STUDIES OF THE CHEMICAL MECHANISM OF HYDROCHLORIC ACID SECRETION

I. Electrolyte Variations in Human Gastric Juice

By H. A. BULGER, C. M. STROUD, and M. L. HEIDEMAN

(From the Department of Internal Medicine, Washington University School of Medicine, and Barnes Hospital, St. Louis, Missouri)

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INTRODUCTION

The literature on the chemistry of gastric secretion contains extensive data concerning hydrochloric acid variations and numerous studies of the changes in concentration of chloride but there are very few observations on the other electrolytes. In the present investigation fluctuations in the base, phosphate and chloride were determined in human gastric juice. It was expected that the data thus obtained would give some indication of the mechanism by which a strongly acid secretion is produced from slightly alkaline blood and possibly some insight into the pathology of gastric secretion. While this work was in progress the account of the beautiful and significant experiments of Gamble and McIver (1) appeared showing the relative changes of base and chloride in the secretion of the Pavlov pouches of dogs.

METHODS

In any study of the chemistry of gastric contents special care must be taken that one is dealing with actual secretion. It is remarkable that only in the past few years has much rational consideration been given to the influence which factors inherent in methods may have on the results obtained from gastric analysis. Gorham (2) appears to be chiefly responsible for calling attention to these factors which are rather obvious but had never been properly emphasized. By far the most important factor is the influence of dilution which may be affected by the test meal itself. Gorham used 400 cc. of water to stimulate the secretion. In the water he placed phenolsulphonephthalein. Assuming that no significant amounts of either water or phenolsulphonephthalein were absorbed by the stomach, he calculated the water in the secretion by means of the percentage of

phenolsulphonephthalein which remained. In the following studies this procedure has been used as carefully as possible and the results of analysis have been corrected accordingly.

Subjects were studied in the morning while fasting. They were instructed to drink no water and to swallow no saliva until the examination had been completed. The studies were usually made an hour or more after the usual breakfast time. At this late hour it was surprising how frequently considerable acid was found in the fasting contents. It seemed possible that we might be dealing with a periodic secretion occurring at the usual time for breakfast. Though the procedure was most often carried out in the laboratories adjoining the wards, patients had seen others eating their breakfasts, and it is possible that the secretion was the result of psychic stimulation. However this may be, numerous acid specimens were obtained without corresponding specimens free from acid and suitable for comparison. After the stomach was emptied as completely as possible the subject was given 400 cc. of water containing 1 cc. of phenolsulphonephthalein solution usually employed for kidney function tests, about 10 cc. of the mixture being withheld to use as a standard. At a given interval the stomach was again completely emptied and the material mixed thoroughly. In a few instances small specimens were obtained at given intervals by aspirating, mixing and returning the secretion several times before a fraction of the contents was preserved for analysis.

The acid and phenolsulphonephthalein determinations were made as soon as possible. The determination of phenolsulphonephthalein was not always satisfactory. Alkalization was usually accompanied by a precipitate of protein which was removed by centrifuging. Occasionally there resulted a slight cloudiness which made comparison with the standard difficult. The possible error was estimated by adding known amounts of phenolsulphonephthalein to gastric juice and following the same procedure. Although errors as high as 15 per cent were sometimes obtained the fact does not seem to detract from the general conclusions to be drawn. Excess strong acid was determined by titrating with Toepfer's reagent to pH 3.7 to 4.0. This will be referred to without further discussion as free hydrochloric acid. By total acid is meant the amount of alkali which was required to produce the first faint color to phenolphthalein. Chloride was determined by the Volhard-Harvey method. Values for phosphate were obtained by the method of Benedict and Theis (3) after removing protein by trichloracetic acid. In some specimens it was impossible to determine phosphate because of the cloudiness which developed.

