PARTICIPATION OF THE VASCULAR COMPONENT IN THE HORMONAL MECHANISM OF PANCREAS STIMULATION

É. K. Kuznetsova and I. T. Kurtsin

Laboratory of Cortico-visceral Pathology and Chair of Normal Physiology of the S. M. Kirov Military-Medical Order of Lenin Academy (Head, Prof. I. T. Kurtsin), Leningrad
(Presented by Academician V. N. Chernigovskii)
Translated from Byulleten' Éksperimental' noi Biologii i Meditsiny, Vol. 51, No. 5, pp. 14-18,
Original article submitted June 16, 1960.

With the discovery by Beilis and Starling [9] of the hormonal mechanism of pancreas stimulation, the problem of the physiological action of secretin has been discussed many times under its most diverse aspects [1]. Particular attention of the investigators was attracted to the problem of direct and indirect effect of the hormone on the secretory cells of the pancreas. A theory has been advanced that the secretory effect obtained via administration of an HCl solution into the duodenal cavity and injection of the extracts of the duodenal mucosa was caused by an increased blood supply to the pancreas and the effect of vasodilating substances.

However, experiments with the use of secretin, purified of vasodilators, as well as crystalline secretin, showed that this hormone stimulates pancreatic activity without increasing its blood flow [13]. The latter phenomenon takes place only in cases when an obstacle to blood outflow is created which leads to an increased secretory pressure in the duct [10, 11, 12].

Thus, the majority of authors accept at present the specificity of secretin action and deny the participation of the vascular factor in this process. However, such an assertion is based on the results of acute experiments, when in an animal which had been anesthetized and subjected to surgical trauma, the secretion of pancreatic juice and the blood flow rate in pancreatic vessels were simultaneously recorded. It is possible that this form of an experiment is acceptable for the solution of this problem, and it is, therefore, possible to be in accord with the concept of the specificity of secretin. But, when we speak of the dynamics of pancreatic secretion under normal physiological conditions, it is scarcely possible to concur with the categorical denial of the role of the vascular component in this process.

This assumption follows not only from the general physiological regularity, according to which each functioning organ is better supplied with blood, but from facts obtained in recent years in regard to the blood supply of the stomach during its secretory activity [2, 3]. In chronic experiments on dogs with isolated ventricles, as per Pavlov, and special electrodes leading from thermoelectric Rein clocks and implanted in a gastric vessel, it was established that the food intake causes long before the appearance of secretion an accelerated blood flow in gastric vessels which increases with the development of the secretory process, reaches its maximum during the period of the most intensive function of the gastric glands and abates with the cessation of secretion. Consequently, these experiments demonstrated the participation of the vascular component not only in the complex reflex phase, but also in the neuro-chemical secretory phase when the glandular activity is caused mainly by hormonal influences.

This fact prompted us to carry out an experimental study of the vascular component in the hormonal mechanism of pancreatic stimulation.

METHOD OF EXPERIMENTS

The study of pancreatic secretion and the blood flow rate in the gland was carried out on dogs, weighing 15-20 kg, in acute and chronic experiments.

The acute experiments were conducted under urethan anesthesia (10% solution intravenously). The secretion was collected in a cannula inserted in the large pancreatic duct; the small duct was ligated; the stomach was separated from the duodenum at the expense of the mucous membrane. Recording of the secretion was taken every minute via pneumatic transmission to a horizontally situated menometric scale; in addition, the total quantity of secretion, collected during the entire secretory period, was measured in milliliters. An interval of not less than an hour was maintained between the employment of each stimulus. Changes in the blood flow rate were determined in Arteria pancreaticoduodenalis by means of a Rein thermoelectric clock. These changes were elicited by processing the photokymograms and were conditionally expressed in millimeters of the rise or fall of

