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PANCREAS

Extrapancreatic glucagon in humans

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New research shows that the pancreas is not the only source of glucagon in humans — patients who had undergone complete pancreatectomy had measurable circulating glucagon levels, and extrapancreatic glucagon contributed to hyperglycaemia after an oral glucose dose.

Glucagon has traditionally been considered a pancreas-specific hormone, secreted by pancreatic islet α cells. Patients with type 2 diabetes mellitus (T2DM) often have hyperglucagonaemia. "The mechanisms behind this hyperglucagonaemia are unclear," explains corresponding author Filip Knop. "We have previously observed that patients with T2DM only exhibit inappropriate glucagon responses to orally administered glucose, while intravenously administered glucose suppresses plasma glucagon."

In the new study, the investigators measured glucagon responses to an oral glucose tolerance test (OGTT) and isoglycaemic intravenous glucose infusion (IIGI) in patients who had undergone total pancreatectomy but did not have T2DM ($n = 10$) and matched healthy controls ($n = 10$). Mean baseline circulating glucagon concentrations were 5.4 pmol/l in patients with no pancreata, compared with 8.3 pmol/l in healthy controls, a difference that was not statistically significant. Patients who had undergone total pancreatectomy showed hyperglucagonaemia during the OGTT, a response not seen in the same patients during IIGI. Endogenous glucose production, stimulated by glucagon, was higher during OGTT than during IIGI in patients without pancreata.

"Our results suggest that the hyperglucagonaemic response to oral glucose in totally pancreatectomized patients is involved in the pathogenesis of postabsorptive hyperglycaemia" concludes first author Asger Lund. The researchers hope to identify the source of extrapancreatic glucagon in future studies, and believe preproglucagon-expressing enteroendocrine L cells are leading candidates.

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ORIGINAL ARTICLE Asger, L. *et al.* Evidence of extrapancreatic glucagon secretion in man. *Diabetes* http://dx.doi.org/10.2337/db15-1541