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T H Steele, H F DeLuca

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Research Article

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Influence of Dietary Phosphorus on Renal Phosphate Reabsorption in the Parathyroidectomized Rat

THOMAS H. STEELE and HECTOR F. DELUCA

From the Departments of Medicine and Biochemistry, The University of Wisconsin, Madison, Wisconsin 53706

ABSTRACT Inorganic phosphate (P_i) reabsorption was studied during P_i infusion, after acute or chronic thyroparathyroidectomy (TPTX), in rats stabilized on a high-phosphorus (1% P) or a low-phosphorus (0.02% P) diet. After acute TPTX, there were no consistent differences in P_i reabsorption between the high- and low-phosphorus dietary groups. After chronic TPTX, the rats stabilized on the low-phosphorus diet exhibited nearly complete P_i reabsorption at every plasma P_i level, while the animals receiving the high-phosphorus diet manifested a marked phosphaturic response to P_i infusion. In addition, P_i reabsorption was significantly increased in the chronic TPTX low-phosphorus rats which achieved the highest filtered P_i loads, while their urine remained essentially phosphate-free. Dietary phosphorus-dependent alterations in P_i reabsorption may play a significant role in establishing the rate of P_i excretion per nephron under certain circumstances and should be considered in the interpretation of studies investigating renal P_i handling. The ability of phosphorus-depleted animals to maintain a phosphate-free urine during P_i loading would favor the rapid repletion of body phosphorus stores.

INTRODUCTION

For many years, the renal regulation of inorganic phosphate (P_i)[1] excretion has been attributed to the tubular reabsorption of appropriate amounts of the P_i filtered by the glomeruli. Pitts originally observed a relationship between the fraction of filtered P_i excreted (FE_{P_i}) and the plasma P_i concentration (1). Subsequently, Pitts and Alexander demonstrated that P_i reabsorption appears to be limited by a maximum transport capacity (Tm_{P_i}) which may be demonstrated by elevating the filtered load of P_i (2). Although several endocrine, metabolic, and physiologic parameters are known to affect P_i reabsorption (3), it is generally thought that parathyroid hormone (PTH) plays a primary role in the physiologic regulation of P_i excretion.

Recent studies in the phosphorus-depleted vitamin D-deficient rat (4), as well as older observations in the rat (5) and man (6, 7), have suggested that P_i reabsorption may be accentuated during phosphorus depletion. Presumably, the excretion of a P_i-free uring during phosphorus depletion has been attributed to hypophosphatemia and the resulting decrease in filtered P_i, both of which are known to decrease the urinary P_i (1, 2). Our results indicate that renal P_i reabsorption is enhanced substantially in the chronically thyroparathyroidectomized phosphorus-depleted rat, independently of the plasma P_i concentration and the degree of extracellular fluid volume expansion.

METHODS

Renal clearance studies were performed in male Holtzman rats weighing 150–250 g which had free access to food and water. They had been stabilized for 2 wk on either a "high-phosphorus" diet containing 1.0% P, or a "low-phosphorus" diet containing 0.02% P, both of which contained adequate vitamin D (8). The high-phosphorus diet contained 1.6% calcium, and the low-phosphorus diet contained 0.6% calcium. The sodium content of the high-phosphorus diet was 10 meq/100 g, and that of the low-phosphorus diet was 14 meq/100 g.

All animals underwent thyroparathyroidectomy (TPTX), either immediately (acute TPTX) or 48 h (chronic TPTX) before the experiments, which commenced at the same hour in the morning. The rats were anesthetized with Inactin

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[1] *Abbreviations used in this paper:* FE_{Na}, fractional excretion of sodium; FE_{P_i}, fractional excretion of P_i; GFR, glomerular filtration rate; P_i, inorganic phosphate; PTH, parathyroid hormone; TCA, trichloroacetic acid; Tm_{P_i}, maximum transport capacity; TPTX, thyroparathyroidectomy.