Total base was determined by a modification of Fisk's urine method (4). Considerable difficulty was experienced in obtaining accurate results in the presence of phosphates by various adaptations to blood analysis which had been suggested. By modifying the procedure by which sulphate was precipitated with benzidine and by titrating directly, total base could be determined with an accuracy of 1 per cent in inorganic solutions containing 150 mM. of base and 10 mM. of phosphate. The base in the form of sulfate and phosphate salts was

obtained in a manner essentially the same as that described by Stadie and Ross (5). The residue was dissolved in 10 cc. of water and any slight residue of sulphuric acid was titrated with 0.02 N NaOH. After adding 1 cc. N hydrochloric acid to the solution it was placed on the steam bath for 30 minutes to convert metaphosphate to orthophosphate. A dilute benzidine solution was then added very slowly, one drop at a time with vigorous stirring to prevent adsorption of benzidine phosphate by the precipitate. The 15 per cent stock solution of benzidine hydrochloric acid was diluted one to four and 8 cc. were used in each determination. After about 10 minutes the precipitate was filtered through a 5.5 cm. ash-free filter and the beaker and filter washed with 95 per cent acetone, first with three 1 cc. portions and then with three 3 cc. portions. The filter was then returned to the same beaker, and 10 cc. of water and a drop of 0.08 per cent phenol red added. The contents were heated to boiling and while hot were titrated with 0.02 N NaOH to the first pink color which persisted with further boiling. A considerable error was noted which might be caused by carbonate in the 0.02 N NaOH solution. This solution should be prepared as free as possible from carbonate. During each titration, before the endpoint is reached, and while the mixture is still distinctly acid it should be boiled and vigorously stirred for about thirty seconds or more. The base combined with phosphate in determinations upon accurately prepared inorganic solutions was constantly in the proportion of one mM. of base for each mM. of phosphate. To the benzidine titration in the case of unknown solutions, an equivalent correction therefore was added. In this series when phosphate was not determined an arbitrary value of 6 mgm. per 100 cc. was taken in making this correction.

EXPERIMENTAL

Numerous studies of the changes in concentration of chloride in gastric juice have indicated that the curve of chloride secretion is similar to and only slightly higher than the curve of hydrochloric acid secretion. Curiously many of these reports have not included the chloride determinations on the fasting contents. When this has been included the concentration has been similar to that found an hour or so after the test meal. It seems quite probable that the lower concentrations which were found early in the curve were due to dilution by the test meal. Gorham, Stroud and Huffman (6) have made similar studies but corrected their data for dilution and find that the chloride concentration remains about the same throughout. The extent to which dilution may obscure the true electrolyte concentration in the secretion is illustrated in the studies recorded in table 1 where the data both before and after correction are given.

In the tables the concentration for all electrolytes except phosphate is expressed as the equivalent of 0.1 N acid or base per 100 cc. of secretion. The notations in the columns headed "time" indicate first whether the secretion was collected from the fasting stomach or after the test meal and secondly the interval between the test meal and the collection.

Some examples of characteristic changes in the electrolytes of gastric juice associated with the secretion of hydrochloric acid are

TABLE 1

Changes in gastric secretion following test-meal showing especially the effects of dilution

(Data are expressed as equivalent cc. of 0.1 N acid or base per 100 cc.)

Case number	Time	Analysis of gastric secretion as obtained				Corrected for dilution indicated by the phenolsulphonephthalein		
		Base	Chloride	Free HCl	Phenol-sulphone-phthalein	Base	Chloride	Free HCl
		cc.	*cc.*	*cc.*	*per cent*	*cc.*	*cc.*	*cc.*
12	Fasting	110	99	0		110	99	0
	½ hour	31.5	51	19	49	62	100	38
31	Fasting	118	120	0		118	120	0
	¾ hour	45	54	12	56	102	122	28
22	Fasting	97	85	0		97	85	0
	1 hour	43.5	73	24	25	58	98	32
	1–½ hour	50	110	53	3	51	114	55
	2 hours	72	102	20	Trace	72	102	20
30	Fasting	104	136	39		104	136	39
	¾ hour	55	135	68	15	65	159	80
28	Fasting	113	107	0		113	107	0
	¾ hour	11.5	24.8	11	80	58	124	5

collected in table 1. The data from the first two cases shows what has been found most frequently, little change in the chloride concentration after a considerable increase in acid. They also show that the increase in acid has been accompanied by a corresponding decrease in base. Less frequently a definite increase in chloride has been noted as is indicated by the next three examples. But even here the decrease in base generally plays the more prominent rôle.

