INTRAGASTRIC PRESSURE AS A FACTOR INFLUENCING THE REDISTRIBUTION OF PEPSINOGEN AND CHLORIDES SECRETED IN THE GASTRIC JUICE AND EXCRETED IN THE URINE

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The relationship between the secretory and motor activity of the stomach in a fasting state and during digestion has been the subject of many clinical and experimental investigations [5]. However, intragastric pressure, which varies within wide limits as a result of the motor activity of the stomach [1], has not been taken into account as a factor capable of influencing the volume of gastric secretion and the composition of the secretion.

In the present investigation the effect of differences in intragastric pressure was studied on the exosecretion of pepsinogen and its excretion in the urine (uropepsinogen), i.e., the movement of the proenzyme from the cells of the gastric glands along the exosectretory and incretory pathways. A parellel study was made of the effect of intragastric pressure on the excretion of chlorides in the gastric juice and urine, for there is an intimate relationship between these indices [10].

EXPERIMENTAL METHOD

Experiments were carried out on 7 dogs with large isolated gastric pouches (about one-third of the secreting surface of the gastric mucous membrane; the pouches were isolated by the method of Pavlov, Savich, and Ugolev) and with ureters exteriorized by Pavlov's method. During the experiment, which lasted for 6-8 h, the gastric secretion and urine were collected in a fasting state, and their volumes were measured at the end of every hour. The pepsinogen content in the collected secretion and urine was determined by an adsorption-colorimetric method [3] and the chlorides by a mercurimetric method [4]. The secretion and excretion of pepsinogen and chlorides were characterized by two indices: their concentration (in mg% and percent and their excretion in unit time ("intensity of excretion" in μg and mg/h).

The pressure in the isolated gastric pouch was varied by means of a device consisting of a pressure vessel with mercury, a glass reservoir of air, and a control mercury manometer. The apparatus was connected to a graduated tube, fixed hermetically every hour of the observation to the fistula tube of the gastric pouch. By means of this apparatus, a negative (20, 30, 40, mm Hg) or positive (10-15 mm Hg) pressure was created inside the gastric pouch after every 2-hour period of observation of the secretion of juice and exretion of urine at atmospheric pressure.

The series of experiments whose results are described in this paper was carried out in a fasting state without the use of stimulants of juice secretion, and in the absence of free hydrochloric acids in the secretion at the beginning of the experiment.

EXPERIMENTAL RESUTLS

The results obtained with all the experimental animals were consistent.

An increase in intragastric pressure to 10-15 mm had a marked effect on the exosecretion of pepsinogen (Fig. 1), shown by a significant fall in the amount of pepsinogen contained in the gastric secretion in unit time. This decrease in the exosecretion of the proenzyme became progressively more marked with time, and took place as a result not only of a decrease in the volume of secretion, but also of the concentration of pepsinogen in the juice. In some experiments, in the first hour of increased pressure in the gastric pouch, the secretion produced contained a small concentration of free hydrochloric acid, but later, as a rule, this was not observed.

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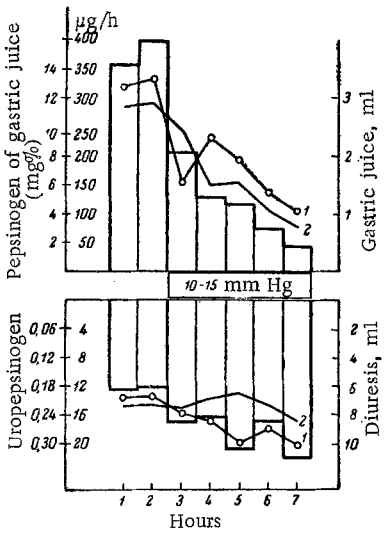

Fig. 1. Effect of a positive intragastric pressure on the exosecretion of pepsinogen and excretion of uropepsinogen. The columns indicate the secretion and excretion of pepsinogen per unit time in the gastric juice and urine (μg/h). 1) Concentration of pepsinogen in juice (above) and in urine (below); 2) volume of gastric secretion (above) and diuresis (below). Volume of gastric secretion and diuresis in ml, secretion and excretion of pepsinogen in juice and urine (μg/h).