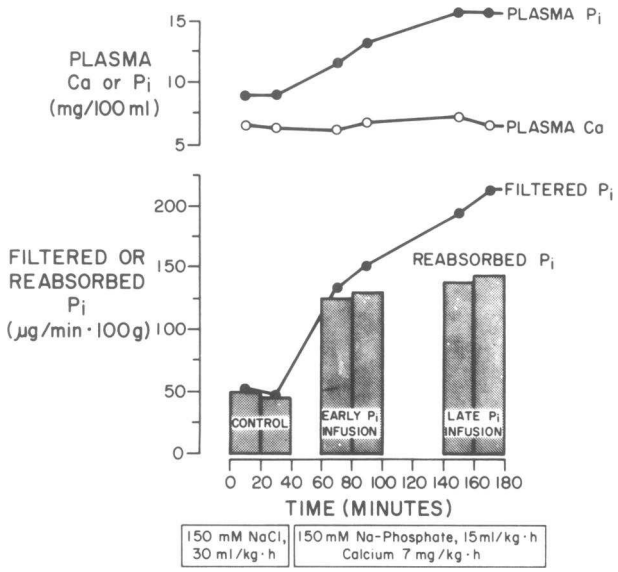

FIGURE 1 Diagrammatic representation of the experimental format. After a two-period control phase during NaCl diuresis, sodium phosphate infusion was begun at half the rate of the previous NaCl infusion. Specimens were collected for "early" and "late" phosphate infusion phases as the plasma and filtered phosphate increased.

(Promonta, Hamburg) 80–100 mg/kg intraperitoneally, and a tracheostomy was performed with PE 360 tubing (Clay Adams, Div. of Becton, Dickinson & Co., Parsippany, N. J.). One carotid artery and both external jugular veins were cannulated with PE 50 tubing. The bladder also was catheterized with PE 50 tubing through a short abdominal incision, and ligated in such a way as to minimize dead space. Each rat received 150 mM NaCl, 10 ml/kg, to replace surgical losses and was placed on an electrically heated platform where the body temperature was maintained at 37–38°C, monitored rectally with a thermistor probe. An 8% inulin solution was administered at a priming dose of 1 ml/kg, and continued as a sustaining infusion at 4 ml/kg·h. In addition, each rat received 150 mM NaCl, 30 ml/kg·h, throughout a preliminary 1-h equilibration interval and during two 20-min control clearance periods. The control periods were not begun until at least 1 h had elapsed after all surgical procedures. Sufficient arterial blood was obtained at the midpoint of each clearance period to allow the separation of 80 μl of plasma. Urine was collected under mineral oil and the volume determined by differential weighing.

The protocol utilized in the clearance studies is illustrated diagrammatically in Fig. 1. After two control periods. the NaCl infusion was changed to 150 mM sodium phosphate (Na_2HPO_4 and NaH_2PO_4 at approximately a 4:1 ratio, adjusted to pH 7.4) which was administered for the remainder of the study at half the rate of the previous NaCl infusion (i.e., at 15 ml/kg·h). At the time of commencing the phosphate infusion, the 8% inulin was replaced with a similar solution which also contained 0.17% calcium (as calcium chloride) and continued at 4 ml/kg·h, a rate which delivered calcium at 7 mg/kg·h, in order to prevent tetany. During the interval between 20 and 60 min after commencing the phosphate infusion, specimens for two 20-min "early" phosphate infusion clearance period were obtained. Similarly, specimens were obtained for two 20-min "late" phosphate infusion clearance periods during the interval between 100 and 140 min.

Ultrafilterable plasma P_i was determined in separate groups of chronic TPTX rats which had been stabilized on either the high- or low-phosphorus diet. They received the same infusions as the rats in the clearance experiments, either with or without phosphate loading. Plasma was equilibrated with 5% CO_2 under mineral oil and ultrafiltrates were obtained by centrifuging through collodion bags (Schleicher & Schuell, Inc., Keene, N. H.) at 37°C.

Plasma, urine, and plasma ultrafiltrates were diluted appropriately in an acidified 1% lanthanum, 5% trichloroacetic acid (TCA) solution and determinations of inulin and P_i were made by semiautomated colorimetric methods on the lanthanum-TCA supernates as reported previously (9). Calcium was measured by atomic absorption spectrophotometry. Sodium and potassium were measured by flame photometry utilizing a lithium internal standard.

The glomerular filtration rate (GFR) was estimated by the clearance of inulin. Values of GFR, filtered load, and solute excretion are expressed per 100 g of body wt. For each experiment, the results from both clearance periods of each of the three phases were averaged separately. These averages for the control, early phosphate infusion, and late phosphate infusion phases were utilized in the figures and in computing the means for the tables. Statistical comparisons were made by utilizing the paired or unpaired Student's t test, as appropriate (10). Results are expressed in the text as mean±SEM.

