugars should be avoided. This diet can help prevent reactive hypoglycemia due to a sudden influx of glucose into the blood.

The use of a fiber supplement before meals also helps control the rate of absorption of dietary carbohydrates. Alcohol, caffeine, tobacco, and other stimulants should be avoided because they are capable of precipitating a hypoglycemic attack. Small meals taken often during the day are recommended to control the amount of carbohydrates entering the system and to prevent rapid declines in blood glucose levels.

LIFE EXTENSION FOUNDATION RECOMMENDATIONS

If you are diabetic and using medications, talk to your physician immediately if you are experiencing hypoglycemic symptoms. You may need your medication adjusted.

The following supplements are suggested for assistance in maintaining normal blood glucose levels:

- **Chromium** —200–400 micrograms (mcg) chromium polynicotinate daily
- **L-glutamine powder** —3 to 5 grams daily between meals
- **NAC** —500 milligrams (mg) daily

HYPERGLYCEMIA SAFETY CAVEATS

An aggressive program of dietary supplementation should not be launched without the supervision of a qualified physician. Several of the nutrients suggested in this protocol may have adverse effects. These include:

Chromium

- Consult your doctor before taking chromium if you have hyperglycemia or type 2 diabetes. See your doctor and monitor your blood glucose level frequently if you take chromium and have hyperglycemia or type 2 diabetes.

L-Glutamine

- Consult your doctor before taking L-glutamine if you have kidney failure or liver failure.
- L-glutamine can cause gastrointestinal symptoms such as nausea and diarrhea.

NAC

- NAC clearance is reduced in people who have chronic liver disease.
- Do not take NAC if you have a history of kidney stones (particularly cystine stones).
- NAC can produce a false-positive result in the nitroprusside test for ketone bodies used to detect diabetes.
- Consult your doctor before taking NAC if you have a history of peptic ulcer disease. Mucolytic agents may disrupt the gastric mucosal barrier.
- NAC can cause headache (especially when used along with nitrates) and gastrointestinal symptoms such as nausea and diarrhea.

For more information see the Safety Appendix