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GASTRIC SECRETION AFTER HISTAMINE: SODIUM AND POTASSIUM CONTENT AND PEPSIN ESTIMATION

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Since Prout (1824) first demonstrated the presence of HCl in the gastric juice and Beaumont (1833) reported the demonstration by Dunglinson and Emmett of the bases, K, Na, Mg, and Ca, the composition of the secretion of the stomach has been repeatedly studied. The literature has been reviewed by Rosemann (1920), Carlson (1923), MacLean and Griffiths (1928), Gamble and McIver (1928), Bulger et al. (1928) and McCann (1929). The recent introduction of histamine as a stimulant of gastric secretion following the work of Popielski (1920) and the subsequent studies, reviewed by Ivy, (1930) has made it possible to secure gastric juice undiluted by test meal. Polland, Roberts and Bloomfield (1928) have demonstrated the value of measuring the rate of secretion of the constituents of the gastric juice following histamine stimulation. In their studies they measured the bases as total base. We have carried out similar studies fractionating the total base into its separate ions and report briefly our results.

From the studies in the literature it is clear that the course of gastric secretion whether stimulated by some type of test meal or by histamine is typically characterized by a rise in the curve of volume secretion associated normally in the mixed juice with rise in acid and chloride concentration, fall in sodium concentration (sodium constituting usually the larger part of the total base), approximate constancy of potassium concentration, concentrations of Ca and Mg always so small as to make difficult the measurement of their changes, fall of nitrogen concentration and change in character of the juice to a less mucoid, more watery consistency. Toward the close of the response to stimu-

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lation these changes are reversed. Fundic pouches give a similar picture but one that is free from the effects of swallowed saliva, mixture of secretion from various parts of the stomach, dilution and buffering by the test meal, and the occasional regurgitation of duodenal contents.

METHODS

In the gastro-intestinal clinic of the Hospital of the University of Pennsylvania under the direction of Dr. T. Grier Miller patients were selected who had been thoroughly studied, usually after complete gastro-intestinal x-ray investigation. On the day of study the patient came without breakfast to the clinic. While reclining comfortably a small Rehfuss tube was cautiously introduced into the stomach and the fasting contents of the stomach removed as completely as possible by gravity and very gentle suction with a syringe. The subsequent fasting secretion collected continuously through the tube for 20 to 40 minutes was separated into samples representing 10 minute periods of collection. Either the specimens or the results of the analyses of the individual samples were combined to constitute "prehistamine" data. Histamine acid phosphate in a dose of 0.3 to 0.5 mgm. as 1:1000 solution of the phosphate was injected subcutaneously. Continuous removal with partition of samples at 10 minute intervals was carried out until the response was subsiding, usually after 60 to 80 minutes. Volume of secretion and acid titration were measured on each specimen. The other analyses were made on certain specimens selected with respect to the volume and acid curve, the size of the specimen, and the freedom of the specimen from blood or bile. Chlorides were measured in all of the subjects, but K, Na, and N only in those indicated in the tables.

Preparation. Each specimen was measured in a cylinder, and passed through ash free filter paper before sampling for analysis.

Acid titration was performed on 1 cc. samples with N/50 NaOH using Topfer's reagent to both the salmon and lemon end points, and phenolphthalein. The lemon end point of Topfer's was used in the human cases to determine the total HCl. This has been recommended by Michaelis (1926) and our data indicate in the human material that the sum of equivalents of total base and total HCl so measured approximately equals the equivalents of total chloride. It is evident that the further titration to the phenolphthalein end point represents for the most part combination of the NaOH with buffer substances in the specimen.

Chlorides were measured by Van Slyke's method as modified by Wilson and Ball (1928).

Phosphates were determined by an adaptation of the method of Fiske and Subbarow (1925) for total phosphorus. One cubic centimeter of juice was digested, with 2 cc. of 2.5 N H_2SO_4 and the later addition of 1 drop of concentrated HNO_3 in long Pyrex tubes, graduated at a volume of 10 cc. After partial dilution and

the addition of reagents, the solution was diluted to the 10 cc. mark. The unknown was compared in a colorimeter with a standard of approximately equal strength, three standards of different strengths being employed.

Nitrogen was determined by the Kjeldahl method.

Bases were determined after ashing a sample in silica or platinum beakers with H_2SO_4 and superoxol the final stages being conducted in an electric oven at a temperature not exceeding 500°C. After complete disappearance of carbon, 1 drop of concentrated H_2SO_4 acid was added to the ash and the heating in the oven repeated at the same temperature. The ash was dissolved in water made up to volume and aliquots taken for the following analyses.

Total base was measured by the method of Stadie and Ross (1925) on the ash from 1 cc. of juice.

Potassium was measured by the titrimetric method of Shohl and Bennett (1928) on the ash from 1 cc. of juice. Known solutions of potassium were analyzed in duplicate with each series.

Sodium was measured by the method of Barber and Kolthoff (1928) using Jena glass filtering crucibles for collection of the precipitates and employing the ash from 1 cc. of juice. Known solutions of sodium were analyzed in duplicate with each series.

Pepsin was estimated by a modification of the method of Polland and Bloomfield (1929). In their method a number of tubes each containing 300 mgm. of edestin are prepared with increasing dilution of the unknown pepsin solution to constant total volume and acidity. They are permitted to digest in a water bath at 37°C. for the same selected time measured to the minute. At the end of the period of digestion the remaining edestin is precipitated with trichloracetic acid, its volume read after centrifugation and the amount of edestin digested is estimated by difference from blank tubes containing edestin but no pepsin. To this point we have followed their method precisely as they described it. Polland and Bloomfield then, in principle, divide the edestin digested by the amount of original pepsin solution present in the tube and plot this value, the edestin digested per unit of pepsin solution, against the dilution of the original pepsin solution in the tube. Such a plot rises to a maximum at some dilution and then, in their experience, falls. They take the edestin digested per unit of pepsin solution at the crest of this curve as a measure of the pepsin concentration of the unknown solution. We were unable to obtain reproducible estimates by this method of interpreting our data.

