Studies on the Release of Serotonin and Catecholamines in the Pancreato-Duodenal Area.* (28099)

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Experiments performed in our laboratory (1) and in that of Dr. Young(2) have demonstrated that, under certain experimental conditions, administration of growth hormone to normal dogs and cats causes the appearance of a hyperglycemic material in the blood of the pancreato-duodenal vein. At first, this material was believed to be glucagon and the results were interpreted as additional evidence for the alphacytotrophic action which several investigators attribute to growth hormone; however, Sirek and Best(3) later demonstrated that the rise in blood glucose could be blocked by dihydroergotamine (DHE), a drug which does not interfere with the hyperglycemic action of glucagon. Results of further work suggest that under different experimental conditions, the pancreato-duodenal area may secrete at least 2 types of hyperglycemic substances: one type which, like glucagon, originates in the pancreas and is effective in animals pretreated with DHE(4) and another type which seems to originate in the duodenum and, like serotonin and the catecholamines, is blocked by DHE(5). The latter appears following injection of STH(3), whereas the material acting in a manner similar to glucagon is liberated during insulin hypoglycemia(6,7) or following injection of deserpidine(8). The exact nature of these materials is unknown: the pancreas, which is the major source of glucagon, is rich in 5-hydroxytryptophane decarboxylase necessary for production of serotonin(9) and contains abundant autonomic structures which may be a source of catecholamines(10,11); on the other hand, the duodenum, which contains abundant chromaffine tissue and is a major source of serotonin, is known to produce significant amounts of glucagon-like materials. Abnormal quantities of 5-hydroxyindolacetic acid, the urinary metabolite of serotonin, have been found in the urine of rabbits treated with STH(12), while significant quantities of catecholamines have been found in splenic and portal blood of patients with portal hypertension(13). Recent evidence also demonstrates that glucagon itself may cause the liberation of catecholamines from the adrenal glands(14). The 4 substances, glucagon, epinephrine, norepinephrine and serotonin, have a hyperglycemic action: the action of epinephrine and glucagon is potent and well known, that of norepinephrine is weak(15), that of serotonin not only requires relatively large doses(4) but probably is secondary to the release of epinephrine(16). This communication reports attempts to measure the effects of STH, ACTH or deserpidine on concentration of epinephrine, norepinephrine and serotonin in the blood of the pancreato-duodenal vein.

Materials and methods. Thirty-one dogs of both sexes, which would submit meekly to intravenous injections, were anesthetized by means of intravenous injections of pentobarbital sodium (35 mg/kg) and barbital sodium (100 mg/kg), a mixture which provides rapid induction and lasting, uniformly deep anesthesia with complete muscle relaxation. The pancreato-duodenal artery and the pancreato-duodenal vein were exposed through a midline incision and cannulated as described previously(17). The animals were heparinized‡ and, to avoid venous stasis, the pancreato-duodenal blood was allowed to flow into the femoral vein using a 3-way connection, through which the desired blood samples could be obtained. Deserpidine‡ (1 mg/cc/kg); STH[4] (batch No. 5-PWR 3.5 mg/cc/kg), ACTH§ (40 U/dog) or saline were injected into the pancreatic artery or into an

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TABLE I.

