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Letter to the Editor

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In comparison to i.v. glucose loading oral, glucose causes a more rapid fall in blood sugar from maximum value[16]. This finding is supported by insulin determinations carried out in dogs and humans. In spite of identical maximum values for blood sugar, the significantly higher blood insulin levels were evoked by oral glucose loading as compared with i.v. administration[1, 9]. These findings raised the question of the participation of hepatic and intestinal factors in the mechanism of insulin secretion. Injection of secretin during parenteral administration of glucose accelerates the fall of blood glucose to such an extent that half-life values are reduced by 50%[5]. We therefore tried to prove a possibly direct acting, glucose-independent, stimulation of insulin secretion by secretin, utilizing isolated pancreatic tissue.

Pancreatic tissues from dogs and rabbits with a maximal thickness of 1 mm and a weight of 150 to 200 mg were used. After a pre-incubation period of 30 min in Krebs-Ringer bicarbonate buffer the tissue segments were incubated for 2½ hrs. in 4 ml of Krebs-Ringer bicarbonate buffer, saturated with oxygen, containing 0.16 M of fumarate, lactate and pyruvate.

Secretin (Vitrum, Stockholm) containing no intrinsic insulin activity or immuno-insulin was used in concentrations of 0.01 and 0.1 U/ml. Determinations of insulin-like activity (ILA) and of immunologically measurable insulin (IMI) were carried out according to the standard methods of our laboratory[4, 11] based on the original procedures of MARTIN et al.[8] and YALOW et al.[17].

Table. *Secretion of insulin in vitro from pieces of dog and rabbit pancreatic tissue following incubation in Krebs-Ringer bicarbonate buffer, buffer and 200 mg% glucose, buffer and 0.01 U secretin/ml and 0.1 U secretin/ml*

		Controls		Glucose 200 mg %		0.01 U/ml Secretin		0.1 U/ml Secretin	
		ILA	IMI	ILA	IMI	ILA	IMI	ILA	IMI
RABBIT	X	260	105	1120	645	1080	295	1260	575
	σ_m	± 37	± 27	± 138	± 107	± 243	± 40	± 257	± 54
	n	8	9	9	9	10	12	10	13
DOG	X	900	145	2020	350	2440	260	2920	380
	σ_m	± 149	± 7	± 246	± 26	± 137	± 31	± 194	± 37
	n	16	13	11	6	13	13	11	13

X = μU insulin (ILA = insulin-like activity and IMI = immunological measurable insulin),
σ_m = standard error of the mean,
n = number of experiments.

The results obtained are given in the table. First we examined the release of insulin into the incubation medium with glucose concentration. Maximal insulin release (ILA+IMI) was obtained at 200 mg%, up to 6-fold of the release without glucose. This effect was also elicited by both secretin dilutions (0.01 and 0.1 U/ml) in the absence of glucose, the values being slightly higher after the administration of 0.1 U/ml. From the results described it may be reasonably concluded that the intestinal local hormone secretin *per se* stimulates insulin secretion independent of the blood glucose concentration.

Clinical implications might be found in a better understanding of the theoretical basis of the measuring of glucose assimilation (the k-value) following i.v. administration of small amounts of glucose[2, 3], the minor role of release of pancreatic insulin, the shorter half-life of glucose given i.v. following primary oral glucose administration[6], the smaller increase in blood glucose and the greater increase in insulin, following the second of the two glucose loads in the oral glucose tolerance test according to STAUB-TRAUGOTT[14].

Furthermore, in slightly older diabetics satisfactorily controlled by diet alone as well as in pre-diabetics, oral glucose administration often leads to a definite increase in insulin[13, 7], whereas i.v. administered glucose remains ineffective, with regard to the increase of plasma insulin[12]. All of these observations might be explained by the action of secretin on insulin liberation, which always takes place upon entrance of glucose into the body. Eventually, spontaneous hypoglycemia observed following oral carbohydrate in post-gastrectomized cases (Dumping-Syndrome) can also be attributed to the rapid secretion of secretin, effected by glucose, reaching the duodenal and jejunal cavity directly. As is generally known, the clinical picture of the Dumping-Syndrome can be reproduced in normal subjects by intrajejunal administration of glucose[15]. By this procedure the discrepancy between low blood glucose and high insulin levels is further enhanced[10a].

Addendum: Similar observations concerning direct stimulation of insulin secretion *in vitro* by secretin were made by MCINTYRE et al.[10b]. Unfortunately, the secretin preparations used by MCINTYRE et al. (Boots, Nottingham) showed both immuno-insulin[10b] and insulin-like activity (own unpublished observation). However, the insulin concentrations and activities

measured in these preparations were far below the insulin quantities released from pancreatic pieces following addition of secretin[10b] (own unpublished observation), and in no way invalidates the finding of an insulin-stimulatory action of secretin.

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A more detailed report will be given elsewhere.

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