It is to be expected that, in the neighborhood of half digestion of the edestin, the relation of pepsin concentration to edestin digested will obey Schutz' law

$$\log S = K + \frac{1}{2} \log E$$

where S is the amount of substrate digested, E is the concentration of enzyme, and K is a constant characteristic for the enzyme and substrate under constant conditions and for uniform time and temperature.

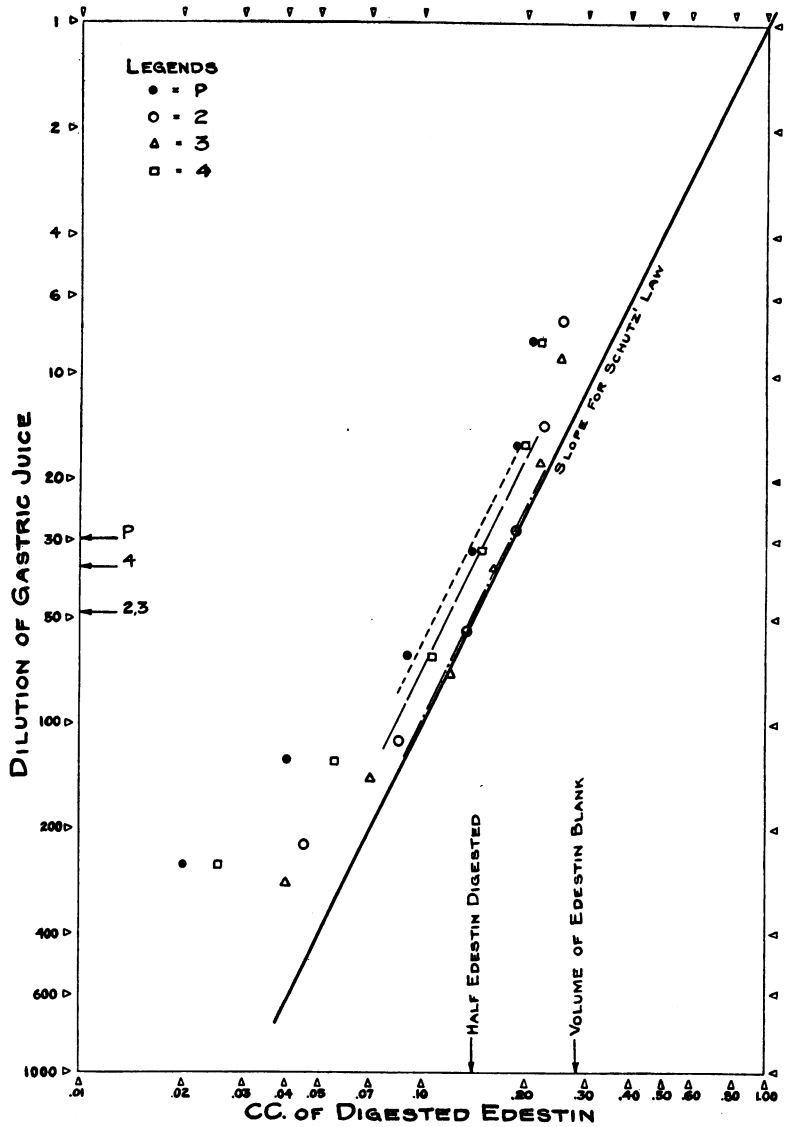

FIG. 1. METHOD OF INTERPRETING PEPSIN READINGS (CASE BR, SPECIMENS P, 2, 3, AND 4)

For the range between 0.09 and 0.20 cc. of edestin digested (abscissae) the values for each specimen approximate the slope of Schutz' law. The intersections of these slopes with the 0.14 ordinate representing half digestion of the edestin, give the dilutions shown by arrows on the left hand margin, which are taken as proportional to the concentration of pepsin in the original specimens.

TABLE 1

Clinical material

Case	Sex	Age	Weight	Nitrogen measured	Blood*	Bile*	Diagnosis
				High acid			
		years	*pounds*				
W	M.	33	119	+			Cholelithiasis
AB	F.	29	115	+			Visceroptosis
AE	M.	37	137	+	Trace		Gastric ulcer
AL	M.	44	115	+	Trace 3 to 7	+ in 1	Arteriosclerosis, hypertension
AN	M.	41	127	+	Traces	+3 and 5	Ulcers; gastroenterostomy; partial obstruction
AO	M.	40	142	+		+4 to 6	Chronic constipation
AP	M.	37	145	+			Diabetes mellitus; constipation
AQ	M.	53	148				Hyperthyroidism; BM + 39 per cent
AZ	F.	25	114	+			Chronic constipation
BF	F.	41	152	+			Chronic cholecystitis
BI	F.	47	130	+			Cholelithiasis
BK	M.	33	147	+			Duodenal ulcer
BP	M.	22	150	+		+2 to 4	Normal student
BQ	M.	59	150	+		+P, trace later	Chronic constipation
BR	M.	21	150	+	+3 to 6	+P	Normal student
BS	M.	24	132	+	+2 to 5	+1, 4, 5	Normal student
BU	M.	23	140	+			Normal student
				Low acid			
B	M.	61	111		Traces		Tuberculosis (?); anemia
U	M.	53	158	+			Arteriosclerosis
V	M.	23	150	+			Duodenal ulcer
AR	M.	71	116				Carcinoma stomach; retention
AT	F.	48	155	+	Traces		Cholelithiasis
AU	M.	43	127		++, except 4		Carcinoma stomach
AV	M.	62	190	+			Chronic constipation
BD	F.	25	115	+			Duodenal adhesions
BE	M.	48	147			+, except 2	Chronic arthritis
BJ	F.	44	146				Intestinal adhesions
BO	M.	22	150				Normal student

* Figures refer to the fractional 10 minute periods following histamine in which blood or bile appeared, P indicating the prehistamine period.

