

## A Review and Management of Hypoglycemia

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### Abstract

Hypoglycemia is often defined by a plasma glucose concentration below 70 mg/dL; however, signs and symptoms may not occur until plasma glucose concentrations drop below 55 mg/dL. The symptoms of Whipple's triad have been used to describe hypoglycemia since 1938. For the Whipple triad, the practitioner must first recognize hypoglycemia symptoms, obtain low blood glucose, and finally, demonstrate immediate relief of symptoms by the correction of the low blood glucose after treatment.

**Keywords:** Gluconeogenesis; glycogenolysis; hepatocytes; pharmacologic intervention; hypoglycemia

### Introduction

Hypoglycemia is defined as a condition where plasma glucose concentration is low, which may expose patients to possible harm. This is common amongst persons who have type 1 diabetes, with an annual incidence of severe hypoglycemia ranging from 3.3% to 13.5%. While patients treated with insulin or insulin secretagogues (sulfonylureas and meglitinides) are generally at higher risk, severe hypoglycemia is less common in patients with type 2 diabetes.

Glucose-lowering medications that do not cause unregulated insulin secretion, such as dipeptidyl peptidase-4 inhibitors, metformin, glucagon-like peptide-1 receptor agonists, thiazolidinediones, and sodium-glucose cotransporter-2 inhibitors are associated with lower risk of hypoglycemia, unless used in combination with insulin or insulin secretagogues.

In patients with diabetes, it is not easy to determine a specific plasma glucose concentration that is diagnostic of hypoglycemia, because the threshold for the appearance of hypoglycemia symptoms varies among patients. This threshold drops due to recurrent episodes of hypoglycemia and rises in individuals with uncontrolled diabetes.

The current classification of hypoglycemic episodes in diabetes includes three levels corresponding to the severity of hypoglycemia.

**Level 1 hypoglycemia:** defined as plasma glucose concentration < 70 mg/dL but > 54 mg/dL. Plasma glucose of 70 mg/dL constitutes the threshold concentration below which neuroendocrine responses to hypoglycemia usually appear in individuals without diabetes. Many patients with diabetes suffer from impaired defense mechanisms against hypoglycemia and/or lack of hypoglycemia awareness; therefore, plasma glucose concentrations < 70 mg/dL are defined as clinically significant in diabetes and require intervention irrespective of symptom severity.

**Level 2 hypoglycemia:** defined as plasma glucose concentration below 54 mg/dL requiring immediate intervention to correct the hypoglycemia.

**Level 3 hypoglycemia:** defined as a serious event characterized by a change in the mental status or impairment in the patient's physical ability to

function that requires intervention by another person to correct the glucose concentration.

### Symptoms of hypoglycemia

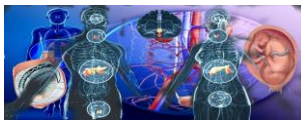
Symptoms of hypoglycemia include autonomic symptoms and neuroglycopenic symptoms. These vary among patients according to age and diabetes duration. For example, children may demonstrate emotional and behavioral changes secondary to hypoglycemia in addition to classic autonomic and neuroglycopenic symptoms.

### Pathophysiology

The body has inherent counter-regulatory mechanisms to prevent hypoglycemic episodes. All of these counter-regulatory mechanisms include an interplay of hormones and neural signals to regulate the release of endogenous insulin, to increase hepatic glucose output, and to alter peripheral glucose utilization. Among the counter-regulatory mechanisms, the regulation of insulin production plays a major role. Decrease in insulin production as a response to low serum glucose isn't the body's first line of defense against hypoglycemia. For endogenous glucose production to take place, particularly hepatic glycogenolysis, low insulin levels are necessary. As plasma glucose levels decline, beta-cell secretion of insulin also decreases, leading to increased hepatic/renal gluconeogenesis and hepatic glycogenolysis.

### Treatment

Identification of a hypoglycemic patient is critical due to potential adverse effects, including coma and/or death. Severe hypoglycemia can be treated with intravenous (IV) dextrose followed by infusion of glucose. For conscious patients able to take oral (PO) medications, readily absorbable carbohydrate sources (such as fruit juice) should be given. For patients unable to take oral agents, glucagon should be administered. Glucagon can be given intramuscularly, or intranasally with the newest available formulations.



### Conclusion

Hypoglycemia in diabetes is associated with increased morbidity and constitutes a barrier to glycemic control. Much effort must be invested in hypoglycemia prevention, including patient education, appropriate dietary and exercise regimens, adjustment of the treatment regimen, and implementation of glucose monitoring systems as appropriate.

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