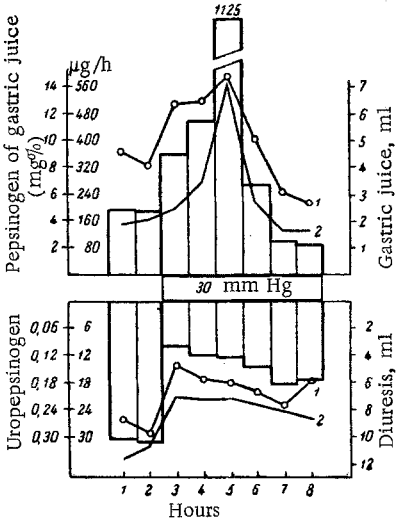

Fig. 2. Effect of a negative intragastric pressure on the secretion of pepsinogen in the gastric juices and its excretion in the urine. Legend as in Fig. 1.

With a decrease in the secretion of proenzyme in the juice excretion of uropepsinogen regularly increased, and a leading role in the phenomenon was due to the increase in the concentration of pepsinogen in the urine.

The creation of a negative pressure (30 mm; Fig. 2) within the isolated gastric pouch had the opposite effect: during the first 3-4 h the exosecretion of pepsinogen rose sharply, but later (until 6-8 h) it fell to lower values than those characteristic of the exosecretion of proenzyme at atmospheric pressure within the gastric pouch. The increase in exosecretion at a negative pressure took place as the result of an increase in the concentration of proenzyme in the secretion and of an increase in the volume of secretion. The subsequent fall in the secretion of pepsinogen in the juice took place as a result of a decrease in the volume of secretion and in the concentration of proenzyme in the juice.

With the increase in exosecretion of pepsinogen under the influence of the negative intragastric pressure, the excretion of uropepsinogen decreased as a result of a decrease of the diuresis and of the concentration of proenzyme in the urine.

In the third variant of the experiments a negative presssure in the gastric pouch was maintained at different levels for 2 h at each. In some experiments the pressure was changed from -20 to -40 mm, in others from -40 to -20 mm Hg. These experiments showed that a pressure of -20 mm increased the exosecretion of pepsinogen to a lesser degree than a pressure of -30 mm. A pressure of -40 mm always depressed the secretion of pepsinogen in the gastric juice, irrespective of whether the experiment began at this pressure of whether it was created at the end of the experiment, as in Fig. 3.

In this variant of the experiments also, the reciprocal relationships between the exosecretion and incretion of pepsinogen were clearly revealed (the magnitude of the latter could be judged indirectly from the excretion of uropepsinogen) depending on the level of the intragastric pressure.

The level of the pressure in the gastric pouch was also important for the "redistribution" of chlorides secreted into the gastric juice and excreted in the urine (see table). A negative pressure in the isolated gastric pouch increased the secretion of chlorides in the juice, by increasing their concentration, but had no marked effect on the synthesis of hydrochloric acid in the gastric mucous membrane. The increase in

Secretion of Chlorides in Gastric Juice and Their Excretion in the Urine Depending on the Level of Intragastric Pressure (Mean Results of 11 Experiments on the Dog Damka).

Experiments of variant I					Experiments of variant II					Experiments of variant III				
Time (in hours)	juice		urine		Time (in hours)	juice		urine		Time (in hours)	juice		urine	
	in %	in mg/h	in %	in mg/h		in %	in mg/h	in %	in mg/h		in %	in mg/h	in %	in mg/h
1	1,44	47	0,82	40	1	1,19	24	0,62	70	1	1,53	91	0,93	77
2	1,47	45	0,80	41	2	1,32	30	0,63	65	2	1,57	96	0,89	69
Pressure +10–15 mm					Pressure –30 mm					Pressure –20 mm				
3†	1,40	84	0,86	50	3	1,70	43	0,57	39	3	1,70	159	1,12	57
4	1,42	35	0,96	53	4	1,63	59	0,63	44	4	1,59	183	0,93	44
5	1,11	20	0,99	50	5	1,64	122	0,68	43					
6	0,82	14	1,06	56	6	1,54	41	0,66	49	Pressure –30 mm				
7	—	—	1,18	59	7	1,36	22	0,76	60	5	1,90	135	0,76	44
					8	1,10	24	0,63	57	6	1,71	126	0,84	50
										Pressure –40 mm				
										7	1,45	30	0,85	65
										8	1,57	30	0,91	65

† The presence of free hydrochloric acid was found in the sample of juice at this hour