TABLE 2

Summary of analyses on clinical material

	High acid group Maximum total acid > 60, 18 cases									Low acid group Maximum total acid < 60, 13 cases								
Period	P	1	2	3	4	5	6	7	8	P	1	2	3	4	5	6	7	8
	Prehistamine	0–10 minutes	10–20 minutes	20–30 minutes	30–40 minutes	40–50 minutes	50–60 minutes	60–70 minutes	70–80 minutes	Prehistamine	0–10 minutes	10–20 minutes	20–30 minutes	30–40 minutes	40–50 minutes	50–60 minutes	60–70 minutes	70–80 minutes
Amount, cc. per 10 minutes:																		
Maximum	29	24	37	59	36	58	21	27		30	50	44	29	23	16	12	22	
Minimum	5	2	5	8	5	2	4	2		1	1	1	1	1	4	3	2	
Average	12	14	23	25	21		13			12	19	17	15	10		9		
Cl, m.Eq. per liter:																		
Maximum	131	148	159	156	156		147			127	132	132	134	133		136		
Minimum	67	99	64	107	95		75			68	68	57	57	68		58		
Average	105	123	133	137	138		126			89	98	96	95	95		94		
Total acid m.Eq. per liter:																		
Maximum	81				116*					35		47*						
Minimum	−13		64*							−25		−8*						
Average	30			99*						−4			22*					
K, m.Eq. per liter, average	15		15				13			13		14				13		
Na, m.Eq. per 10 minutes, average	0.45		0.57				0.55			0.29		0.36				0.43		
N, m.Eq. (NH_3) per 10 minutes, average	0.49		0.57				0.58			0.81		0.49				0.51		

*Crest of acid curve.

If the edestin digested be plotted on logarithmic paper against the dilution of unknown solution, then in the neighborhood of half digestion of the edestin the data should fall along a straight line whose slope is given by the equation.

TABLE 3

Potassium concentration (m.Eq. per liter)

Case	P	1	2	3	4	5	6	7	8
	Prehistamine	0–10 minutes	10–20 minutes	20–30 minutes	30–40 minutes	40–50 minutes	50–60 minutes	60–70 minutes	70–80 minutes
High acid									
W	10	8	10			10			
AE	15	14		14				16*	
AL	14		13				7		
AN	14		17	15				15	
AO	10	14	18			15			
AP	17	19	32			13		14	
AQ									14
AZ			13				14		
BF							13		
BP	22	21	23	20					
BQ			13		13	13			
BR	17		18	17	16				
BS	14	11	17		15				
BU	17			16					
Low acid									
U				11			5		
V	9	9		10			5		
AR						15	14		
AT	16	15	16						
AU	15	13		16					
AV	13								
BD					16	17			
BE						16			
BO	11	17		16				18	

*Broken columns in this and other tables indicate a combination of material from several periods, 6, 7 and 8 in this instance.

Figure 1 shows that in the neighborhood of half digestion of the edestin the observations exhibit this relationship. A line whose slope is that of the equation is accordingly drawn through the points near the locus of half digestion. The dilution indicated by this line at half digestion is taken as the concentration of pepsin in arbitrary units in the original unknown solution.

RESULTS OF CLINICAL STUDIES

The patients studied are listed in table 1 with respect to sex, age, and diagnosis. All were used in studying volume rate of secretion, acid titration and chlorides; but only those indicated in tables 1, 3, and 4 for the measurement of N, K, and Na. In no instances were these latter measurements made on specimens containing more than traces

TABLE 4

Sodium excretion (m.Eq. per liter)

Case	P	1	2	3	4	5	6	7	8
	Prehistamine	0–10 minutes	10–20 minutes	20–30 minutes	30–40 minutes	40–50 minutes	50–60 minutes	60–70 minutes	70–80 minutes
High acid									
W	65	62	14			20			
AB	64	70	35		27	20			
AE	29	38		14				16	
AL	80		39				61		
AN	31		23						40
AO	42	38	22				11		
AP	42	17	8			3		6	
BP	19	14	4	2					
BQ			56		13	13			
BR	50		23	12	8				
BU	20			36					
Low acid									
B	49		31						
U	56	56		29			30		
V	73	65		54			46		
BO	27	32		24				37	

of bile or blood and usually the specimens employed were not visibly contaminated with either.

Examination of our data revealed no significant correlation with the diagnoses accepted other than the well recognized correlation of certain conditions with high or low acid titrations. Our material has been divided arbitrarily into those subjects whose maximum total HCl acid titration (lemon end point with Topfer's reagent) exceeded 60 m.Eq. per liter and those failing to reach this acidity. In dealing

with each component we direct attention either to its concentration or to its rate of secretion depending upon which proves to be as a rule the more constant through the period of response to stimulus. Following this criterion we have directed attention to the concentration of chloride and of potassium and to the rate of secretion of sodium, nitrogen, and acid. The results with respect to these components are shown in summary in table 2, supplemented by tables 3 and 4 and

