

Endocrinology, Diabetes & Metabolism Grand Rounds



**DATE: 4/13/2021 TIME: 8:00-9:00 AM
ZOOM**

SPEAKER: Filip K Knop, MD PhD

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TOPIC: “My Gut Feeling About Glucagon.”

Abstract

Hyperglucagonemia (in the fasting as well as in the postprandial state) is considered a core pathophysiological component of diabetes and is found to contribute substantially to the hyperglycemic state of diabetes. Hyperglucagonemia is usually viewed upon as a consequence of pancreatic alpha cell insensitivity to the glucagon-suppressive effects of glucose and insulin. Since we observed that the well-known hyperglucagonemic response to oral glucose in patients with type 2 diabetes is exchanged by normal suppression of plasma glucagon levels following isoglycemic intravenous glucose administration in these patients, we have been focusing on the gut and gut-derived factors as potential mediators of diabetic hyperglucagonemia. In a series of clinical experiments, we have elucidated the role of gut-derived factors in diabetic hyperglucagonemia and shown that glucose-dependent insulinotropic polypeptide promotes hyperglucagonemia and that glucagon, hitherto considered a pancreas-specific hormone, may also be secreted from extrapancreatic tissues – most likely from proglucagon-producing enteroendocrine cells. Furthermore, our observation that fasting hyperglucagonemia is unrelated to the diabetic state, but strongly correlates with obesity, liver fat content and circulating amino acids, has made us question the common ‘pancreacentric’ and ‘gluco-centric’ understanding of hyperglucagonemia and led to the hypothesize that steatosis-induced hepatic glucagon resistance (and reduced amino acid turnover) and compensatory glucagon secretion mediated by increased circulating amino acids constitute a complete endocrine feedback system: the liver–alpha cell axis. In this lecture, the physiological regulation of glucagon secretion in humans will be summarized and new findings suggesting that the liver and the gut play key roles in determining fasting and postabsorptive circulating glucagon levels will be disseminated.

Zoom Link

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