RESULTS

In five chronic TPTX rats stabilized on the high-phosphorus (1% P) diet, the concentration of P_i in plasma ultrafiltrates averaged 107.1±1.8% of the total plasma P_i concentration; ultrafilterable P_i averaged 103.5±1.4% of total plasma P_i in six other high-phosphorus dietary animals which received phosphate infusions. Similarly, ultrafilterable plasma P_i averaged 103.5±2.1% of total in six chronic TPTX rats stabilized on the low-phosphorus (0.02% P) diet, and 100.0±1.5% in seven other low-phosphorus dietary rats which received phosphate infusions. Ultrafilterable P_i neither differed significantly between corresponding high- and low-phosphorus dietary groups, nor was there a statistically significant difference in ultrafilterable P_i between animals which did and did not receive phosphate infusions. Furthermore, ultrafilterable P_i did not differ significantly from total P_i, after phosphate infusion in either group. Because of this and because ultrafilterable P_i was not measured in the animals actually undergoing the clearance experiments, the filtered P_i loads were computed simply as the product of the GFR times the total plasma P_i concentration.

In 16 acute TPTX and 20 chronic TPTX rats undergoing clearance experiments (Fig. 1), GFR remained stable during phosphate infusion (Table I). In both of the low-phosphorus dietary groups, the plasma P_i remained significantly less than in the corresponding high-phosphorus groups, until the late

TABLE I

Dietary Phosphorus and P_i Excretionin Acute and Chronic TPTX Rats

	GFR		Plasma P_i			$FE_{P_i} \times 100$			$FE_{Na} \times 100$		
	Control	Early P_i infusion	Late P_i infusion	Control	Early P_i infusion	Late P_i infusion	Control	Early P_i infusion	Late P_i infusion	Control	Early P_i infusion	Late P_i infusion
	ml/min·100 g			*mg/100 ml*			%			%		
Acute TPTX												
High-phosphorus (1% P) diet (n = 8)												
	0.80	0.77	0.91	8.3	13.6‖	17.6‖	1.24	3.34	23.3§	0.75	0.55	0.75
	±0.13	±0.10	±0.12	±0.3	±0.5	±1.1	±0.72	±1.34	±5.7	±0.22	±0.10	±0.12
Low-phosphorus (0.02% P) diet (n = 8)												
	1.07	0.98	0.84	4.6	10.9‖	17.5‖	0.16	0.10	9.29	0.86	0.75	0.62
	±0.06	±0.14	±0.10	±0.2	±0.8	±1.5	±0.03	±0.02	±5.30	±0.26	±0.22	±0.30
	NS	NS	NS	$P < 0.001$	$P < 0.05$	NS	NS	$P < 0.05$	NS	NS	NS	NS
Chronic (48-h) TPTX												
High-phosphorus (1% P) diet (n = 7)												
	1.28	1.15	1.08	9.9	15.1‖	18.9‖	10.1	20.8§	30.6‖	1.4	1.5	1.0
	±0.10	±0.13	±0.10	±0.3	±0.5	±0.6	±1.9	±3.1	±1.8	±0.3	±0.3	±0.1
Low-phosphorus (0.02% P) diet (n = 13)												
	1.11	0.86*	0.97	4.3	10.0‖	17.5‖	0.19	0.15	0.20	1.1	1.0	0.62
	±0.08	±0.09	±0.09	±0.2	±0.5	±0.9	±0.02	±0.06	±0.05	±0.2	±0.3	±0.21
	NS	NS	NS	$P < 0.001$	$P < 0.001$	NS	$P < 0.001$	$P < 0.001$	$P < 0.001$	NS	NS	NS
Acute vs. chronic												
High-phosphorus												
	$P < 0.01$	$P < 0.05$	NS	$P < 0.01$	$P < 0.05$	NS	$P < 0.005$	$P < 0.001$	NS	NS	$P < 0.01$	NS
Low-phosphorus												
	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS

Values are mean±SEM. Symbols indicate significant paired changes from control, within the same experimental group: * $P < 0.05$; ‡ $P < 0.02$; § $P < 0.01$; ‖ $P < 0.001$. P values indicate unpaired comparisons between different groups during similar experimental phases. NS, not significant.

phosphate infusion phase. During control and early phosphate infusion phases, plasma P_i was elevated significantly in the high-phosphorus chronic TPTX group, as compared to acute TPTX.

In the high phosphorus *acute* TPTX group, fractional P_i excretion (FE_{P_i}) increased significantly during the late phosphate infusion phase (Table I). In contrast, late phosphate infusion FE_{P_i} values in the low-phosphorus acute TPTX group did not increase to a statistically significant degree because of wide variation. In the *chronic* TPTX rats, FE_{P_i} in the high-phosphorus group significantly exceeded that in the low-phosphorus group in all three phases (Table I). Whereas plasma P_i was significantly increased in the former group during control and early phosphate infusion phases, there was no significant difference during late phosphate infusion. Yet, FE_{P_i} averaged 30.6±1.8% in the high-phosphorus chronic TPTX group, as compared to 0.20±0.05% in the low-phosphorus group ($P < 0.001$). In the low-phosphorus chronic TPTX rats, the urine remained essentially phosphate-free, and FE_{P_i} uniformly remained less than 1%, even with plasma P_i values as high as 20 mg/100 ml (Fig. 2).