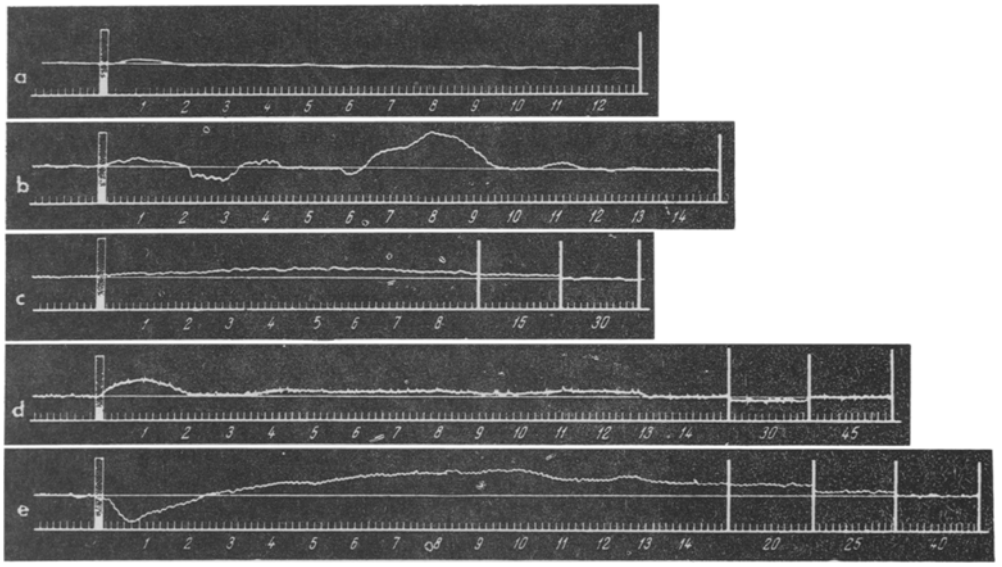

Fig. 1. Dynamics of changes in the blood flow rate in the pancreas upon administration of secretin. Designation of curves (top to bottom): photokymogram of the blood flow rate; mean initial level of blood flow (horizontal lines); time mark in seconds (each division – 10 seconds; minutes are designated with numbers). a) Administration of "Mebiol-Secretin" in acute experiment; b) administration of the extract of duodenal mucosa in acute experiment; c) administration of "Lilly-Secretin" in chronic experiment; d) administration of "Mebiol-Secretin" in a chronic experiment; e) administration of the extract of duodenal mucosa in a chronic experiment. Columns on the left – time of administration of secretin or extract.

the blood flow in relation to its initial level. As a stimulus of pancreatic secretion, we employed 10% solutions of crystalline "Lilly-Secretin" and "Mebiol-Secretin" in 1-2 ml quantities and an extract from cat's duodenal mucosa obtained by the usual method in 10-20 ml quantities. These substances were administered intravenously. As control, we employed a physiological solution injected in the same quantities. A total of 32 acute experiments was staged; the secretory effect of secretin was tested 65 times.

Chronic tests were carried out on four dogs with a chronic fistula of the pancreatic duct, as per Pavlov, (two dogs), and with electrodes implanted into the pancreatic artery, from Rein's thermoelectric clocks. A total of 39 chronic experiments was carried out.

The obtained secretion was examined for the content of total and free lipase, according to the Bondi-Rozhkova method, trypsin – per Serensen, and amylase – per Volgemuth. The titrated alkalinity and viscosity of the secretion were also determined.

RESULTS OF EXPERIMENTS

The results of acute experiments were as follows. Administration of extracts from duodenal mucosa of secretin solutions produced non-uniform vascular effects. Most frequently, a very slight and transitory acceleration of the blood flow was observed (Fig. 1, a); this effect was noted in 44 cases out of 65 (68%). A definite increase of the blood flow was observed in five cases only (7%); in the rest, an increase of blood flow alternated with its reduction (Fig. 1, b). This took place in 25% of cases; it usually originated when extracts had been used.