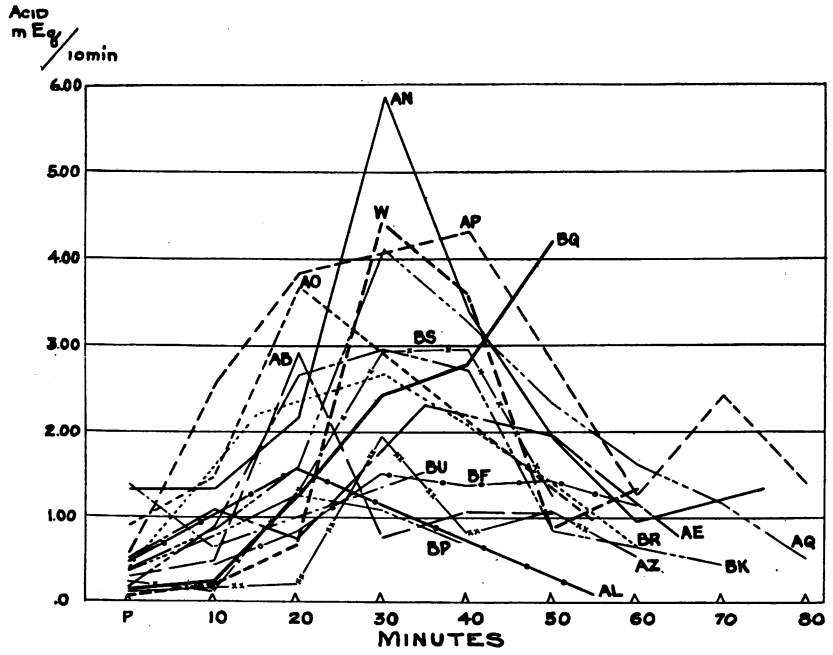

FIG. 2. RATE OF ACID SECRETION IN HIGH ACID GROUP

figures 2 to 7, for it is clear that the significance of the course of the individual curves is somewhat masked in the presentation of table 2.

In the high acid group, the maximum response is about 30 minutes after histamine, with rise of Cl^- and acid concentrations and fall of Na^+ and N concentrations. The rate of Na^+ and N secretion are usually slightly increased but the crest of these curves is earlier, usually 10 to 20 minutes after the stimulus.

In the low acid group the volume secretion rises during the first 10

minutes, as in the high acid group, but then begins to fall off. The difference between the two groups lies not only in the marked difference