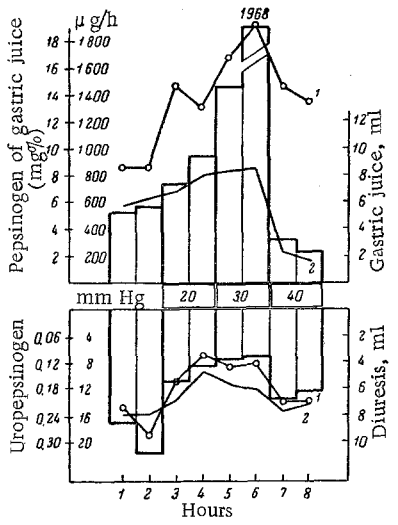

Fig. 3. Effect of different negative pressures on the secretion of pepsinogen in the gastric juice and its excretion in the urine. Legend as in Fig. 1.

the secretion of chlorides in the gastric juice was accompanied by a regular decrease in their excretion by the kidneys. Similar results in response to active stimulation of gastric secretion were obtained by Ya. P. Sklyarov [10]. The depression of the exosecretory elimination of chlorides with a positive intragastric pressure led to an increase in their excretion in the urine.

According to the findings of Janowitz and co-workers [15, 16], 99% of the pepsinogen synthesized in the gastric mucous membrane leaves it in the gastric secretion, while 1% passes into the blood stream, from which it is excreted by the kidneys in the urine. This is an extremely widely held view, but evidence has increasingly been obtained recently that there are no serious grounds for insisting upon a relationship of direct proportion between the exosecretion of the proenzyme, its secretion into the blood stream, and the excretion of pepsinogen in the urine [2, 6, 7, 11, 12, 17, 18].

This is also suggested by experimental results obtained in the authors' laboratory, demonstrating that the extrarenal excretion of the pepsinogen secreted by the stomach into the blood stream may take place and that the excretion of uropepsinogen may be increased at a time when gastric secretion is inhibited [3]. The scale of the excretion of uropepsinogen and the concentration of pepsingen in the blood stream give information primarily about the "peptic potential of the stomach" (the total gastro-peptic mass of cells [13, 14]), a marked change in which is reflected in the excretion of pepsinogen in the urine. The results described provide a further argument in support of the view that the pepsinogen synthesized in the gastric mucous membrane may leave it by both exosecretory and incretory pathways in different quantitative proportions. Depression of exosecretion in response to an increase in intragastric pressure (and also in the presence of edema of the gastric mucous membrane [8, 9]) increases the secretion of pepsinogen into the blood stream and its excretion in the urine.

LITERATURE CITED

1. A. S. Belousov, I. I. Malkiman, and A. M. Sorin, Vestnik Akad. Med. Nauk SSSR No. 2, 71 (1964).
2. I. I. Ionova, Kazansk. Med. Zh., No. 2, 37 (1964).
3. G. F. Korot'ko, The Incretion and Excretion of Pepsinogen [in Russian], Tashkent (1965).
4. L. N. Lapin and R. Kh. Zamanov, in the book: Collected Scientific Publications of the I. P. Pavlov Samarkand Medical Institute [in Russian], Samarkand (1956), Vol. 9, p. 126.
5. E. M. Matrosova, The Motor Activity of the Stomach and its Connection with the Secretion of Gastric Juice [in Russian], Moscow, Leningrad (1964).
6. V. B. Mel'nitskii, Klin. Med., No. 2, 35 (1962).
7. Yu. D. Popov, Vrach. Delo, No. 10, 24 (1964).
8. O. G. Sizov, Lab. Delo, No. 11, 48 (1962).
9. O. G. Sizov, Importance of Determination of the Uropepsin Activity in Clinical Surgery, Author's abstract of candidate dissertation, Riga (1965).
10. Ya. P. Sklyarov, The Gastric Secretion [in Russian], Moscow (1961).
11. G. P. Fedorova, Vrach. Delo, No. 12, 25 (1964).
12. A. I. Frolova, Ter. Arkh., No. 5, 68 (1964).
13. O. A. A. Bock, G. Arapakis, L. J. Witts, et al., J. Brit. Soc. Gastroenterol., 4, No. 2, 106 (1963).
14. B. J. Hirschowitz, J. Lab. a. Klin. Med., 46, No. 4, 568 (1955).
15. H. D. Janowitz, M. H. Levy, and F. Hollander, New York Acad., 26, 281 (1950).
16. H. D. Janowitz and F. Hollander, J. Appl. Physiol., 4, No. 2, 53 (1951).
17. J. R. Jude and A. H. Harris, Arch. Surg., 79, No. 5, 761 (1959).
18. G. Van Goidsenhowen, L. Wilkoff, and J. B. Kirsner, Gastroenterology, 34, No. 3, 421 (1958).