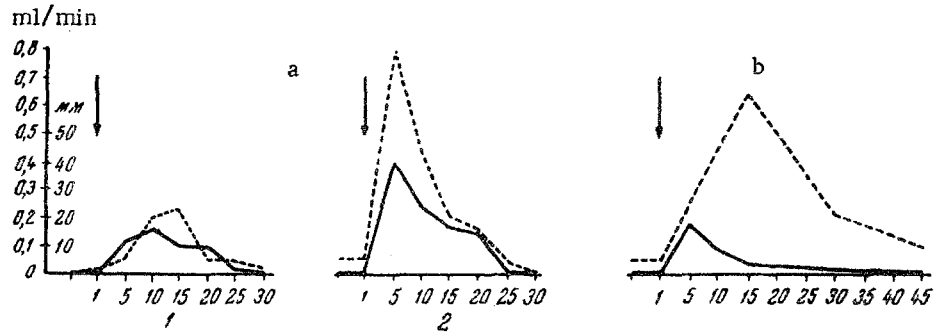

Fig. 2. Correlation between the vascular and secretory reactions of the pancreas following administration of secretin. —— change of blood flow rate (in millimeters); ---- change of intensity of pancreatic secretion (in milliliters per minute). Along the ordinate axis: quantity of secretion (in milliliters), blood flow rate (in millimeters); along the abscissa axis: time (in minutes). 1) Experiment January 13, 1960; 2) experiment January 20, 1960; a) Administration of extract of duodenal mucosa; b) administration of "Mebiol-Secretin." Arrows indicate the moment of secretin administration.

Secretin solutions most frequently caused an abundant pancreatic secretion. The latent period of secretion did not exceed 55-70 seconds. Maximal secretion was observed on the 2nd-3rd minute. The duration of the effect was 15-20 minutes. Total amount of secretion fluctuated in various dogs within wide limits (from 5 to 18 ml).

In some experiments a definite connection was elicited between the secretory activity of the pancreas and the character of changes in the blood flow rate. Thus, for instance, in the test with double administration of one ml of a 10% solution of "Mebiol-Secretin" the blood flow acceleration after the first administration of the solution took place within 200 seconds, after the second administration—within 20 seconds. Correspondingly, the volume of secretion for the entire secretory period comprised 10.5 ml after the first administration of the solution of secretin, and 15 ml—after the second administration. The enzymic content in the secretion in cases of a rapid and intensive acceleration of the blood flow and increased secretion was usually lower, as compared to cases when the acceleration of the blood flow proceeded slowly after a prolonged latent period and a scanty secretion.

However, such clear dependence between changes of blood flow rate and the intensity of pancreatic performance did not take place in every case—a fact which in our opinion can be connected with the conditions of an acute experiment and with the difference in the depth of narcosis in particular.

We obtained clearer results in chronic experiments. An important feature of these results, as compared to the results of acute experiments, was the blood flow acceleration in response to secretin administration. It was observed in all four dogs. The range of blood flow acceleration in various dogs at diverse time periods fluctuated between 7 and 40 mm.

The effect of "Lilly-Secretin" was studied on dogs Dik and Kozyr'. The latent period of the vascular reaction is generally 10-25 seconds, the duration of the reaction comprised 15 minutes in Kozyr' and 30 minutes in Dik. The blood flow reached the highest acceleration during the first 6-8 minutes (Fig. 1, c).

In the dog Ramzai with a permanent fistula of the pancreatic duct, the increase of blood flow rate in the pancreatic artery upon administration of "Mebiol-Secretin" took place within 5-10 seconds after reaching its

maximum (18-20 mm) which occurred during the first few minutes after the injection of secretin; within 15-20 minutes, the blood flow rate reverted to the initial level (Fig. 1, d). The pancreatic secretion in these cases would start only within 50-60 seconds after injection of secretin and lasted 20-30 minutes; the maximal secretory activity was usually reached toward the 15th minute. During the entire secretory period about 15-20 ml of juice was secreted, on the average (Fig. 2, b).

In the dog Tsygan, also with a permanent fistula of the pancreatic duct, the secretory and vascular reactions to intravenous administration of the extract from the duodenal mucosa were investigated. Upon its injection in the blood, the blood flow acceleration (10-40 mm) occurred at various periods—from scores of seconds to several minutes—and lasted 30 to 40 minutes (Fig. 1, e). The highest rise occurred on the 10th-12th minute. Pancreatic secretion started after the emergence of vascular reaction and reached its maximum on the 5th-15th minute; it ceased within 30 minutes after the administration of the extract (Fig. 2, a).