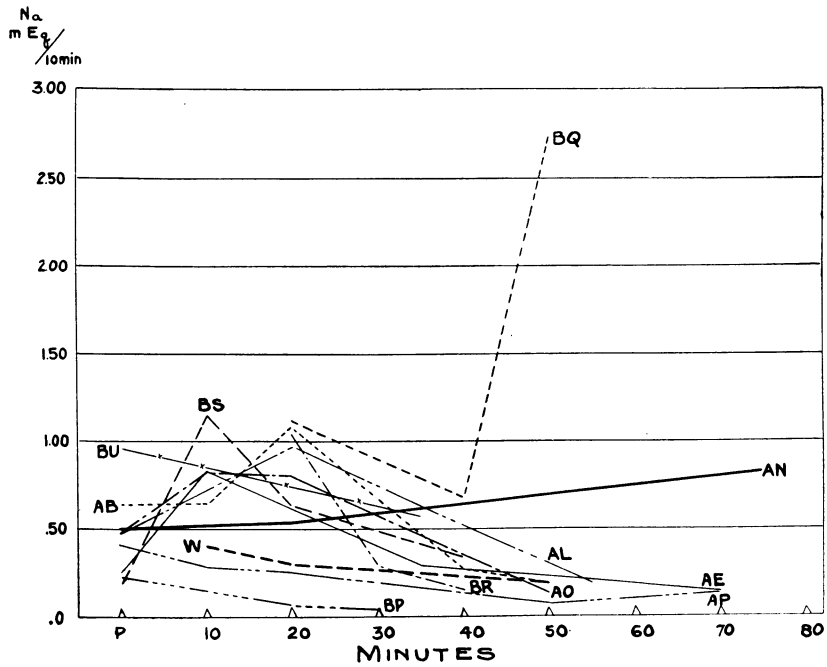

FIG. 3. RATE OF SODIUM SECRETION IN HIGH ACID GROUP

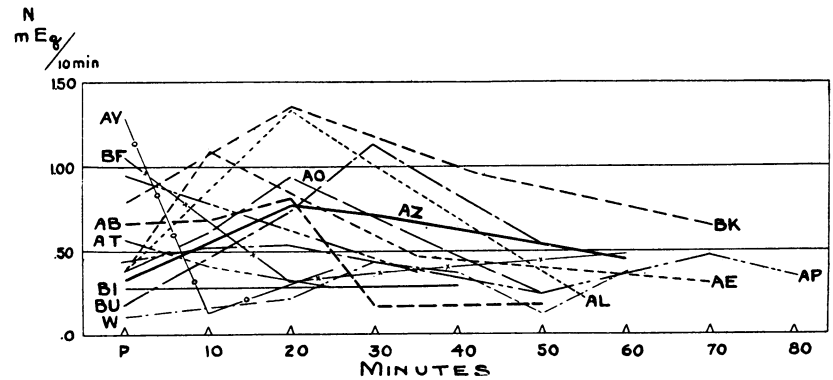

FIG. 4. RATE OF NITROGEN SECRETION EXPRESSED AS m.Eq. NH_3 IN HIGH ACID GROUP

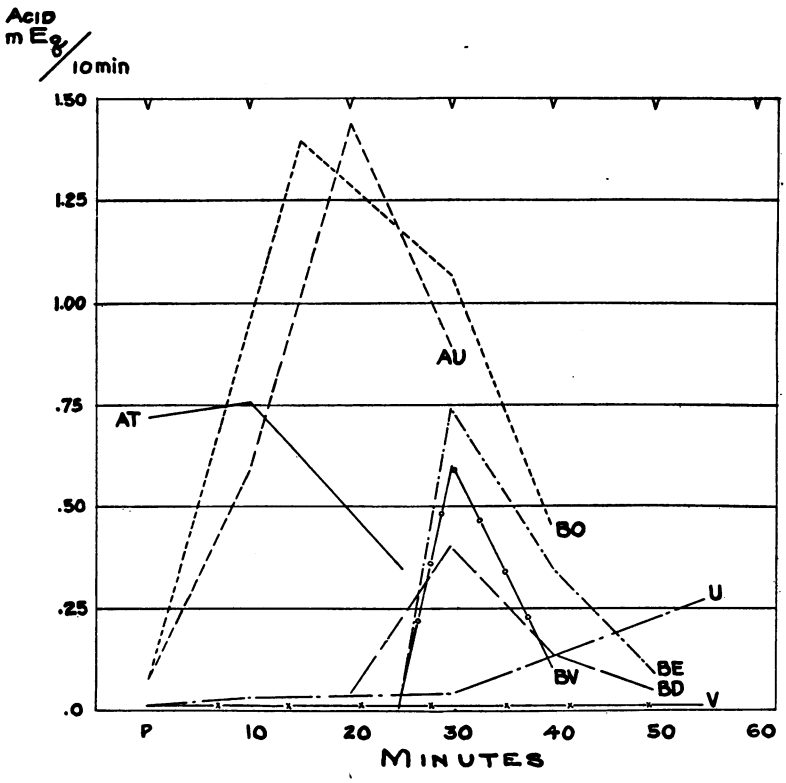

FIG. 5. RATE OF ACID SECRETION IN LOW ACID GROUP
Note that ordinates are on a larger scale than those of figure 2

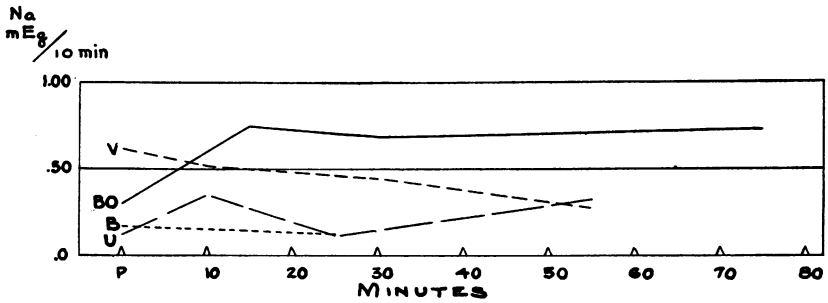

FIG. 6. RATE OF SODIUM SECRETION IN LOW ACID GROUP

in rate of HCl secretion but in less tendency to a rise in rate of secretion of Na and N in the low acid group. The correlation between N and Na^+ secretion is a rather striking one as shown in figure 8. Since in this graph rates of secretion and not concentrations are compared a misleading apparent correlation due to dilution of both by increased secretion of HCl is avoided.

The K^+ concentration is relatively constant throughout. The chloride concentration approaches at its maximum the figures of Carl-

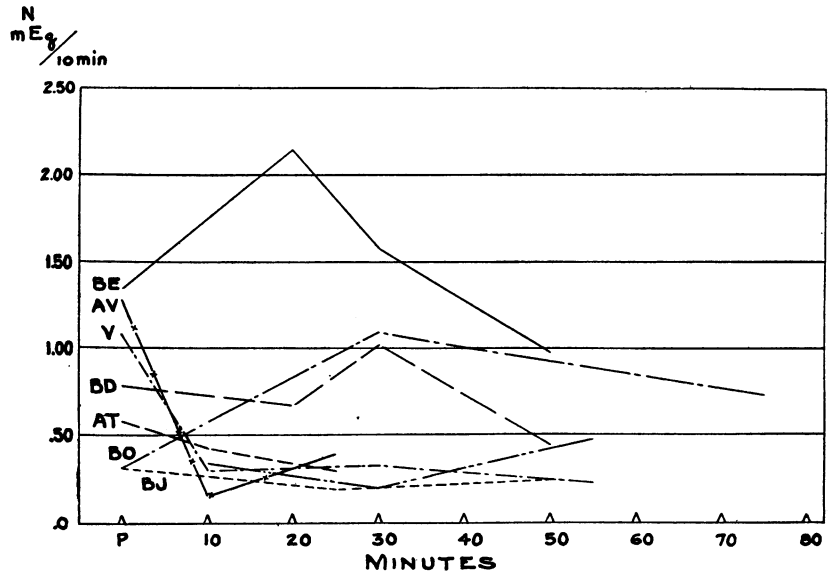

FIG. 7. RATE OF NITROGEN SECRETION EXPRESSED AS m.Eq. NH_3 IN LOW ACID GROUP

son (1923) (150–165 m.Eq. per liter) on gastric fistula juice from man and of Gamble and McIver (1928) on juice from fundic pouches in dogs but never quite reaches these values. In the periods of lower stimulation, and especially in the low acid group, it may reach only 35 per cent of these values. In the low acid group, a chloride concentration as low as 64 m.Eq. per liter was observed in a subject with active secretion amounting to 31 cc. per 10 minutes. If we interpret the gastric secretion as consisting of a mixture of an acid secretion

containing HCl 135 m.Eq. per liter and KCl 15 m.Eq. per liter and a second mucoid secretion containing mucus, nitrogen, and NaCl, the evidence suggests that the NaCl concentrations in the mucoid secretion averages about 50 m.Eq. per liter, which is much lower than the HCl concentration of the acid secretion; the low acid group under this interpretation is characterized by marked depression of the HCl secre-

