

blood did not differ significantly. It is important to note that after 24 h, the indices of the hemodynamics in the surviving animals were better than 3 h after resuscitation. At the same time, if cerebral cortical edema was present after 24 h, the indices of the hemodynamics were only approaching their initial levels, whereas in the absence of cerebral edema considerable hyperperfusion was observed. It can be postulated on the basis of the facts described above that the prolonged reduction in the volume blood flow is a factor of considerable importance in the formation of cerebral edema associated with posthypoxic states. This conclusion is in agreement with data in the literature [5-8], and it emphasizes the need for the correction of hemodynamic disturbances during the first day of the resuscitation period after clinical death.

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EFFECT OF ANTRECTOMY ON GASTRIC SECRETION INDUCED BY INSULIN HYPOGLYCEMIA IN DOGS

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Antrectomy causes a sudden and lasting depression of reflex secretion of the gastric fundal glands in response to insulin hypoglycemia in dogs. The reduction in the secretion of acid and pepsin is on average twice that observed after histamine stimulation. A tendency for the indices of secretion to recover is observed after 3-5 months, and during the next 7 months secretion is maintained at a constant level.

KEY WORDS: *antrectomy; gastric secretion; insulin hypoglycemia; histamine.*

The extent to which antral gastrin participates in the secretory response of the fundal glands to vagal stimulation is not yet clear. In patients with duodenal ulcer, positive correlation has been found between the blood gastrin level and the gastric acid secretion in response to insulin [10]. According to observations described by other workers, the correlation between these parameters is less definite [4, 15]. There is evidence that secretion of acid in response to insulin, 2-deoxyglucose, and sham feeding is reduced in dogs after antrectomy [12]. The same effect has been found in antrectomized patients with duodenal ulcer. Antrectomy caused a significant decrease in acid secretion in a Pavlov's gastric pouch in dogs following injection of small doses of insulin (0.2 unit/kg), but in response to larger doses (0.6 unit/kg), secretion was substantially unchanged [12]. Antreneurolysis or vagal

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TABLE 1. Gastric Secretory Response of Dogs to Insulin Hypoglycemia after Antrectomy ($M \pm m$)

Index	Initial values	After antrectomy (time in months)								
		0.5	1	2	3	4	5	6	7-9	10-12
Volume of secretion, ml/h P	75.2±4.76	40.0±11.72 0.02	40.0±5.02 <0.001	28.0±3.34 <0.001	33.2±10.62 <0.005	32.0±10.62 <0.003	42.8±5.02 <0.001	44.0±7.08 <0.005	35.3±2.12 <0.001	34.0±5.61 <0.002
Concentration of free acid, meq/liter P	117±1.6	76±1.5 <0.001	72±7.6 <0.301	56±7.5 <0.001	61±9.5 <0.001	46±9.7 <0.001	64±8.3 <0.001	82±0.01 <0.001	77±4.0 <0.001	81±5.0 <0.001
Acid production (A _i), meq/h P	8.8±0.71	2.8±0.84 <0.001	2.8±0.33 <0.001	1.6±0.17 <0.001	2.3±1.00 <0.001	2.0±0.17 <0.001	2.8±0.50 <0.001	3.2±0.16 <0.001	2.6±0.21 <0.001	2.7±0.56 <0.001
Pepsin concentration, mg/ml P	0.103±0.01	0.066±0.02 <0.001	0.066±0.01 <0.001	0.066±0.01 <0.001	0.062±0.01 <0.001	0.054±0.013 <0.001	0.056±0.003 <0.001	0.052±0.006 <0.001	0.056±0.002 <0.001	0.057±0.005 <0.001
Pepsin production (P _i), mg/h P	7.3±0.62	2.8±1.51 <0.02	2.8±0.33 <0.001	1.6±0.33 <0.001	1.9±0.17 <0.001	2.0±0.67 <0.001	2.0±0.17 <0.001	2.2±0.31 <0.001	1.9±0.26 <0.001	1.9±0.34 <0.001
A _i /P _i P	1.21±0.13	1.17±0.305 >0.9	1.14±0.243 >0.8	0.95±0.059 >0.10	1.20±1.062 >0.9	0.86±0.257 >0.2	1.26±0.251 >0.9	1.47±0.239 >0.3	1.37±0.083 >0.3	1.44±0.163 >0.3

TABLE 2. Gastric Secretory Response of Dogs to Histamine after Antrectomy ($M \pm m$)

Index	Initial values	After antrectomy (time in months)								
		0.5	1	2	3	4	5	6	7-9	10-12
Volume of secretion, ml/h P	122.5±6.19	67.0±2.09 ≤0.001	69.7±7.53 ≤0.001	83.7±11.72 ≤0.01	63.0±14.65 ≤0.001	79.0±6.70 ≤0.001	84.3±2.51 ≤0.001	98.0±7.39 ≤0.05	95.3±6.36 ≤0.01	92.3±4.49 ≤0.001
Acid production (A _h), meq/h P	14.4±0.81	8.0±0.55 ≤0.001	7.4±1.22 ≤0.001	8.3±1.76 ≤0.01	6.4±2.35 ≤0.01	8.5±1.60 ≤0.01	8.5±1.05 ≤0.001	9.3±0.01 ≤0.001	9.8±0.84 ≤0.001	9.3±0.74 ≤0.001
Pepsin production (P _h), mg/h P	3.7±0.25	2.3±0.33 ≤0.001	1.9±0.25 ≤0.001	2.8±0.50 ≤0.1	2.2±0.79 ≤0.1	2.6±0.21 ≤0.01	1.9±0.42 ≤0.001	2.7±0.53 ≤0.1	2.8±0.35 ≤0.05	2.4±0.42 ≤0.03
P _i /P _h P	2.0±0.21	1.2±0.63 ≤0.2	1.4±0.25 ≤0.10	0.6±0.04 ≤0.001	1.0±0.29 ≤0.02	0.7±0.44 ≤0.03	1.2±0.21 ≤0.03	0.8±0.01 ≤0.001	0.73±0.11 ≤0.001	0.78±0.08 ≤0.001
A _i /A _h P	0.60±0.056	0.35±0.075 ≤0.02	0.40±0.052 ≤0.05	0.20±0.067 ≤0.001	0.26±0.059 ≤0.001	0.23±0.053 ≤0.001	0.32±0.084 ≤0.02	0.34±0.01 ≤0.001	0.27±0.028 ≤0.001	0.30±0.078 ≤0.001

denervation of the antral portion in dogs has also been reported [9, 11] to have no effect on insulin-stimulated acid secretion.

