PHYSIOLOGICAL AND HISTOLOGICAL PARALLELS DURING ANALYSIS OF SECRETORY ACTIVITY OF THE GASTRIC MUCOSA IN EXPERIMENTAL ANIMALS AND MAN

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Gastric secretory function in guinea pigs, rats, dogs, and man in response to histamine stimulation was compared with the structure of the fundus of the stomach. In guinea pigs the parietal cells are more numerous than the chief and accessory cells. They are also much larger. In rats the opposite picture is observed: chief cells are more numerous. This accounts for the increased sensitivity of the secretory apparatus of the stomach in guinea pigs to histamine and its relative refractory state in rats. In dogs, equal areas of the stomach contain more parietal cells than in man, accounting for the higher concentration of hydrochloric acid in the gastric juice.

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Few comparative studies of secretory function and structure of the gastric mucosa in different species of animals have been undertaken. However, the close relationship between structures concerned with enzyme-secreting and acid-producing functions of the stomach in mammals is well known.

Histamine has been shown [1-3, 5, 9, 12] to cause direct chemical stimulation of activity of the parietal cells secreting hydrochloric acid. This property of histamine is used to determine the functional reserves of the gastric glands secreting hydrochloric acid. Although animals of different species show well marked general sensitivity to histamine, the possibility of differences in the responses of the gastric secretory apparatus to histamine stimulation must be borne in mind. Nevertheless, no explanation has been given in the literature for this phenomenon and the local mechanisms responsible for it have been insufficiently studied.

The object of the present investigation was to compare the physiological and morphological parameters of gastric secretion in rats, guinea pigs, dogs, and man. Attention was concentrated mainly on the glands in the region of the fundus of the stomach.

EXPERIMENTAL METHOD

Gastric secretion was investigated in fasting rats, guinea pigs, and dogs: total secretion per hour and secretion of hydrochloric acid and pepsin per hour under normal conditions and during histamine stimulation; in dogs either histamine or a natural food stimulus (200 g meat) was used as stimulator. The dose of histamine for intramuscular injection into dogs and guinea pigs was 0.15 mg/kg. To obtain a well marked stimulant effect in rats, the dose of histamine was increased to 10 mg/kg. To establish the normal parameters of gastric secretion, from 5 to 10 experiments were carried out on each animal, and the same number of experiments were used to determine the stimulant action of histamine. To ascertain differences in the histological structure of the gastric mucosa, apparently healthy animals were sacrificed and small pieces excised from them. The material was fixed in 10% formalin and Carnoy's fluid. Sections were stained by Schiff's method or with hematoxylin-eosin. Sections of the fundus of the human stomach were cut from pieces of mucosa obtained by aspiration biopsy by Masevich's method.

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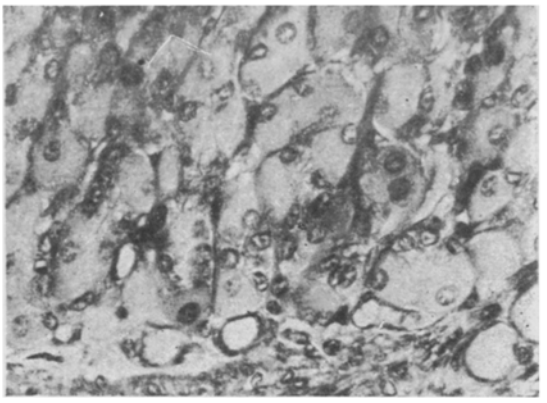

Fig. 1. Gastric mucosa of a guinea pig. Terminal division of fundal glands. Large parietal cells more numerous than small chief cells. PAS reaction, 550 ×.

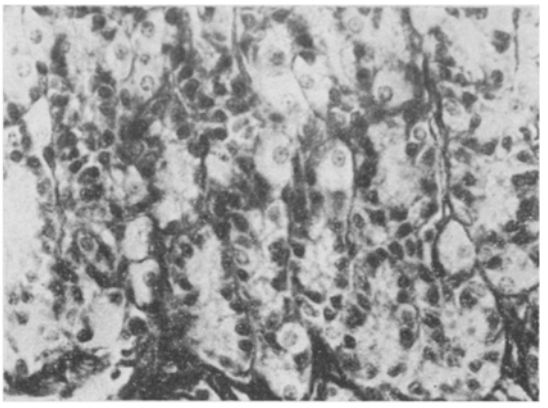

Fig. 2. Gastric mucosa of a rat. Terminal division of fundal glands. Chief cells much larger than parietal. PAS reaction. 550 ×.

