THE ABSORPTION AND EXCRETION OF CALCIUM AND PHOSPHORUS IN THREE PATIENTS WITH COLOSTOMY AND ILEOSTOMY

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It is generally believed that calcium and phosphorus are absorbed from the small intestine and excreted through the kidneys and the colon. The chief factors which influence the absorption from the small intestine are the hydrogen ion concentration of the content of the bowel, the peristaltic rate, and the proportion of the various types of food in the diet. Macfadyen, Nencki and Sieber in 1891 (1), McClendon in 1915 (2) and numerous investigators (3, 4, 5) more recently found the content of the small intestine to be acid most of the time. The strength of the acidity decreases from a pH of about 1.5 in the stomach to approximate neutrality at the ileocecal valve. In spite of this experimental work, one commonly encounters the statement that the content of the small intestine is alkaline. The pancreatic and biliary secretions are in fact alkaline, but these secretions are readily neutralized by excess of acid secretion from the stomach and intestine. The peristaltic rate, or rate of propulsion of the intestinal content, is largely controlled by the nature and bulk of ingested food. A marked increase in the rate of propulsion of content would decrease the time for absorption of calcium and phosphorus as well as other minerals and foodstuffs and would increase the amount of materials retained in the lumen. Diets containing large amounts of fats, excesses of either calcium or phosphorus and highly alkaline diets have been shown by Farquharson, Salter, Tibbets and Aub (6) and others to decrease calcium and phosphorus absorption from the bowel, while acid foodstuffs and proper calcium-phosphorus ratios lead to increased calcium and phosphorus absorption.

In man it has not been possible heretofore to study calcium and phosphorus exchange in the small bowel independent of colonic excretion, due to the difficulty of distinguishing dietary calcium and phosphorus retained in the stool from that excreted into the intestine. An unusual opportunity for study of the interchange of calcium and phosphorus through the small intestine independent of colonic excretion was afforded by three patients in whom tumor of the cecum necessitated both ileostomy and colostomy, thereby permitting separate collection of colonic and ileal excretion.

METHODS OF STUDY

After the patients had recovered from operation they were given weighed diets composed of foods of known calcium and phosphorus content. An effort was made to give a diet as near the normal as possible. The urine was collected under toluene in twenty-four hour samples. The excreted ileal content was collected in colostomy pouches which were held against a flat piece of rubber sheeting cut to fit snugly around the base of the colostomy opening by an elastic belt. The flat rubber was pasted to the skin by a layer of yeast between the skin and rubber sheeting. In this manner no material was lost and ulceration of the skin was prevented. The colon was irrigated daily by the injection of 100 grams of distilled water into its proximal opening, and the material was collected as it was expelled through the anus. Usually about 80 per cent of the water was expelled about twenty minutes after its injection. These washings always contained a mucoid, opaque, colorless material free from feces or bile, thus showing the absence of any leakage of ileal content into the colon. The pH of all excreta was determined by the glass-electrode method as modified by Hemingway (7). The ileal content and colon washings were dehydrated either over a water bath or in an electric oven at about 95° C. No attempt was made to dehydrate to a constant weight. The dehydrated material was powdered and one gram samples of the ileal content and all of the colon washings were wet-ashed with concentrated sulphuric and nitric acids. When necessary, superoxyl was added drop by drop to obtain a colorless solution. Aliquot samples of urine were wet-ashed as above. The calcium content of the ashed material was determined by the method of Tisdall and Kramer (8) and the quantity of phosphorus determined by the method of Fiske and Subbarow (9). The ileal content corresponding with any experimental period was marked with carmine or charcoal. The identifiable substances appeared at the ileal opening two to three hours after oral ingestion. Controls on results of analyses consisted of reagent blanks, known solutions, and known solutions added to unknowns run simultaneously with the unknowns. Results not checking to within five per cent were repeated except in the colon washings,

where larger variations were expected because of the very low calcium and phosphorus content of the material analyzed.