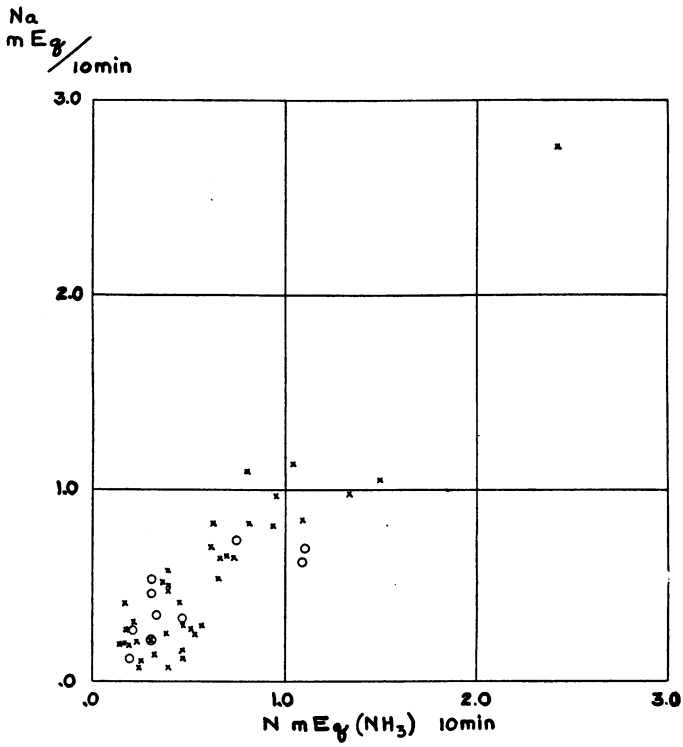

FIG. 8. COMPARISON OF RATE OF SODIUM AND NITROGEN SECRETION IN HIGH ACID (*x*) AND LOW ACID (*o*) GROUPS

tion, while the mucoid secretion with its mucus, N, and NaCl is only a trifle depressed. With this interpretation one would have to postulate that both secretions contain potassium in about equal concentration (10 to 20 m.Eq. per liter) since regardless of the character of the secretion, K^+ concentration remains relatively constant. Our measurements of total base by the method of Stadie and Ross were compared in 51 specimens with the sum of Na^+ and K^+ measured individ-

TABLE 5

Secretion from fundus, pyloric end, and duodenum

	Time	Amount	Rate	Acid titration			Cl	K	Na	N	Acid secretion	Na secretion	
				Topfer		Phenol-phthalein							
				Salmon	Lemon								
		cc.	*cc. per 10 minutes*	*m.Eq. per liter*	*m.Eq. per liter*	*m.Eq. per liter*	*m.Eq. per liter*	*m.Eq. per liter*	*m.Eq. per liter*	*m.Eq. per liter*	*m.Eq. per 10 minutes*	*m.Eq. per 10 minutes*	
Fundus	10:59–11:23	0	0										
	11:23–11:34	10	9.1	38	60	72	151			42	0.54		Tinged with blood
	11:34–11:44	11	11.0	93	110	118	157	14	34	20	1.21	0.37	Very thin, watery, clear
	11:44–11:59	16	10.7	121	134	139					1.43		
	11:59–12:11	11	9.2	129	141	146					1.30		
	12:11–12:22	13	11.8	125	141	146	158	11	17	8	1.66	0.20	
Pylorus*	10:59–12:22	3	0.36	−23	−12	2	141	29	156	60		0.56	Thick mucus
Duodenum	10:59–12:22	14	1.69	−87	−46	2	117	14	163	41		0.28	Blood stained thin fluid

* Because the specimens for analysis were small and measured with great difficulty owing to the highly viscous mucus, these figures are only roughly approximate.

ually. The difference, which includes the sum of the errors of the three methods, ranges from −4 to +15 m.Eq. per liter with a mean of +4.04. This mean figure agrees approximately with the few analyses made for Ca, giving about 2 m.Eq. per liter, and for Mg, giving about 1 m.Eq. per liter. Total base concentrations in our data range from 18 to 101 m.Eq. per liter with variations from period to period in a given fractional study of from 10 to 65 m.Eq. per liter. Attention directed to total base concentration seems to us less illuminating than to K^+ concentration and rate of Na^+ secretion. Total phosphorus was measured in 18 specimens from 6 of the early cases studied. In 11 specimens from 3.0 to 0.2 mM per liter of PO_4 was found, and in 7, less than 0.1 mM. per liter. It was higher in the fasting contents. It was not followed further.

We have measured the pepsin concentration in several of our observations following histamine stimulation. It suffices to record that no consistent correlation of pepsin concentration with curve of secretion or acidity was observed. The pepsin concentration was as a rule more constant than either rate of secretion or acidity. Sodium concentration varied from 2 to 81 m.Eq. per liter.

That histamine stimulates frequently the secretion of a juice high in HCl, undiluted by test meal, is apparent both in our studies and in those of others. As will be pointed out by Gammon and Miller (1931) in a more extensive clinical study of the histamine test it is probable that the conditions of the histamine test, lacking as it does any diluting meal, do not afford opportunity for demonstrating the tendency, which Michaelis (1926) points out as characteristic of the normal stomach, of secreting enough acid to bring the pH of its contents to a relatively constant value, indicated by a free HCl of about 20 to 40 m.Eq. per liter. If this be true, a most important regulating mechanism, highly characteristic of normal gastric function, is masked under the conditions of the histamine test.

EXPERIMENTAL STUDIES

For comparison with the clinical material, we studied with the same chemical methods the secretion of fundic pouches in dogs after stimulation by food and by histamine. For the preparation of these pouches we are indebted to Dr. I. S. Ravdin, Professor of Surgical Research.

