ANALYSIS OF THE CHLORIDE-SECRETING FUNCTION OF THE STOMACH IN EXPERIMENTAL ANIMALS AND IN MAN

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Heidenhain's theory, according to which the synthesis of hydrochloric acid takes place in the oxyntic cells, played an important role in the study of the chloride-secreting function of the stomach. For this reason, this function has always been regarded as secondary, depending on the intensity of acid formation. However, the results of histochemical investigations carried out in recent decades [3] have shown that the synthesis of hydrochloric acid takes place extracellularly, in the region of the gastric pits. The oxyntic cells secrete neutral chlorides only. These results make it necessary to re-examine the question of chloride secretion as an independent aspect of the activity of the gastric cells, taking place before acid formation.

The present paper describes the results of a study of the chloride-secreting function of the stomach and of an analysis of the activity of the different cells found in the gastric glands.

EXPERIMENTAL METHOD

Twenty-one experiments were carried out on two esophagectomized dogs with a Basow gastric fistula. The gastric juice was collected continuously, changing the flasks every 15 min. The fasting observations began after the stomach had been washed out, and ended with the termination of secretion. After sham feeding with meat or bread, a further 8 samples of gastric juice were collected. The volume of juice was measured, and the acidity and the chloride content determined. The blood chlorides were determined at the same time intervals. Altogether 324 parallel estimations of all the indices were made. The chlorides were determined by Ruszniak's method.

Investigations were also carried out on 41 persons. All had recovered from either dysentery or acute gastro-enterocolitis, but at the moment of investigation they were in a stage of late convalescence. Samples were taken through a thin stomach tube. Initially four samples of fasting gastric juice were taken at intervals of 15 min, and sham feeding with bread was then carried out for 5 min, after which a further 8 samples of juice were withdrawn. Blood was taken at the same time from the finger, and the chloride content estimated. Altogether 420 parallel investigations of samples of blood and gastric juice were made.

EXPERIMENTAL RESULTS AND DISCUSSION

The concentration of total chlorides in the gastric juice varied from 70 to 190 meq/liter. Their mean value was 140.03±1.64 meq/liter; at the height of secretion the concentration of total chlorides was usually 130-160 meq/liter, corresponding to the figures given in the literature [1, 2, 4].

The content of neutral chlorides in the gastric juice of the dogs also varied considerably. To discover the causes of these variations, a statistical comparison of the neutral chlorides of the gastric juice with the blood chlorides and the total acidity was made (see table).

The fasting content of neutral chlorides was 106 meq/liter, i.e., it was isotonic with the blood plasma in accordance with the accepted normal values. In these experiments, because of the wasting of the animals, the blood chloride level was somewhat depressed. However, even in these circumstances a distinct linear relationship was observed between the changes in the neutral chlorides and the blood chlorides. At the same time, no correlation was found between the changes in the neutral chlorides and the acidity of the gastric juice.

As the secretory process developed, a progressive decrease in the content of neutral chlorides was observed. Despite the simultaneous decrease in the concentration of blood chlorides, their link with the variations in the neutral chlorides gradually weakened and then became negative in character. At the same time the relationship

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Index		Experimental animals			Human subjects	
			total acidity in meq/liter			
		0-30	30-100	100-150	0-20	20-100
		fasting	after sham feeding fast		fasting	after sham feeding
Blood chlorides		64,75	61.50	62.26	74.56	70.24
Curvilinear correlation between blood chlorides and						
neutral chlorides		+0.593	-0. 588	-0.396	+0.645	+0.443
Neutral chlorides of gastric juice		106.50	74.50	19.88	61. 96	44.39
Correlation between neutral chlorides	Curvilinear	_	-0.887	-	_	-0.488
and total acidity	Rectilinear	-	_	-0.689		-
Total acidity of gastric juice		20.50	51.00	125.49	9.78	39.39
Number of parallel investigations		80	80	164	92	328

Note. All indices in meq/liter (mean values).

between the variations in the neutral chlorides and the acidity of the gastric juice became, at first, curvilinear and, later, rectilinear (inversely proportional).