Case 1. G. M., a 62 year old white male who was in good health until 1930, when he experienced heart burn and gas pains following meals. January, 1934, he noticed a progressive weakness and weight loss which by March, 1934, compelled him to stop work. Examination March, 1934, revealed weight loss and a palpable tumor mass in the right lower quadrant. There was an associated melena and a secondary anemia, hemoglobin 46 per cent, (Sahli, 17 grams per 100 cc. blood equals 100 per cent) and 4.75 million erythrocytes per cubic millimeter of blood. X-ray examination of the colon revealed a filling defect in the cecum through which peristalsis did not pass. March 28, 1934, the cecum, the proximal four inches of the ascending colon, and the terminal six inches of the ileum were resected because of an adenocarcinoma (microscopic diagnosis) of the cecum. The free ends of the colon and ileum were brought to the surface through a colostomy opening. One month later, when the anemia was corrected and peristalsis was normal, the patient was used for these studies. This patient is well (November 1936), and no evidence of recurrence or metastasis has been found.

Case 2. Mrs. A. R., age 63, had been constipated for twenty-five years. Prior to the last few years the patient had an occasional attack of pain in the right upper quadrant associated with chills, fever, and less often, jaundice. In 1932 she began having attacks of intermittent colicky pain in the right lower quadrant of the abdomen associated with nausea, vomiting, and abdominal distention. These attacks came on more often during 1934. She had lost twenty-two pounds of weight during the four months prior to admission in November, 1934. There was a firm, nodular, fixed mass in the right iliac fossa. The size of this mass varied considerably from time to time. X-ray examination of the colon revealed a constant irregular filling defect through which peristalsis did not pass. No shadow of the gallbladder was found at any time during a cholecystographic study. The hemoglobin was 66 per cent (Sahli), and the red blood cell count was 3.3 million per cubic millimeter of blood. Other laboratory tests were normal. December 1934, six inches of terminal ileum, the cecum, and about six inches of ascending colon were resected because of a suspected carcinoma. The mass on microscopic examination proved to be a carcinoid tumor of the cecum. The gallbladder at operation was thickened and contained stones but was not removed. This patient's convalescence was greatly prolonged because of inability to retain adequate amounts of food. She also lost large amounts of fluid through the ileostomy opening until it was closed. She was in good health in November, 1936.

Case 3. Mrs. M. M., age 50, noticed a small mass in the right lower quadrant in the fall of 1934 which produced very few symptoms. In February 1935, she experienced alternating periods of diarrhea and constipation. The mass began to grow rapidly. Examination at that time showed a somewhat undernourished pale female with movable mass in the right iliac fossa, about three inches in diameter. X-ray examination revealed a filling defect in the cecum which could not be differentiated from a granuloma, carcinoma, or carcinoid of the cecum. Hemoglobin was 57 per cent (Sahli) and there were 2.62 million red blood cells per cubic millimeter of blood. There was occult blood in the feces; other tests and examinations gave normal or negative results. At operation, a large tumor mass was found involving the cecum and appendix. The cecum and the adjacent ten inches of terminal ileum and nearly all of the ascending colon were resected. The proximal end of the colon and the terminal end of the ileum were brought to the surface through a colostomy opening. On microscopic examination the tumor proved to be a gelatinous carcinoma of the cecum. The immediate convalescence was uneventful, but about one year later the patient developed bone metastasis for which she was given roentgen-ray therapy. The patient died from cachexia on June 13, 1936. Postmortem examination confirmed the above diagnosis.

RESULTS

The patient G. M. was able to follow prescribed diets, but became very restless and refused to remain sufficiently long to permit more than one three-day period of study without change of procedure. In Patient A. R. a calcium and phosphorus balance study was made before the operation with considerable difficulty because constant persuasion was necessary to get the needed cooperation. Following operation the patient refused to eat any constant diet; in fact, her stay in the hospital was prolonged for months because of anorexia and a marked diarrhea through the ileal opening with a loss of large amounts of ileal content until the ileum and colon were anastomosed. However, colonic washings were satisfactorily obtained. Samples of ileal content were obtained from the ileal opening at various times for determination of the pH, but a complete collection was not possible. Satisfactory colon washings were obtained on five occasions. Table I lists the volume and pH of urine obtained from Patient G. M. and the daily amount of ileal elimination in terms of wet and dry weights. The colon washings were similarly measured and recorded. The pH was determined on freshly obtained wet materials from the ileum and colon. The patient G. M. was given a diet containing food and water as indicated in Table I. The diet

was changed two days before the beginning of the first and third periods, thereby reducing the error introduced by excreta from a previous period being mixed with that of a subsequent period. The urine volume follows closely the fluid intake during the first three periods. The urine collection of 215 cubic centimeters during April 30 was incomplete since the creatinine, calcium, and phosphorus excretion in that specimen was too low when compared with other collections of