Time	Before				0-15 min				15-30 min			
Exp	NE, γ/l	E, γ/l	NE + E, γ/l	5-HT, γ/ml	NE, γ/l	E, γ/l	NE + E, γ/l	5-HT, γ/ml	NE, γ/l	E, γ/l	NE + E, γ/l	5-HT, γ/ml
STH, P-D A Samples, P-D V (6)	2.00 ± .88	.53 ± .56	2.53 ± 1.24	.34 ± .43	1.44 ± .84	2.10 ± .12*	3.80 ± 1.51	.50 ± .64	1.23 ± .96	2.02 ± .86*	3.23 ± 1.37	.70 ± .86
STH, F.V. Samples, P-D V (7)	2.49 ± 1.40	.73 ± .32	3.23 ± 1.27	.56 ± .54	2.76 ± 1.09	1.15 ± 1.26	3.91 ± .90	.58 ± .52	3.60 ± 1.94	1.34 ± .72	4.94 ± 2.07	1.12 ± 1.04
ACTH, P-D A Samples, P-D V (5)	.96 ± .52	1.11 ± .82	2.07 ± .31	.12 ± .08	3.58 ± 3.02	1.39 ± .43	4.97 ± 3.22	.40 ± .45	4.09 ± 3.80	1.12 ± .39	5.15 ± 3.50	.37 ± .45
Deserpidine, P-D A Samples, P-D V (6)	3.07 ± .45	1.54 ± 1.24	4.62 ± .65	1.93 ± 1.67	5.08 ± 3.26	2.09 ± .47	7.17 ± 3.49	2.21 ± 1.91	7.20 ± 3.27	2.38 ± .79	9.59 ± 3.77	2.31 ± 1.53
Deserpidine, P-D A Samples, F.V. (5)	1.50 ± .96	.57 ± .81	2.33 ± 2.50	.18 ± .19	3.75 ± 1.85	.70 ± 1.04	4.45 ± 5.18	.30 ± .20	7.31 ± 2.81	1.20 ± 1.38	8.52 ± 4.42	.71 ± .59
Saline, P-D A Samples, P-D V (4)	2.00 ± 1.41	.79 ± .49	2.79 ± 1.35	.19 ± .19	2.05 ± 1.16	.60 ± .15	2.66 ± 1.20	.25 ± .26	2.31 ± 1.17	.94 ± .34	3.25 ± 1.11	.14 ± .18

NE, norepinephrine; E, epinephrine; 5-HT, serotonin; P-D A, pancreato-duodenal artery; P-D V, pancreato-duodenal vein; F.V., femoral vein.
Avg values ± S.E.
* $P < .01$.

exposed femoral vein. Samples of pancreato-duodenal venous blood were collected before injection of the test substance and during the first and second 15-minute periods thereafter. This technic allowed the slow collection of relatively large amounts (40 cc) necessary for the chemical analysis. Serotonin was determined by the method of Waalkes(18), catecholamines by the method of Weil-Malherbe and Bone(19,20). An Aminco spectrophotofluorometer was used.

Results. The results are shown in Table I. No statistically significant changes in concentration of epinephrine, norepinephrine or serotonin in the blood of the pancreato-duodenal vein were observed after injection of any of the substances studied into the femoral vein or after injection of deserpidine, ACTH or saline into the pancreatic artery. Only the injection of STH into the pancreatic artery caused a significant increase in concentration of epinephrine in the pancreato-duodenal blood.

Discussion. These experiments were designed to investigate the possibility that liberation of catecholamines or serotonin from the pancreato-duodenal area may be the cause of the rise in blood glucose concentration noted by several investigators following intravenous injections of STH. Since this hyperglycemic reaction occurs within 30 minutes of hormone administration, blood catecholamines and serotonin levels were not measured after that period. Of the 3 substances measured, norepinephrine and serotonin did not increase within this period; epinephrine did increase, but only when STH was injected directly into the pancreato-duodenal artery. It may be concluded that the hyperglycemia observed after intravenous injections of STH is probably not due to liberation of catecholamines or serotonin, and remains unexplained. The increase in epinephrine concentration suggests that under certain conditions the pancreato-duodenal area may be a source of this hormone. This is in agreement with previous observations(13) and should be investigated further.

Summary. The concentration of epinephrine, norepinephrine and serotonin in the blood of the pancreato-duodenal vein was measured following injection of STH, ACTH, deserpidine or saline into the pancreato-duodenal artery or the femoral vein of normal anesthetized dogs. Intravenous injections of STH, ACTH or deserpidine do not cause a statistically significant rise in blood catecholamines and serotonin. The hyperglycemia which sometimes follows intravenous injection of STH remains unexplained.

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