In a fasting state, therefore, when signs of activity of the oxyntic cells were absent, the secretion of chlorides by the remaining cells was passive in character (simple filtration). There are no grounds for supposing that at the height of secretion the elimination of chlorides from these cells by filtration was altered, and yet the concentration of neutral chlorides fell considerably. Special calculations showed that this result could not be explained by Heidenhain's theory. Nor could the decrease be attributed to the development of a reciprocal relationship between the neutral chlorides and the acidity of the gastric juice.

An explanation can be found for these phenomena on the assumption that the synthesis of hydrochloric acid takes place extracellularly. In this case all the chlorides present in the secretion, regardless of their origin, are utilized for the formation of hydrochloric acid. When there is considerable production of acid, their utilization is considerable, the level of nonutilized chlorides falls sharply, and in connection with this, they begin to bear an inversely proportional relationship to the amount of hydrochloric acid produced.

The excess of chlorides in the gastric juice is formed as a result of the active secretion of chlorides by the oxyntic cells. In the present experiments in some cases a concentration of total chlorides of about 200 meq/liter was observed. Usually this was in a fasting state, when very little gastric juice was being secreted (not more than 1.0-1.5 ml), but it still contained free hydrochloric acid. It may be postulated that in such cases the chloride concentration reached the upper limit and was maintained by the working of mainly the oxyntic cells. The figure of 200 meq/liter is also known to be the maximal equivalent concentration of electrolytes possible in the tissue cells [5].

Hence, in relation to the chlorides, the gastric juice is a mixture of two fluids: the secretion of the chief and accessory cells, containing about 100 meq/liter of chlorides, and the secretion of the oxyntic cells, with a chloride concentration varying from 0 to 200 meq/liter. The total chloride concentration of the gastric juice depends on the proportions in which these secretions are mixed.

On the basis of the results described above an attempt can be made to give a mathematical definition of the proportions in which these secretions are mixed. The concentration of chlorides in the secretion of the chief and accessory cells is taken to be 100 meq/liter. Two equations were formed:

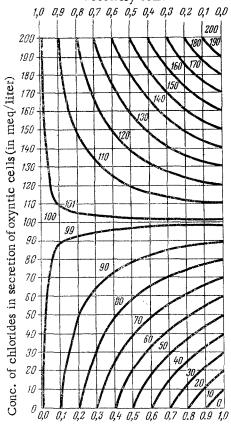
$$100 \cdot SCA + Z \cdot SO = TC \cdot GJ$$
 and $SCA + SO = GJ$,

where SCA is the volume of secretion of the chief and accessory cells; SO the volume of secretion of the cells; GJ the total volume of gastric juice; TC the total chlorides; and Z the concentration of chlorides in the secretion of the oxyntic cells. Hence:

$$SCA = \frac{Z - TC}{Z - 100} \cdot GJ \text{ and } SO = \frac{TC - 100}{Z - 100} \cdot GJ.$$

From these equations curves were plotted to illustrate the states of affairs described above (see figure).

Proportion of secretion of chief and accessory cells



Proportion of secretion of oxyntic cells Influence of concentration of chlorides in secretion of oxyntic cells on its proportion in the composition of the gastric juice. The curves and numbers on them denote the concentration of total chlorides in the gastric juice (in meq/liter).

After the analysis of the experimental data it was interesting to ascertain the degree to which these relationships held good in man.

In all the human subjects investigated after sham feeding, a marked increase in acidity was observed. In 23 of them free hydrochloric acid was absent from the fasting juice. Because of their state of late convalescence and their positive secretory reaction, it was expected that the relationships studied would be reasonable close to normal (see table).

As the table shows, the same changes were observed in the human subjects as in the animals. With free hydrochloric acid absent from the fasting juice, the level of neutral chlorides varied in close relationship with the changes in the blood chloride concentration. As the secretory process developed, this relationship became less marked, and in its place a relationship appeared between the neutral chlorides and the total acidity. The absence of a rectilinear correlation may be attributed to the fact that the indices of acidity did not exceed 100 meq/liter.

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