TABLE I

The quantity and pH of urine, ileal content, and colon washings obtained from patients with colostomy and ileostomy openings

Date	Daily intake		Urine		Ileal elimination			Ratio of wet weight to dry weight	Colon washings returned		
	Water	Weight of food as served	Cc.	pH	Wet	pH	Dry		Wet	pH	Dry
		grams			*grams per 24 hours*		*grams per 24 hours*		*grams*		*grams*
CASE G. M.											
April 29, 1934	750 cc.	609	246		273.7		23.1		70.0		1.27
April 30, 1934	Control period		215*		298.0		24.1		97.0		1.52
May 1, 1934			270		292.4		23.2		72.5		1.49
Average			**263**		**288.1**		**23.5**	**13.3**			
May 2, 1934	2000 cc.	609	1200		316.4		27.5		94.5		1.27
May 3, 1934			1808		295.5		21.9		89.2		1.25
May 4, 1934			1555	5.4	354.8	5.4	26.2		50.7	8.3	0.64
Average			**1521**		**322.2**		**25.2**	**12.8**			
May 7, 1934	1500 cc.	812	331	5.6	410.5	5.3	31.8		62.2	8.2	1.00
May 8, 1934			713	6.4	418.0	5.7	28.3		95.3	8.3	1.49
May 9, 1934			837	6.8	442.4	5.6	32.3		97.0	8.0	1.37
Average			**627**		**423.6**		**30.8**	**13.8**			
May 10, 1934	1500 cc.	812	938	6.9	346.3	5.4	25.7		49.1	8.2	1.15
May 11, 1934	Viosterol 750 D		1105	6.6	372.5	5.6	31.1		103.5	8.0	1.50
May 12, 1934	(3 cc.) t.i.d.		1553	6.4	392.1	5.5	29.6		97.0	7.2	1.47
Average			**1199**		**370.3**		**28.8**	**13.0**			
May 13, 1934	1500 cc.	812	1533	6.5	241.0	5.0	26.1		89.7	8.0	1.22
May 14, 1934	Parathormone		2140	6.4	231.4	5.3	25.8		41.6		0.98
May 15, 1934	40 units b.i.d.		1043	6.5	215.0		24.5		84.2	8.2	1.08
Average			**1572**		**229.1**		**25.5**	**9.0**			
CASE A. R.											
February 5, 1935 to February 11, 1935	Inconstant diet				Very large volume 2000 to 4000 grams	6.07 to 6.68			150 50	8.6 8.3	
April 6, 1935 to April 11, 1935					1369 to 1575 grams	6.37 to 6.84			60 76 58	8.2	
CASE M. M.											
March 14, 1935	Not controlled					7.63			44	8.7	
March 15, 1935						6.56					
March 17, 1935						7.09			6.7	8.3	

* Urine collection incomplete—Values not used in obtaining average values.

that period. No adequate explanation is apparent for the small twenty-four hour urine collection of 331 cc. on May 7, 1936. It was complete, for the creatinine and mineral excretion values were comparable with those of other collections for the same period. The fourth and fifth periods show diuretic effects of viosterol and parathormone. pH determinations were not made during the early part of this study because the glass electrode potentiometer was not available.