Dog I, male, weight 13 kilos, was operated upon on October 4, 1929 by Dr. I. S. Ravdin who constructed a Pawlow pouch in the fundus of the stomach. Juice was collected during the periods of study by continuous aspiration through a fenestrated tube introduced into the pouch and leading to a collecting bottle. The animal was fed once daily on an adequate ration of casein, sugar, lard, salts, and vitavose. Weight was maintained approximately constant and the dog remained in good condition.

Three feeding experiments (IF1, IF2, and IF3) were conducted, in each of which, after commencing the collection of pouch contents, the daily feeding was given and the contents of the pouch collected, for 24 hours in the first two experiments and 10⅓ hours in the third. These experiments were conducted on November 15, November 25, 1929 and January 2, 1930. Two histamine experiments (IH1, and IH2) were conducted on November 19, and November 22, 1929. In these experiments the collection from the pouch was commenced in the fasting dog; histamine acid phosphate was injected subcutaneously. On November 19th, 5 cc. of 1:1000 solution were injected which resulted in marked conjunctival congestion and excitement; on November 22nd, 3 cc. of 1:1000 solution were injected and resulted in slight conjunctival congestion and a mild degree of restlessness. The dog drank water frequently. The collection was continued until the secretion had ceased which occurred after 3½ and 2½ hours respectively.

Dog II, male, weight 11.5 kilos, was operated upon on October 11, 1929 by Dr. I. S. Ravdin and a Heidenhain pouch constructed in the fundus of the stomach. Studies were conducted in a manner similar to those on Dog I. Two feeding experiments (IIF1 and IIF2) were performed on November 15, and 25, 1929, and a histamine experiment (IIH1) on November 22, 1929. In the latter, 3 cc. of 1:1000 solution of histamine were given subcutaneously and resulted in conjunctival congestion, mild excitement, slight incoordination, and apparent confusion.

Because of great variation in rate of secretion it was not considered practical to divide the collection over predetermined intervals. Instead the periods of collection were closed as sufficient juice for analysis had accumulated, the collecting tubes being emptied as completely as possible at the close of each period and the time of each period noted. The tabulation of the results is rendered somewhat difficult for this reason. We have accordingly prepared Chart 1 in which each of the components is presented for each period of each experiment either with respect to concentration or rate of secretion in horizontal blocks which represent the duration of the period and its location in time with respect to the stimulation by food or histamine. In only one experiment, IF3, were we able to collect any secretion before stimulation.

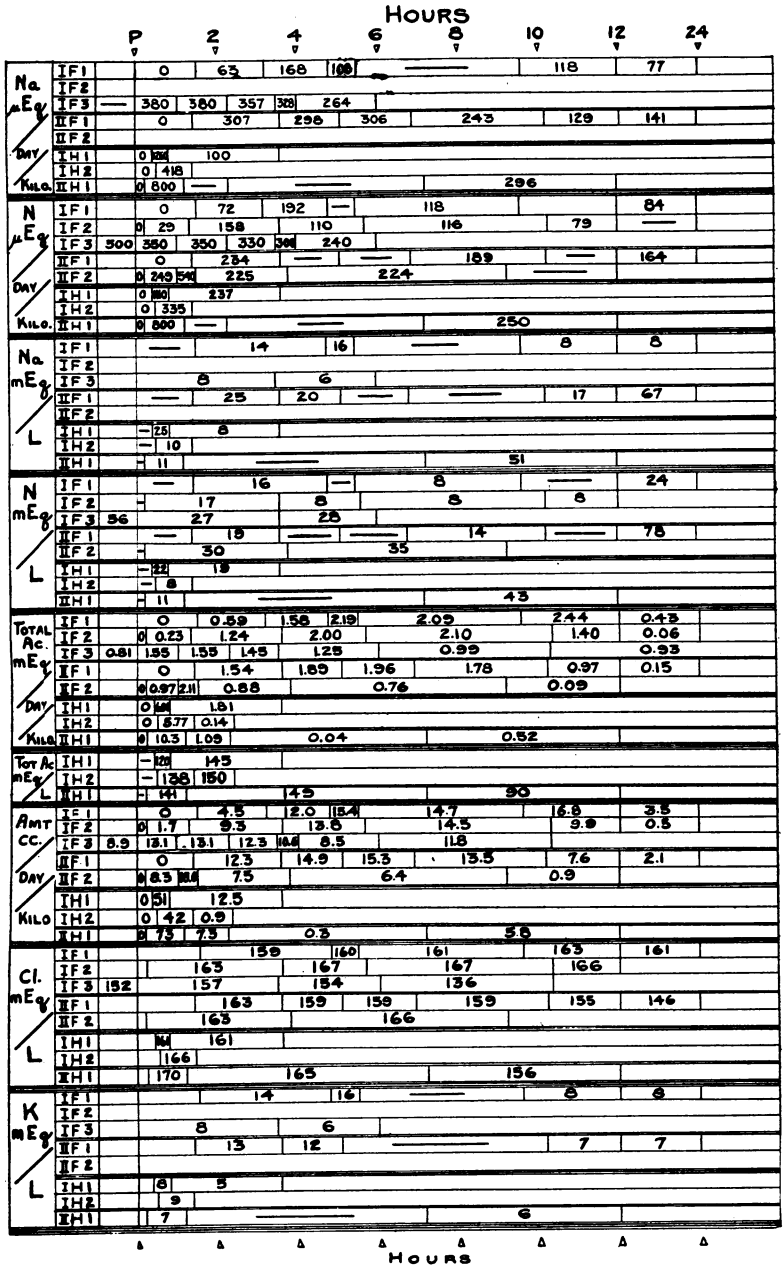

CHART 1. EXPERIMENTS ON FUNDIC POUCHES IN DOG I, PAWLOW POUCH, AND DOG II, HEIDENHAIN POUCH

F indicates stimulation by feeding; *H*, stimulation by histamine. *P* indicates the time of stimulation. Figures show rate of excretion or concentration of the various constituents for the period in hours indicated by the position and length of the block in which the figure is placed. Zero time, "*P*," indicates the time of feeding or giving histamine. Dash in a block indicates no measurement made during that period.