The object of this investigation was to assess the effect of antrectomy on the dynamics of acid and pepsin secretion stimulated by insulin hypoglycemia.

EXPERIMENTAL METHOD

Chronic experiments were carried out on three adult male dogs weighing from 11 to 13.8 kg. A gastric fistula was formed by Basov's method 1-1.5 cm away from the greater curvature. Antrectomy was performed 1-2 cm proximally to the boundary defined with the aid of Congo Red. The duodenum was anastomosed with the edge of the residual part of the stomach closer to its greater curvature with minimal invagination of the mucosa. By using this method, practically all the gastric juice can be obtained [13] and regurgitation of the duodenal contents is prevented. Contamination with bile was found in 7 of the 498 portions of gastric juice tested. Portions contaminated with bile were discarded. The dogs were used in the experiments 25-30 days after formation of the fistula. The secretory function of the stomach was investigated at least 3 times before antrectomy, 2 weeks after the operation, and thereafter monthly. Integrity of the vagal innervation of the gastric fundus was verified by Hollander's criterion and by methods developed in the writers' laboratory [3]. Tests were carried out after the animal had been deprived of food (but not of water) for 16-18 h. The gastric juice was collected in 15-min portions for 1 h before injection of the stimulus and thereafter in the course of 2-2.5 h after injection of insulin in a dose of 1.5 unit/kg or of histamine dihydrochloride in a dose of 0.126 mg/kg. The doses of insulin and histamine chosen produced maximal secretion of acid in dogs [6]. The secretory tests were repeated at intervals of 1-3 days.

EXPERIMENTAL RESULTS

Antrectomy caused a sudden and lasting decrease in the secretory activity of the fundal glands in response to vagal stimulation (Table 1). The volume of secretion 2 months after the operation was reduced by 62.7%, acid formation by 80.0%, and pepsin production by 78.1%. Starting from the third month, a tendency was observed for the indices of secretion to rise. The volume of secretion and the acid production after 5 months reached the values observed 2 weeks after antrectomy and later they were maintained at that level. Pepsin production remained low between 3 and 12 months after the beginning of the experiments. The dynamics of acid and pepsin secretion as described above were due to changes not only in the volume of secretion, but also in the acidity of the juice and the concentration of pepsin in it. After antrectomy the ratio between the output of acid (A_i) and of pepsin (P_i) in response to insulin remained practically unchanged throughout the experiment.

In response to maximal stimulation by histamine during the first 3 months after antrectomy, the volume of secretion fell on average by 42.5%, A_h by 47.4%, and P_h by 37.8%. After the fourth month, there was a tendency for these indices to return to normal (Table 2). On the whole, the secretory response of the stomach to histamine was depressed by 33-50% less than that to insulin. Whereas the pepsin secretion in response to insulin was twice as high as that to histamine before antrectomy, after the operation they were almost equal. The level of acid secretion in response to insulin, which before the operation was 60% of that to histamine, also fell sharply after antrectomy and was only 20-32% of the response to histamine.

After removal of the antral portion of the stomach, the secretory response of the fundal glands to vagal stimulation was thus persistently depressed by about two thirds of its initial value. Such a decrease in the production of acid and pepsin and the similar dynamics of the changes in these indices during the year after antrectomy are evidence that the parietal and chief cells equally require antral gastrin for their normal response to vagal stimulation. A close connection between endogenous gastrin and pepsin secretion was established previously [2].

Depression of the secretory response of the fundal glands to insulin hypoglycemia after antrectomy was due to the absence of antral gastrin, normally liberated in response to vagal stimulation and, naturally, to the absence of synergic interaction between gastrin and acetylcholine [7]. The results can be explained from the standpoint of interaction between the receptors of the secretory cells of the fundal glands [8]. In the absence of antral gastrin, the sensitivity of the acetylcholine and, to a lesser degree, of the histamine receptors of

the parietal and chief cells of the stomach is evidently considerably reduced. This decrease in gastric secretion cannot be explained either by loss of a small part of the fundal portion (the resection was carried out only 1 cm proximally to the antral portion) or by incomplete collection of juice on account of its rapid evacuation through the gastroduodenostomy (which was prevented by the position of the cannula), or by regurgitation of the duodenal content (in the basal period 2-5 ml of mucus was secreted per hour, and in response to the stimulus the juice obtained was not contaminated by bile). The two last possible explanations are also ruled out by differences in the secretory response of the stomach to histamine and insulin, as well as by the characteristic changes in pepsin secretion. The absence of gastrin, known to have a trophic action on the fundal glands [5, 14], causes hypoplasia of the fundal glands and this is reflected in a further decrease in their secretory response.

In patients with duodenal ulcer, insulin hypoglycemia has been shown to induce a higher and longer increase in the blood gastrin concentration than in healthy persons [1].

These observations and the results of the present experiments indicate that antrectomy would be beneficial in patients with gastric hypersecretion due not only to excessive gastrin production but also to hypervagotonia.

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