Correlation of the Time Between the Appearance of Secretion and the Change of the Blood Flow Rate in the Dog's Pancreas After the Intravenous Administration of Secretin

Date of experiment	Time of appearance of secretion and blood flow change (in seconds)		Date of experiment	Time of appearance of secretion and blood flow change (in seconds)	
	Blood flow	Secretion		Blood flow	Secretion
January 9th	120	210	January 16th	120	380
January 11th	20	50	January 17th	80	200
January 13th	125	240	January 18th	10	40
January 14th	170	360	January 19th	360	50
January 15th	130	360	January 20th	20	60

There was usually a correspondence between the secretory and vascular reactions, in the sense that a higher acceleration of the blood flow was accompanied by a more intensive pancreatic secretion and the changes in the blood flow rate always preceded the emergence of the secretory effect (see table).

Most frequently a direct interdependence was observed between the increased rate of the blood flow and the enzymic content of the juice which had been secreted in response to secretin administration: with the increase of blood flow rate, a larger quantity of enzymes was secreted. Analogous relationship was noted between the magnitude of the blood flow rise and the titrated alkalinity of the secretion. Pancreatic juice, secreted in response to secretin administration, always had lower viscosity than the juice secreted in response to food stimulation.

Thus, the obtained results attest to the fact that extracts from the duodenal mucosa as well as pure secretin not only stimulate the secretory pancreatic activity, but also increase its blood supply. Since this effect is less pronounced under conditions of an acute experiment and is always present under normal physiological conditions, there is reason to believe in the importance of the development of this effect in the normal functioning of the nervous system, especially after investigations of a number of authors [4-8] have established the dependence of the secretin stimulation of the pancreas on the nervous system.

Changes in the pancreatic blood supply appear before the start of secretion. The marked constancy of these reactions, observed in chronic experiments, permits the assumption that such changes of the blood flow rate in the organ are very essential to the course of normal pancreatic secretion. At the same time, our data indicate the principal possibility of a humoral stimulation of the pancreas without changes in its blood supply. However, since these phenomena had been elicited only under conditions of an acute experiment with the use of narcosis and manipulations of a traumatic character to the nervous system, they can scarcely be regarded as physiological reactions.

LITERATURE CITED

1. B. P. Babkin, The Secretory Mechanism of the Digestive Glands [in Russian] (Leningrad, 1960).
2. A. D. Golovskii, Secretory and Vascular Reactions of the Stomach in Various Functional States of the Higher Sections of the Central Nervous System [in Russian], Author's Report, Candidate's Dissertation (Leningrad, 1957).
3. I. T. Kurtsin and V. I. Medvedev, Theses of Reports at the Conference on Problems of Cortico-visceral Physiology and Pathology [in Russian] (Leningrad, 1953) p. 101.
4. O. G. Onisko, Transactions of the I. P. Pavlov Institute of Physiology [in Russian], 6, (Moscow, 1957) p. 366.
5. V. E. Robinson, Byull. Éksp. Biol. i Med., 39, 2 (1955) p. 12.
6. Ts. V. Serbenyuk, Participation of the Nervous System in the Realization of the Effect of Chemical Regulating Factors of Pancreatic Secretion [in Russian], Author's Report, Candidate's Dissertation (Moscow, 1952).
7. A. V. Solov'ev, Byull. Éksp. Biol. i Med., 28, 2, 8 (1949) p. 108.
8. V. V. Troitskaya and A. D. Troinikova, Transactions of the I. P. Pavlov Institute of Physiology, 3, (Moscow, 1954) p. 127.
9. A. L. Bennett and E. U. Still, Am. J. Physiol., 106 (1933) p. 454.
10. R. Gayet and M. Guillaumie, C. R. Soc. Biol., 105 (Paris, 1930) p. 373.
11. C. Maltesos and R. H. Watson, Pflüg. Arch. ges. Physiol., 241, 516 (1939).
12. M. M. Weaver, Am. J. Physiol., 85 (1928) p. 410.

All abbreviations of periodicals in the above bibliography are letter-by-letter transliterations of the abbreviations as given in the original Russian journal. *Some or all of this periodical literature may well be available in English translation.* A complete list of the cover-to-cover English translations appears at the back of this issue.