This is in agreement with the work of Gamble and McIver (1) on the secretion of Pavlov's pouches in dogs, in which it was found that during hydrochloric acid secretion the chloride level remained relatively constant but the base fell in proportion to the increase in acid. In table 2 are grouped thirteen studies where specimens containing free hydrochloric acid were obtained shortly after satisfactory specimens of fasting gastric contents, i.e., fasting specimens which did not

TABLE 2

Examples of the usual changes in gastric secretion associated with hydrochloric acid production

(The data have been corrected for dilution and are expressed as the equivalent cc. of 0.1 N acid or base per 100 cc.)

Case number	Fasting					Interval	After test meal				Phosphate
	Base	Chloride	Free HCl	Total acid	Phosphate		Base	Chloride	Free HCl	Total acid	
	cc.	*cc.*	*cc.*	*cc.*	*mgm. per cent*	*hours*	*cc.*	*cc.*	*cc.*	*cc.*	*mgm. per cent*
1	77	94	0	15	6.0	¾	53	89	28	50	5.0
4	95	97	0	18	5.3	¾	70	95	10	14	4.3
8	116	103	0	14	4.8	1	52	97	52	68	6.8
9	104	94	0	15		½	71	85	22	38	
12	110	99	0	31		½	62	101	38	94	
15	101	82	0	4	6.9	1	56	100	32	51	4.8
15	122	102	0	3	8.6	1½	61	111	27	41	7.4
17	103	96	0	15		1	71	84	10	26	
22	97	85	0	19	5.9	1	58	98	32	60	6.7
22	97	85	0	19	5.9	1½	51	114	55	69	5.3
33	97	85	0	19	5.9	2	72	101	20	40	5.6
28	113	107	0	12		¾	58	124	55	75	
31	118	120	0			¾	102	122	22		
Average..	104	96	0	15	6.2		64	102	31	52	5.5

contain free acid. The data here, and in the remaining tables, have been corrected for the dilution. The average of this group probably illustrates more exactly the usual changes during hydrochloric acid secretion. We may consider the averages of the two groups as ordinary specimens of gastric chyme the second containing in 100 cc. the equivalent of 31 cc. of free hydrochloric acid. With this increase in hydrochloric acid the total chloride increased only the equivalent of 6 cc. but there was a decided drop of 40 cc. in the base.

It appears that, during hydrochloride acid production by the stomach, chloride continues to be secreted at about the same concentration as in the fasting state. This is somewhat similar to the concentration of chloride in serum. In other words chloride ions and water leave the blood at the same relative rate, maintaining

TABLE 3

Analysis of gastric chyme from cases with achlorhydria

(Data are expressed as equivalent cc. of 0.1 N acid or base per 100 cc.)