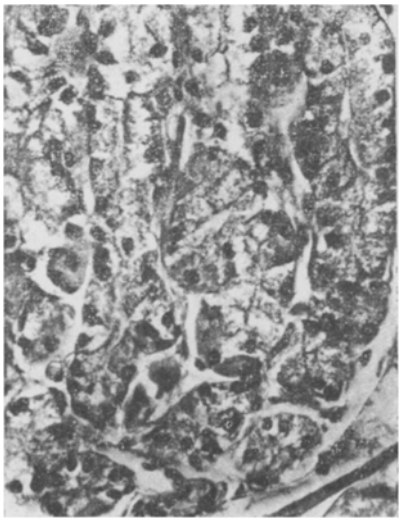

Fig. 3. Gastric mucosa of a dog. Terminal division of fundal glands. Chief and parietal cells. Hematoxylin-eosin, 550 ×.

EXPERIMENTAL RESULTS

Experiments were carried out on 13 guinea pigs, 10 rats, 5 dogs with Basow fistulas, and 4 dogs with isolated Pavlov gastric pouches. Altogether 159 experiments were performed. Indices of gastric secretion in the human subjects were obtained in the author's laboratory (Masevich's data) after continuous aspiration through a thin tube for 1 h (basal secretion) and subsequently for a second hour after injection of histamine.

As Table 1 shows, under the influence of histamine the hourly secretion of gastric juice and the total quantity of hydrochloric acid secreted were increased in all experimental animals; the concentration and total content of pepsin were increased only in dogs, while the quantity of proteolytic enzyme secreted per hour was increased in all animals. In guinea pigs the indices of all studied components of the gastric juice, except for the pepsin concentration, showed a sharp increase.

In man the hourly gastric secretion was increased, and so also were the concentration of hydrochloric acid and its amount secreted per hour; the pepsin production showed only a tendency to increase.

To analyze and interpret the results of investigation of gastric secretion, the histological structure of the glands was studied (Figs. 1-4). The results of examination of many histological sections taken from the fundus of the stomach show that in guinea pigs the fundal glands constitute between 4/5 and 5/6 of the thickness of the mucosa and are lined mainly with parietal cells, the number of chief and accessory cells being comparatively small. In addition, the parietal cells were from 3 to 4 times larger in size than the chief cells and they appeared swollen. This feature of the gastric gland cells was particularly conspicuous when their sizes, and particularly their numbers, were compared in guinea pigs and rats (Figs. 1 and 2); in the latter the chief cells were much more numerous and relatively few parietal cells were present.

Data in the literature [7, 8, 10, 11, 13, 14] suggest a correlation between the number of parietal cells and hydrochloric acid secretion. In Marks's opinion [13], in man 50 million parietal cells function after maximal stimulation with histamine (injection of 0.4 mg/10 kg body weight), secreting hydrochloric acid at the rate of 1 meq/h. It may also be concluded from the results of the present investigation that the quantity of hydrochloric acid and pepsinogen secreted per hour depends on the number of chief and parietal cells. This explains why the highest hydrochloric acid indices are found in the gastric juice of guinea pigs both