The amount of ileal elimination varied directly with the quantity of water and food ingested. Food and fluid when taken in the usual amounts tended to increase peristalsis and decrease the time for absorption from the small intestine. This point is well illustrated by comparing the first period with the second. The diet was identical in both periods excepting that during the second period water consumed was increased from 750 cc. to 2000 cc. daily. This resulted in an increase in average daily ileal excretion of 34.1 grams wet weight and only 1.7 grams of dry substance. The ratio of dry to wet ileal excretion increased from 1 to 13.3 to 1 to 12.8, showing that the increased elimination was chiefly water loss. During the third and subsequent periods the bulk of the diet was increased by one-third, four meals were given instead of three. With this increase in bulk there was an increase in both wet and dry substance in the ileal excretion. The ratio of dry substance to wet weight was 1 to 13.8. Since both the bulk and water content of the diet were changed in this period, a simple comparison with the previous two periods is not possible. When viosterol was added to this diet (next period), a diuresis resulted, and there was a marked decrease in the wet weight and smaller decrease in the dry weight of the ileal excretion, the ratio changing from 1 to 13.8 to 1 to 13. The ileal excreta was less fluid than previously, but still was liquid. During the last period viosterol was discontinued and parathormone was injected. The patient became dehydrated as indicated by a dry skin, a cessation of gain in weight, a large urinary output, and sensation of thirst. The colon washings at this time contained formed plugs of mucus which previously had been liquid. The ileal excreta was semi-solid and almost pasty. The wet weight of the ileal excreta decreased from 370.3 grams to 229.1 grams with a less marked decrease in the elimination of dry substance (from 28.8 grams to 25.5 grams). The dry to wet ratio increased from 1 to 13 to 1 to 9. The absolute decrease in dry substance indicates a better absorption from the small intestine. These effects from viosterol and parathormone administration probably represent a more rapid absorption of water due to hemoconcentration resulting in a slower rate of propulsion of ileal content and a longer time for absorption of foodstuffs from the small intestine rather than any specific effect of viosterol or parathormone upon the mucosa of the intestine. Later, it will be shown that the decrease in both calcium and phosphorus content of the ileal excreta after viosterol and parathormone administration parallels decreased water content.

The content of the terminal ileum in the case of G. M. was quite acid at all times. As previously stated, the daily ileal elimination was collected in two portions of approximately twelve hours each, the 7 a.m. to 7 p.m. collection representing chiefly the food residue and the 7 p.m. to 7 a.m. representing the fasting excretion. The pH of the excreta collected during the period of fasting averaged about 0.2 lower (more acid) than the dry excreta. This difference became more marked when samples taken three to four hours after meals, a time when maximum elimination occurred, were compared with pH readings from material obtained after fourteen hours of fasting. Following meals, the material became about neutral, readings of 6.5 to 6.9 were obtained and readings as low as 4.3 were obtained during the fasting state. In the case of A. R. the daily ileal elimination was 1300 to 1600 grams. The patient was unable to take a constant amount of either fluid or food preventing any balance study. The pH of the content of the terminal ileum varied from 6.07 to 6.8, a slightly acid reaction. These readings for the most part represent fasting values, since the patient was able to take but little food until after the ileostomy was closed. The last patient, M. M., found it necessary to take a very high bulk coarse diet to prevent a large fluid loss from the ileostomy opening. It is possible that this diet may have been a factor in producing an approximately neutral reaction of the ileal content. This is

suggested by the above mentioned observation of a tendency for the content to approach neutrality following meals and becoming decidedly more acid in the fasting state. It will be noted in the case of G. M. that an increase in dietary bulk did not influence the average pH; however, the ratio of bulk to other foods remained the same. The difference in reactions of the ileal content in these cases may represent individual differences. Robinson (10), working with dogs, concluded that the pH of the content of any segment of small intestine was controlled by secretions from the wall of that segment. Of course, any rapid ingress of intestinal content having a decidedly different