Case number	Time	Base	Chloride	Free HCl	Total acid	Phosphate
		cc.	*cc.*	*cc.*	*cc.*	*mgm. per cent*
2	Fasting	92	71	0	4	9.5
2	¾ hour	60	45	0	5	10.9
3	Fasting	111	78	0	11	3.4
3	¾ hour	91	60	0	9	11.6
5	Fasting	83	59	0	9	8.7
5	¾ hour	79	51	0	15	5.9
14	Fasting	66	65	0	0	5.9
14	½ hour	76	60	0	16	9.9
14	1 hour	65	60	0	20	7.2
14	1 hour	105	99	0	24	9.8
14	1½ hours	71	75	0	26	6.2
19	Fasting	85	58	0	0	
19	½ hour	82	54	0	0	11.8
19	Fasting	72	68	0	12	8.5
19	1 hour	111	81	0	0	10.4
19	1½ hours	87	67	0	3	9.7
19	Fasting	73	50	0	11	9.5
19	2 hours	73	48	0	9	8.7
20	Fasting	65	48	0	1	4.1
20	1 hour	92	49	0	2	7.6
20	1½ hours	82	46	0	3	10.8
25	Fasting	92	74	0	0	10.2
25	¾ hour	107	75	0	0	
Average.....		84	50	0	8	8.7

about the same relationship as in the serum; acid is freed by retention of base.

The extent of the variations found in a larger number of specimens of gastric juice are recorded in tables 3, 4, 5 and 6, specimens being grouped according to their acid content. The first and second groups (tables 3 and 4) contained no free hydrochloric acid. Those in the

first group (table 3) were from cases which, as far as could be determined, were examples of true achlorhydria. All were cases of pernicious anemia except two; one (case no. 3) was considered a case of sprue, the other (case no. 14) an instance of post-diphtheritic neuritis, which later, after marked improvement again showed ability to secrete acid. In table 3, the electrolytes showed a rather striking contrast to the specimens without free hydrochloric acid of table 4

TABLE 4

Analysis of gastric chyme which contained no free hydrochloric acid. From cases which were known to have the power to secrete acid

(Data are expressed as equivalent cc. of 0.1 N acid or base per 100 cc.)

Case number	Time	Base	Chloride	Free HCl	Total acid	Phosphate
		cc.	*cc.*	*cc.*	*cc.*	*mgm. per cent*
17	Fasting	98	106	0	8	4.5
17	½ hour	128	104	0	23	15.5
17	Fasting	95	94	0	1	5.5
17	1 hour	93	104	0	11	8.2
17	Fasting	85	109	0	25	6.5
17	Fasting	103	96	0		
12	Fasting	110	99	0	30	
13	Fasting	130	117	0	18	4.6
15	Fasting	101	82	0	4	6.9
15	Fasting	122	102	0	3	8.6
15	2 hours	126	100	0	14	8.7
15	Fasting	123	92	0	5	8.1
4	Fasting	95	97	0	18	5.3
8	Fasting	116	103	0	14	4.8
9	Fasting	104	94	0	15	
31	Fasting	118	120	0	21	
22	Fasting	97	85	0	19	5.9
28	Fasting	113	107	0	12	
14	1½ hours	93	109	0	14	13.7
Average.....		108	101	0	14	7.6

which were obtained from other individuals who were known to have the power to secrete acid. The chloride was quite low and the base was also reduced. The average of this group showed a greater excess of base over the chloride than the next group (26 cc. as compared with 7 cc. equivalent). In the next two groups, tables 5 and 6, the secretion contained various amounts of free hydrochloric acid. In table 5

where the acid never exceeded 30 cc. the average concentration of chloride showed little variation from the comparable material without free hydrochloric acid in table 4, illustrating again the decrease in base rather than an increase in chloride when free hydrochloric acid is produced. Specimens showing excessive free hydrochloric

TABLE 5

Analysis of gastric chyme containing moderate amounts of acid

(Data are expressed as equivalent cc. of 0.1 N acid or base per 100 cc.)