TABLE 1. Indices of Gastric Juice

	Volume of gastric juice		Total acidity (in titration units)	Free HCl		Content of HCl		Total HCl secreted		Pepsin content		Total pepsin secreted	
	ml	%		titration units	%	mg/ml juice	%	mg	%	mg/ml juice	%	mg	%
Guinea pig	12±0,6 / 21,8±0,9	100 / 181	91,8±4,7 / 135±3,0	79,6±5,1 / 120±4,6	100 / 163	2,9±0,3 / 4,38±0,2	100 / 148	34,86 / 80,5	100 / 259	5,3±0,6 / 5,4±0,4	100 / 101	66,3±6,2 / 110±0,9	100 / 166
P	<0,001		<0,01	<0,001		<0,01		<0,001		>0,1		<0,001	
Dog	12±0,8 / 19±1,3	100 / 158,3	60±3,2 / 123±4,6	44,2±3,1 / 58±4,6	100 / 131	1,61±0,1 / 2,11±0,2	100 / 134	19,35 / 40,22	100 / 206	12±0,7 / 16±0,8	100 / 133	144±7,0 / 304±6,4	100 / 211
P	<0,001		<0,01	<0,001		<0,01		<0,001		<0,005		<0,001	
Rat	1,6±0,2 / 2,4±0,3	100 / 150	50±3,2 / 60±3,8	32±2,1 / 45±3,1	100 / 140,6	1,16±0,05 / 1,64±0,1	100 / 141	1,86 / 3,94	100 / 211	20,5±1,2 / 20,3±1,4	100 / 99	34±2,3 / 49,7±3,1	100 / 144
P	<0,001		>0,1	<0,001		<0,001		<0,001		>0,1		<0,001	
Man	145 / 210	100 / 144	28 / 45,3	24 / 34,2	100 / 142	0,88 / 1,24	100 / 140	127 / 262,1	100 / 207	— / —	— / —	35 / 40	100 / 114
P	<0,01		<0,001	<0,001		<0,001		<0,001				>0,1	

*Normal values in numerator, values after stimulation with histamine in denominator.

†Values of secretion between meals in numerator, values after stimulation with histamine in dose of 0.5 ml of 0.1% solution over a period of 1 h in denominator.

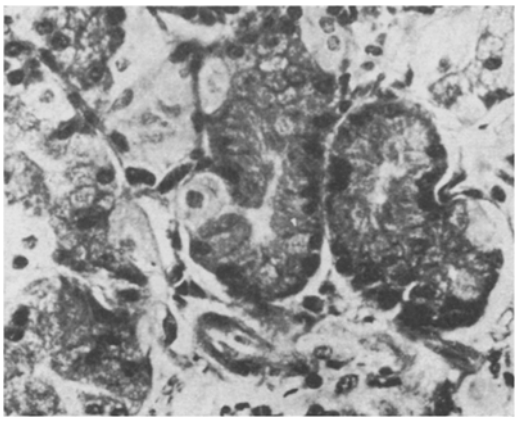

Fig. 4. Human gastric mucosa. Terminal division of fundal glands. Chief and parietal cells. PAS reaction, 550 ×.

under normal conditions and after administration of histamine. Examination of the structure of the terminal divisions of the fundal glands explains the cause of the increased pepsinogen content in the gastric juice (Table 1). In dogs, the number of parietal cells per unit area of gastric mucosa from the fundal part of the stomach is relatively higher than in man, and accordingly their hydrochloric acid concentration in the gastric juice is higher.

By comparing the patterns of secretion and structure of the glandular apparatus of the stomach in dogs, guinea pigs, rats, and man, reasons for differences in sensitivity of the gastric mucosa to histamine and in its secretory response can thus be explained. An answer is also given to the question why the rats occupy first place as regards refractoriness of the gastric mucosa to histamine, followed by the dog, while the guinea pig's stomach exhibits least tolerance to histamine.

LITERATURE CITED

1. B. P. Babkin, Secretory Mechanism of the Digestive Glands [in Russian], Leningrad (1960).
2. L. I. Dvinyaninov, Transactions of the I. P. Pavlov Institute of Physiology, AN SSSR [in Russian], Vol. 9, Moscow–Leningrad (1960), p. 467.
3. I. T. Kurtsin, Hormones of the Digestive System [in Russian], Leningrad (1962).
4. Ts. G. Masevich, Aspiration Biopsy of the Mucous Membranes of the Stomach, Duodenum, and Small Intestine [in Russian], Leningrad (1967).
5. V. I. Uspenskii, Histamine [in Russian], Moscow (1963).
6. J.H. Baron, Gut, 4, 136 (1963).
7. O. A. Bock, W. C. Richards, and L. J. Witts, Gut, 4, 112 (1963).
8. W. I. Card and I. N. Marks, Clin. Sci., 19, 147 (1960).
9. C. F. Code, Fed. Proc., 24, No. 6, 1311 (1965).
10. K. Fischermann and K. Kaster, Gut, 3, 211 (1962).
11. A. W. Kay, Brit. Med. J., 2, 77 (1953).
12. T. M. Lin, Ann. N. Y. Acad. Sci., 99, 30 and 74 (1962).
13. I. N. Marks et al., Am. J. Physiol., 199, 579 (1960).
14. I. N. Marks, Gastroenterology, 41, 599 (1961).