TABLE II

The calcium and phosphorus content of the excreta

Date	Daily intake		Urine		Ileal elimination		Colon washings		Total excretion		Balance	
	Calcium	Phosphorus	Calcium	Phosphorus	Calcium	Phosphorus	Calcium	Phosphorus	Calcium	Phosphorus	Calcium	Phosphorus
	grams per day	*grams per day*	*grams per day*	*grams per day*	*grams per day*	*grams per day*	*grams per day*	*grams per day*	*grams per day*	*grams per day*	*grams per day*	*grams per day*
CASE G. M.												
April 28, 1934	.55	.74	.17	.64	.42	.18	.016	.003				
April 29, 1934	H_2O 750 cc.		.16	.51	.40	.17	.022	.003				
April 30, 1934			.14*	.38*	.38	.21	.007					
May 1, 1934			.18	.61	.40	.20	.003	.002	.57		−.02	
Average			**.17**	**.59**	**.40**	**.20**				**.79**		**−.05**
May 2, 1934	.55	.74	.20	.80	.44	.20	.003	.002				
May 3, 1934	H_2O 2000 cc.		.16	.62	.41	.20	.003	.003				
May 4, 1934			.18	.67	.56	.22	.002	.004	.65		−.10	
Average			**.18**	**.72**	**.47**	**.21**				**.93**		**−.19**
May 7, 1934	.73	1.00	.13	.62	.60	.24	.004	.005				
May 8, 1934			.13	.64	.55	.25	.004	.004				
May 9, 1934			.14	.65	.62	.26	.004	.003	.72		+.01	
Average			**.13**	**.64**	**.59**	**.25**				**.89**		**+.11**
May 10, 1934	.73	1.00	.15	.65	.55	.23	.005	.004				
May 11, 1934	Viosterol 750 D		.17	.68	.60	.27	.004	.004				
May 12, 1934	(3 cc.) t.i.d.		.18	.86	.61	.27	.003	.003	.76		−.03	
Average			**.17**	**.73**	**.59**	**.26**				**.99**		**+.01**
May 13, 1934	.73	1.00	.20	1.36	.53	.24	.003	.003				
May 14, 1934	Parathormone		.35	1.43	.55	.29	.005	.003				
May 15, 1934	40 units b.i.d.		.47	1.06	.43	.20	.004	.004	.84		−.11	
Average			**.34**	**1.28**	**.50**	**.24**				**1.52**		**−.52**
CASE A. R.												
February 12, 1935							.017	.051				
February 14, 1935							.063	.009				
April 6, 1935							.008	.005				
April 7, 1935							.005	.004				
April 10, 1935							.001	.001				
CASE M. M.												
March 16, 1935							.001	Trace				
March 17, 1935							.002	.003				

* Urine collection incomplete—Values not used in obtaining average values.

reaction into another segment of bowel would greatly modify the pH of the content of the receiving segment.

The character, gross appearance, and pH of the colon washings were very similar in all three cases and consisted of white mucin-like material which became less fluid when the patient was dehydrated. Staining and contamination by ileal content was not observed at any time. The pH of material obtained from all three patients varied but little (8.0 to 8.7).

Calcium and phosphorus absorption and excretion data from analyses of urine, ileal and colonic excreta are listed in Table II. Patient G. M. was used for a calcium and phosphorus balance study. As previously stated, the other patients were not suitable for a similar study. The daily values are listed and averaged for each period. This was thought advisable since average figures do not give any information regarding daily variation within a period. Had it been possible to run more than one three-day period on each variation of the study, the listing of daily values would not have been advisable. During the first period and for the preceding two days the patient was given a diet containing 0.55 gram calcium and 0.74 gram phosphorus per day; the average daily urinary excretion of calcium was 0.17 gram and 0.59 gram of phosphorus. The daily ileal excreta contained 0.4 gram calcium and 0.2 gram phosphorus, and the material obtained by washing out the colon contained only a few milligrams of calcium and phosphorus. It is noteworthy that the colon washings did not contain any significant amount of calcium or phosphorus at any time even though during the last period the serum calcium was elevated to 15.3 mgm. per cent by parathormone injection, which resulted in a very significant increase in urinary calcium and phosphorus excretion. The intake of calcium and phosphorus during the second period was the same as during the first, the only change was an increase of water from 750 cc. to 2000 cc. daily. The slight increase of urinary calcium excretion is probably of no significance, but the increase of urinary phosphorus excretion from 0.59 to 0.72 gram per day is a significant one and corresponds to the increase commonly encountered when diuresis occurs. The increase in daily ileal calcium elimination parallels reasonably well the increase in dry material excreted as shown in Table I. The increase in urinary phosphorus and ileal calcium elimination during this period resulted in a small negative balance. It was necessary to increase the diet to permit a gain in weight and to satisfy the patient. This was accomplished by increasing the number of daily meals to four without otherwise changing the diet. Two days after this change the third period was begun. During this period the patient was in a state of calcium balance and a positive phosphorus balance of 0.1 gram per day. When viosterol was added during the fourth period, the urinary excretion of calcium and phosphorus increased while the ileal excretion remained constant, converting the calcium balance to a slight loss and the previously positive phosphorus balance to a balanced state. During the last period the parathormone injections, as previously stated, resulted in a hypercalcemia and a moderately severe dehydration of the patient. There resulted a marked increase of daily urinary calcium and phosphorus excretion and a decrease in ileal calcium and phosphorus elimination which produced a negative balance of both calcium and phosphorus. In Patients A. R. and M. M., except for the first washings in the case of A. R., the colon washings did not contain any appreciable quantities of calcium and phosphorus. The amounts of calcium and phosphorus excreted in the colon washings in all three cases is surprisingly small.