Case number	Time	Base	Chloride	Free HCl	Total acid	Phosphate
		cc.	*cc.*	*cc.*	*cc.*	*mgm. per cent*
16	Fasting	84	115	18	30	5.9
17	1½ hours	82	120	2	8	7.0
17	Fasting	82	98	5	17	6.4
17	2 hours	81	101	6	21	6.7
17	1 hours	71	84	10	26	
18	Fasting	99	104	10	15	2.3
21	2 hours	105	121	17	30	
21	Fasting	87	119	17	28	
22	2 hours	72	101	20	40	5.6
23	1 hour	105	128	16	34	17.0
23	Fasting	90	96	8	11	3.7
27	Fasting	116	128	1	18	3.8
1	Fasting	77	94	1	15	6.0
1	¾ hour	53	89	28	50	5.0
4	¾ hour	70	95	10	14	4.3
7	1 hour	89	91	2		
11	Fasting	69	108	15	25	6.0
12	Fasting	78	79	10	30	
14	Fasting	81	90	14		
14	1 hour	75	106	27		
15	1½ hours	61	111	27	41	7.4
9	½ hour	71	85	22		
31	¾ hours	102	122	22		
27	Fasting	80	115	26		5.3
Average.....		79	104	14	26	5.7

acid are collected in table 6, and exhibit a number of examples of higher chloride concentration. It appears that this group cannot very well be compared with that in table 4, since comparable specimens of gastric juice free from acid were not obtained in most cases. The corresponding fasting secretion generally contained acid and high

chloride. In this group are sixteen examples of chloride concentrations higher than that ordinarily found in serum. It is not likely that these findings can be explained by errors in phenolsulphonephthalein determination and thus by excessive correction for dilution. Chloride concentrations as high as this have been obtained in pure secretion after histamine stimulation. The data indicate that the

TABLE 6

Analysis of gastric chyme containing considerable acid

(Data are expressed as equivalent cc. of 0.1 N acid or base per 100 cc.)

Case number	Time	Base	Chloride	Free HCl	Total acid	Phosphate
		cc.	*cc.*	*cc.*	*cc.*	*mgm. per cent*
8	1 hour	52	97	52	68	6.8
10	Fasting	66	97	47	63	
10	1 hour	51	108	68	80	
11	1 hour	57	123	50	60	4.6
11	Fasting	51	118	71	77	
11	Fasting	89	128	32	42	
11	2 hours	91	123	33	77	3.5
16	1½ hours	76	125	43	55	1.2
16	Fasting	70	101	34	38	5.5
16	Fasting	83	133	31	44	4.6
21	½ hour	83	124	41	52	
21	1 hour	100	138	42	51	
21	1½ hours	97	140	39	49	
22	1½ hours	51	114	55	69	5.3
22	1 hour	58	98	32	60	6.7
26	Fasting	90	128	51	64	5.1
28	¾ hour	56	124	55	75	
29	¾ hour	67	128	68	74	2.0
30	¾ hour	65	159	80	88	
30	Fasting	104	136	39	54	
12	½ hour	62	101	38	93	
15	1 hour	56	100	32	51	4.8
27	¾ hour	79	108	31	43	4.6
Average.....		73	120	46	62	4.5

stomach can secrete chloride ions at a somewhat higher concentration than in the serum. The highest figures which have been obtained approach the molar value of serum total base, or in other words, the level of the serum electrolytes. The fact remains that the chloride in gastric secretion does not deviate far from the chloride concentration of the serum.

The phosphate fluctuations found in the gastric secretion are of considerable interest. The average variations in tables 3, 4, 5 and 6 are as follows:

	mgm. of inorganic P per 100 cc.
Achlorhydria specimens	8.7
Other specimens without HCl	7.6
With free HCl 1 to 30 cc	5.7
With 31 to 80 cc. of free HCl	4.5

It is apparent that the phosphate concentration is almost invariably greater in gastric secretion than in serum. In some in-

TABLE 7

Data showing variations in phosphate grouped according to whether free hydrochloric acid was or was not produced as a result of stimulation

