


TABLE 66-8 SIGNS AND SYMPTOMS OF HYPOGLYCEMIA

AUTONOMIC		
Sweating	Palpitations	Hunger
Pallor	Tachycardia	Nausea
Anxiety	Hypertension	Vomiting
Tremor	Irritability	Paresthesias
NEUROGLYCOPENIC		
Difficulty thinking	Dizziness	Seizures
Fatigue, weakness	Visual blurring	Loss of consciousness
Somnolence	Confusion	Coma
Headache	Abnormal behavior	Death

Pathology

Hypoglycemic disorders can result when there is overproduction of hormones that lower glucose concentrations, underproduction of hormones that serve to elevate glucose levels, deficiency of substrates for endogenous glucose synthesis, or changes in cells and tissues that result in their increased consumption of glucose.

Etiologic Classification

Causes of hypoglycemia by etiologic categories are listed in [Table 66-9](#).

Drug-Induced

The most common causes of hypoglycemia are excess insulin or insulin secretagogues (especially sulfonylureas) administered in the treatment of diabetes. Ethanol is another commonly used drug that can cause hypoglycemia. This most often occurs in the context of chronic alcoholism in an individual who is nutritionally depleted, often after binge drinking for several days or longer. Under these circumstances, hepatic glycogen stores become depleted, and the process of alcohol metabolism blocks gluconeogenesis by depriving the liver of nicotinamide adenine dinucleotide (NAD⁺). Commonly used pharmacologic agents that have been associated with hypoglycemia include β -blockers (especially nonselective β_2 -adrenergic antagonists), ACE inhibitors, pentamidine (through toxic effects on beta cells), quinine, and quinolones.

Excess Endogenous Insulin or Insulin-like Hormones

Alimentary hypoglycemia is a disorder in which low blood glucose levels occur typically 90 to 180 minutes after meals in patients who have undergone gastric outlet surgery with resulting accelerated gastric emptying. This is distinct from the more common *dumping syndrome*, which results from rapid entry of an osmotic load into the small intestine and associated fluid shifts and autonomic responses and is not associated with hypoglycemia. “Reactive hypoglycemia” is a now outmoded term that previously was applied to adrenergic symptoms occurring 2 to 4 hours after a meal in patients who are not hypoglycemic; these individuals may experience decreased symptoms with frequent feedings and avoidance of high-carbohydrate meals.

Tumors of islet beta cells (*insulinomas*) can cause hypoglycemia by producing excess insulin in an unregulated manner. They are uncommon (1 in 250,000 patient-years), but it is important

TABLE 66-9 ETIOLOGIC CLASSIFICATION OF HYPOGLYCEMIC DISORDERS MANIFESTING IN ADULTS

DRUG-INDUCED
Antidiabetic agents (insulin, sulfonylureas, meglitinides)
Alcohol
Other pharmacologic agents (β -blockers, ACE inhibitors, pentamidine, quinine, quinolones and many others)
ALTERED GASTROINTESTINAL FUNCTION
Alimentary hypoglycemia
BETA-CELL INSULIN OVERSECRETION
Insulinoma
Non-insulinoma pancreatogenous hypoglycemia (without or with bariatric surgery)
NON-ISLET CELL NEOPLASMS
Tumor insulin-like growth factor-II secretion
Tumor glucose consumption
AUTOIMMUNE
Circulating insulin antibodies
Insulin receptor activating antibodies
ENDOCRINE DEFICIENCIES
Glucocorticoids (adrenal insufficiency), growth hormone, catecholamines, glucagon
SEVERE ILLNESS
Sepsis
Hepatic failure
Renal failure
MALNUTRITION
Anorexia nervosa

ACE, Angiotensin-converting enzyme.

to recognize them when they do occur. Insulinomas usually are small (1 to 2 cm), benign (>90%), solitary (>90%), and confined to the endocrine pancreas (99%). Some patients have an indolent course extending over many years before diagnosis, but insulinomas can produce profound hypoglycemia. There is a tendency for adrenergic symptoms to become suppressed as a consequence of repeated exposures to hypoglycemia, and neuroglycopenic symptoms may predominate, including sometimes bizarre behavioral abnormalities. Patients may eat frequently in response to the hypoglycemia and exhibit moderate weight gain.

Non-insulinoma pancreatogenous hypoglycemia is a disorder that may manifest with symptoms similar to those of insulinomas, but the pathology involves beta-cell hypertrophy and hyperplasia rather than the presence of a discrete tumor. More recently, the development of hypoglycemia with similar beta-cell hyperplasia has been described in a small number of patients, more often in females, months to years after Roux-en-Y gastric bypass surgery.

Non-islet cell neoplasms are a rare cause of hypoglycemia; they produce an insulin-like growth factor (IGF), usually a partially processed form of IGF-II designated *big IGF-II*, that can have insulin-like effects. The tumors typically are large and malignant and are most often located in the retroperitoneal space, abdomen, or thoracic cavity. Tumor types include hemangiopericytomas, hepatocellular carcinomas, lymphomas, adrenocortical carcinomas, gastrointestinal carcinoids, and mesenchymal tumors. Some large tumors cause hypoglycemia in the absence of detectable insulin-like factors.