DISCUSSION

Vitamin D is commonly believed to increase absorption of calcium from the small intestine. As shown in Table II when viosterol was administered, there was a significant decrease in both the dry and wet weight of the ileal excreta. It was suggested that this possibly was due to a slowed rate of propulsion permitting a longer time for absorption of absorbable material from the small intestine. It was also pointed out that taking of larger amounts of water as in the second period of Table I resulted in a larger wet and dry ileal elimination and that clinical signs of dehydration and a marked decrease in both the wet and dry ileal excretion resulted when parathormone was administered. If these variations were a result

of greater or lesser absorption from the small intestine dependent upon rate of propulsion and time for absorption rather than selective action of viosterol or parathormone upon the mucosa of the intestine, then the mineral excretion should have paralleled the dry weight elimination. Table III lists these data. On the first diet there

TABLE III

Milligrams calcium and phosphorus contained in each gram of dry weight of average daily excreta

	Dry weight of excreta	Daily ileal excretion		Dry weight	
		Calcium	Phosphorus	Calcium	Phosphorus
	grams	*mgm.*	*mgm.*	*mgm. per gram*	*mgm. per gram*
Control period	23.5	400	200	17	8.5
Period of hydration	25.2	470	210	19	8.3
Diet changed					
Control period	30.8	590	250	19	8.1
Viosterol (3 cc.) t.i.d. 750 D	28.8	590	260	20	9.0
Parathormone 40 units b.i.d.	25.5	500	240	20	9.4

were excreted in each gram of dry material 17 and 8.5 mgm. of calcium and phosphorus respectively. When the water intake was increased and the diet otherwise remained constant, there was a greater increase of ileal calcium excretion or less absorption of calcium than during the control period. The phosphorus excretion was not appreciably altered. With the patient on four meals daily and on intermediate water intake, the excreta contained 19 and 8.1 mgm. calcium and phosphorus respectively. Viosterol was then added to the diet, and even though there was a decrease in the grams of dry excreta, the concentration of calcium and phosphorus in this excreta increased. A similar but even more marked effect was noted when viosterol was discontinued and parathormone administered. These data do not support the contention that viosterol increases the absorption of calcium specifically from the intestine, but indicate that through a general increase of absorption from the small intestine there may result some increase in mineral absorption including calcium. It is possible that this increase in absorption is due to slowed rate of propulsion and an increased time for absorption from the intestine.

CONCLUSIONS

In two of three patients studied, the content of the terminal ileum was acid at all times, and in the third patient the content was usually acid, but following the rapid expulsion of very coarse vegetable fiber, the content became approximately neutral.

Following the ingestion of a large amount of water, the ileal excreta became more fluid, and there was an increase in weight of the wet, dry, and mineral excretion.

Viosterol and parathormone administration resulted in a diuresis and a concomitant decrease in the wet and dry weight of ileal excretion. The ileal content became thick and semisolid whereas it had been quite fluid on the same diet during the preceding period. The more concentrated ileal excreta contained more calcium and phosphorus per gram of dry weight than the hydrated.

No evidence was obtained that viosterol in the amounts given to this patient had any specific effect on the absorption of calcium from the intestine.

In these three patients the colon failed to excrete significant amounts of calcium and phosphorus at any time during the study.

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