HCl secretion with test meal		No HCl secretion with test meal	
Fasting	After stimulation	Fasting	After stimulation
mgm. per 100 cc.	*mgm. per 100 cc.*	*mgm. per 100 cc.*	*mgm. per 100 cc.*
6.0	5.0	9.5	10.9
5.3	4.3	3.4	11.6
4.8	6.8	4.5	15.5
6.0	4.6	5.5	8.2
6.9	4.8	8.5	10.4
8.6	7.4	4.1	7.6
5.9	3.7		
5.5	1.2		
4.6	4.1		
5.9	6.7		
Average 6.0	4.9	5.9	10.6

stances it is quite high. From 63 determinations there were nine in which the inorganic phosphorus concentration was greater than 10 mgm. per 100 cc. It also seems evident that there is a decrease in phosphate with increase in acid. One would suspect that salts with buffer values like the phosphates might play a prominent part in the mechanism by which hydrochloric acid is secreted by the stomach. There is nothing in this work, however, which would indicate this. In table 7 the data showing variation in phosphate are placed in two groups according to whether free hydrochloric acid was or was not

produced as the result of stimulation. If free hydrochloric acid was produced there was a decrease in phosphate; while if no free hydrochloric acid was produced there was an increase. Studies in this laboratory have shown that saliva contains considerably more phosphate than blood serum, confirming earlier reports in the literature. Any dilution of gastric juice with saliva will therefore result in a higher concentration of phosphate. The subjects of these experiments showed admirable coöperation and, as far as one could detect, swallowed little or no saliva just before or during the period of examination. But this effect cannot be ruled out in any individual case and may possibly account for phosphate fluctuations in some instances. If the secretion of the mucous glands of the stomach is similar to saliva, the possibility of an analogous effect by such secretion is evident. It seems probable that as a result of the secretion of the mucous glands, gastric juice contains more phosphate than blood serum. If hydrochloric acid secretion containing less phosphate is produced in larger amounts than the secretion of the mucous glands, a fall in phosphate will result due to dilution. Or if a stimulus causes an increased activity of the mucous glands with little or no hydrochloric acid production the concentration of phosphate will increase.

The presence of the secretion from mucous glands may also explain certain variations in chloride. Saliva contains relatively small amounts of chloride and any dilution of gastric juice with saliva will result in a lower concentration of chloride. But with the care taken to exclude this factor it must have been relatively unimportant in these studies. It seems reasonable to believe that variations in the relative amounts of mucous gland secretion in gastric chyme may have an important relationship to the low chloride content which has been observed in the secretion from cases with achlorhydria and in those in which alterations in chloride were associated with various degrees of acidity.

CONCLUSIONS

Relatively little change in the concentration of chloride in human gastric fluid attends acid secretion, but, during secretion, the total base falls in proportion to the increase in acid. It appears that

chloride ions and water leave the blood in the same relative concentration as in serum, acid being liberated by a retention of base.

The concentration of phosphate in gastric contents is generally much greater than in serum. If stimulation does not result in hydrochloric acid secretion the concentration of phosphate as a rule increases. If much acid is produced, however, the concentration falls. The variation in phosphate may be attributed to fluctuations in the relative amounts of secretion from the mucous glands.

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PROTOCOLS

Case 1. A man 35 years old with severe diabetes mellitus complicated by chronic diarrhea. At the time of the gastric analysis he was markedly emaciated and there were several extensive, indolent but freely draining subcutaneous abscesses over his back. Pancreatic ferments were present in the duodenal fluid. Diarrhea was eventually relieved only by hydrochloric acid and atropine per os.

Case 2. A man 59 years old with pernicious anemia complicated by chronic ulcerative colitis and bilateral cataract.

Case 3. A man 35 years old with diarrhea for four years. There was a slight anemia and slight atrophy of the tongue but no neurological symptoms.

Case 4. A man 47 years old complaining of constipation for fifteen years. He had considerable epigastric distress after eating but rarely vomited. No organic disease was demonstrated.

Case 5. A man 45 years old with pernicious anemia. For 6 years he had had frequent attacks of vomiting.