RESULTS

Feeding experiments

Rate of secretion. The secretion, except in experiment IF3, began from 10 to 90 minutes after feeding. In each animal the secretion began earlier in successive experiments, which suggests that nervous factors may have delayed the beginning of secretion in the earlier experiments. The secretion when established was of many hours duration and was usually maximal at about 4 to 10 hours after feeding.

Chloride concentration remained almost constant through most of each experiment but there was a moderate fall toward the end of two of the experiments, IF3 and IIF1.

Total HCl was measured to the phenolphthalein end point. Differing in this respect from our studies on human gastric juice, in the juice from the pouches the sum of the equivalents of total HCl measured to phenolphthalein plus equivalents of total base agreed more closely with the total chloride than did the sum of base and the total HCl measured to the lemon point of Topfer's indicator. Buffer substances in the juice from the pouches and in our human gastric juice would seem therefore to differ. Total HCl ranged in concentration from 72 to 145 m.Eq. per liter and was always above 91 in the first juice collected. Free HCl values were from 47 to 136 and above 68 in the first juice collected. As could be expected from the moderate variation in acid concentration the rate of acid secretion followed approximately the rate of volume secretion.

Potassium concentration when studied ranged from 6 to 16 m.Eq. per liter with a tendency to lower values toward the close of the period of secretion.

Sodium secretion followed almost the same curve as the acid and volume secretion, with a disproportionately high secretion in the resting 12 hour period studied at the end of IIF1. In this period the Na concentration was 67 m.Eq. per liter. Otherwise the concentrations were from 6 to 25 m.Eq. per liter.

Nitrogen secretion was closely correlated with the Na secretion and both were high when the juice was conspicuously mucoid in character.

Histamine experiments

These experiments were characterized by an extraordinarily great outpouring of secretion during the first hour at a rate three or four times the maximum attained after feeding but ceasing after $2\frac{1}{2}$ to $3\frac{1}{2}$ hours. The composition of the secretion was not significantly different from that which followed feeding. The earlier crest of sodium than of acid secretion which we noted in the high acid group of our clinical material is manifested by the data on Na concentration in experiment IH1 and by the fact that the maximal acid concentration occurred always in the period following the maximum rate of volume secretion and of sodium concentration and secretion.

Experiment designed to separate secretion from fundus, pyloric end of stomach and duodenum

Protocol. On April 23, 1930, a dog of about 12 kilos weight which had been fasted 12 hours was anesthetized with amytal anesthesia. At 10 A.M. the abdomen was opened. Four long-jawed clamps protected with rubber were applied to divide the lumen of stomach and duodenum into three portions, care being taken to interfere as little as possible with the blood supply. The first closed the oesophagus at its entrance to the stomach. The second divided the fundus from the pyloric end of the stomach along a line from the angulation of the lesser curvature to the junction of the splenic and pancreatico-duodenal arterial supply of the greater curvature. The third occluded the duodenum at the junction of first and second parts. The fourth was placed a little below the ampulla of Vater. The common bile duct was ligated. Bile was excluded from the duodenum, but not pancreatic juice. Three small incisions were made admitting fenestrated tubes into the fundus, the pyloric end of stomach, and the duodenum opposite the ampulla of Vater respectively. At 10.55 the stomach was emptied. At 10.59 histamine acid phosphate, 2.5 cc. of 1:1000 solution, was injected subcutaneously. Continuous aspiration from the three tubes was maintained until 12.22 with collection of secretion as shown in table 5. Violent peristalsis was noted in stomach and duodenum beginning about 11.02 and persisting with varying intensity for most of the experiment.

Results. In table 5 are collected the analytical data. It is evident in this experiment that the secretion from the pyloric end was negligible in quantity consisting of thick mucus. The secretion of the fundus was similar in character to that of our clinical experiments and fundus pouches. It exhibited the crest of Na secretion early, followed by maximal acid secretion later, as in our other experiments.

It also showed the correlation of Na^+ and N and the more constant K^+ concentration.

SUMMARY

The studies presented furnish direct measurement of the rate of Na and K secretion following histamine stimulation in patients and after stimulation by both feeding and histamine in fundic pouches in dogs.

They indicate that the period of maximal sodium secretion after histamine is before the period of maximal acid secretion and not as the acid secretion is subsiding. A late increase in Na secretion was inferred by MacLean and Griffiths (1928) from the increase in neutral chloride in the gastric juice during subsidence of acid secretion following various types of stimulus other than histamine. The occasional increase in sodium concentration in this period in our studies is due to fall in acid secretion and not due to increased rate of sodium secretion.

The rate of nitrogen and sodium secretion in the low acid group is approximately the same as in the high acid group, not any higher.

Potassium from its constancy of concentration appears to be a constituent in about the same concentration in the gastric secretion whether this be highly acid or neutral.

The correlation in rate of secretion of sodium and of nitrogen suggests that they are constituents of one part of the gastric secretion, a part which appears to be mucoid in character.

Our results appear to be consistent with the studies of Gamble and McIver (1928) and Polland, Roberts, and Bloomfield (1928).

The course of secretion in the fundus pouches is sufficiently like that in the gastric contents of our patients to suggest that the major factor in determining the character of the gastric secretion obtained in our patients is the secretion of the fundus.

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