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SYMPOSIUM

The Physiology of Glucagon

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Abstract

This short review outlines the physiology of glucagon *in vivo*, with an emphasis on its neural control, the author's area of interest. Glucagon is secreted from alpha cells, which are a minority of the pancreatic islet. Anatomically, they are down stream from the majority islet beta cells. Beta-cell secretory products restrain glucagon secretion. Activation of the autonomic nerves, which innervate the islet, increases glucagon secretion.

Glucagon is secreted into the portal vein and thus has its major physiologic action at the liver to break down glycogen. Glucagon thereby maintains hepatic glucose production during fasting and increases hepatic glucose production during stress, including the clinically important stress of hypoglycemia. Three different mechanisms proposed to stimulate glucagon secreted during hypoglycemia are discussed: (1) a stimulatory effect of low glucose directly on the alpha cell, (2) withdrawal of an inhibitory effect of adjacent beta cells, and (3) a stimulatory effect of autonomic activation.

In type 1 diabetes (T1DM), increased glucagon secretion contributes to the elevated ketones and acidosis present in diabetic ketoacidosis (DKA). It also contributes to the hyperglycemia seen with or without DKA. The glucagon response to insulin-induced hypoglycemia is impaired soon after the development of T1DM. The mediators of this impairment include loss of beta cells and loss of sympathetic nerves from the autoimmune diabetic islet.

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Abbreviations: (ACh) acetylcholine, (DKA) diabetic ketoacidosis, (GABA) gamma aminobutyric acid, (GLP) glucagon-like peptide, (IIH) insulin-induced hypoglycemia, (VMH) ventromedial hypothalamus, (T1DM) type 1 diabetes mellitus

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