Case 6. A man 74 years old who complained of a dull pain in the right upper

quadrant. He had vomited at infrequent intervals. There was a mass in the right side of the abdomen which X-ray showed to be extra-alimentary. This was considered a hypernephroma. His condition was too poor to warrant an exploratory operation.

Case 7. A woman 46 years old complaining chiefly of pain in the epigastrium soon after eating and occasional vomiting. She had had one gastric hemorrhage. The diagnosis of gastric ulcer was not confirmed by x-ray.

Case 8. A man 56 years old complaining of abdominal distention and epigastric pains shortly after meals. On several occasions stools contained blood. Diagnosis of gall-bladder disease was made.

Case 9. A colored woman 28 years old with pain in the lower abdomen. No diagnosis made other than chronic constipation.

Case 10. A man 20 years old with pain in the upper abdomen about one hour after eating and marked constipation. No organic disease demonstrated.

Case 11. A man 23 years old presenting neurological signs, a residual of epidemic encephalitis. There were no gastrointestinal symptoms.

Case 12. A white woman 44 years old, complaining of a mass in upper abdomen and cramplike pains after eating. X-ray showed the mass was probably liver. Wasserman reaction ++++. Her condition improved with anti-luetic treatment.

Case 13. A woman 50 years old complaining of headache and pain in the upper abdomen. No organic disease of the gastro-intestinal tract was made out.

Case 14. A boy 18 years old who had diphtheria 2 months before admission to the hospital. Two weeks after the acute symptoms subsided he gradually developed paralysis of the lower extremities and occasionally had regurgitation of food and liquids through the nose. There were no gastro-intestinal symptoms. At the time of the first gastric-analysis, symptoms were marked. They had practically cleared at the time of the last examination.

Case 15. A man 41 years old who entered the hospital because of an irregular heart. This was found to be due to auricular extrasystoles. He had had more or less constipation for years but no other gastro-intestinal symptoms.

Case 16. A colored man 49 years old with pain in the abdomen unrelated to meals. There was no nausea or vomiting. No diagnosis was made other than chronic constipation.

Case 17. A man 30 years old complaining of weakness and epigastric distress after eating. No organic disease demonstrated.

Case 18. A women 22 years old with pain in the epigastrium, usually after meals. The pain radiated to the back and was relieved by belching. No diagnosis other than spastic constipation was made.

Case 19. A woman 48 years old with pernicious anemia complicated with pyonephrosis and hypotension. Duration of symptoms about ten years.

Case 21. A man 51 years old with hypertrophic arthritis of the spine and syphilis. No gastro-intestinal symptoms.

Case 22. A man 51 years old with chronic B. coli pyelitis and without any gastrointestinal symptoms.

Case 23. A man 26 years old with extensive psoriasis. No gastro-intestinal symptoms.

Case 24. A man 23 years old with chronic constipation for several years and epigastric distress after meals. No organic disease was demonstrated.

Case 25. A man 44 years old with typical pernicious anemia.

Case 26. A man 44 years old with a multiplicity of complaints including general malaise, pain in the epigastrium and pain in joints. There was a moderate degree of chronic constipation. No organic disease demonstrated.

Case 27. A man 27 years old with central nervous system lues. For about two years he had had burning in the epigastrium one hour after meals. X-ray of the gastro-intestinal tract was negative.

Case 28. A man 54 years old with a diagnosis of syphilis of the cerebro-spinal meninges and bilateral glaucoma. There were no gastro-intestinal symptoms except chronic constipation.

Case 29. A man 33 years old with a typical history and x-ray findings of duodenal ulcer. There had been no vomiting.

Case 30. A man 27 years old complaining of chronic constipation, loss of appetite, and weakness for about 8 months. No organic disease was demonstrated.

Case 31. A man 62 years old with multiple diverticula of distal colon and carcinoma of the colon. He had had symptoms for 5 years consisting chiefly of dull epigastric pain. Rarely had he had nausea and vomiting. There was a history of syphilis and the Wassermann reaction was positive.