In the *acute* TPTX animals, corresponding values of filtered P_i and absolute P_i reabsorption never differed significantly between the high- and low-phosphorus dietary groups (Table II). P_i reabsorption per unit GFR was significantly increased in the high-phosphorus dietary group during control and early phosphate infusion phases. During late phosphate infusion, however, P_i reabsorption per unit GFR was significantly increased in the *low*-phosphorus dietary group. In both acute TPTX groups, absolute P_i reabsorption increased significantly during early phosphate infusion as compared to control values ($P < 0.01$), but did not show a significant *additional* increase during late phosphate infusion.

In the *chronic* TPTX animals, filtered P_i, absolute P_i reabsorption, and P_i reabsorption per unit GFR were significantly greater in the high-phosphorus dietary group during the control and early phosphate infusion phases (Table II). During late phosphate infusion, when the filtered P_i loads became nearly equal in these two groups, their absolute P_i reabsorption rates did not differ significantly. As was the case in the acute TPTX rats, P_i reabsorption per unit GFR continued to increase further in the low-phosphorus animals during late phosphate infusion. The low-phosphorus chronic TPTX rats reabsorbed amounts of P_i statistically indistinguishable from their filtered P_i loads during all three experimental phases (Table II, Fig. 3). Absolute P_i reabsorption in the high-phosphorus chronic TPTX rats was significantly less than the filtered load during late phosphate infusion ($P < 0.001$), and P_i reabsorption never increased to values significantly greater than control.

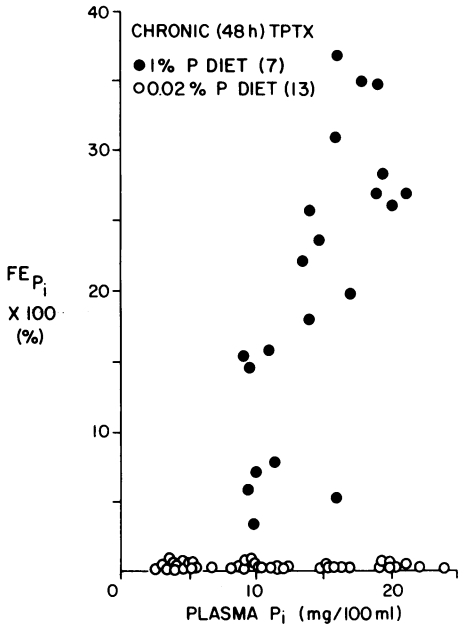

FIGURE 2 FE_{P_i} as a function of plasma P_i in chronically TPTX rats on a high- (1% P) or low- (0.02% P) phosphorus diet. In this and the following figures, each point represents the mean of two clearance periods. Even at plasma P_i concentrations of 20 mg/100 ml, P_i excretion was virtually absent in the rats stabilized on the low-phosphorus diet.

Eight rats of the low-phosphorus chronic TPTX group and all the high-phosphorus chronic TPTX rats achieved filtered P_i values greater than 150 μg/min·100 g body wt. At these high filtered P_i loads, which averaged 204±16 and 189±9 μg/min·100 g body wt in the low- and high-dietary phosphorus groups,

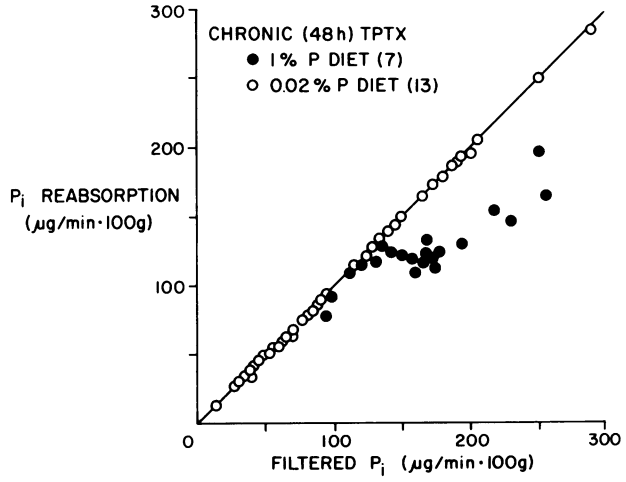

FIGURE 3 P_i reabsorption as a function of the filtered P_i in chronic TPTX rats. In animals stabilized on the low-phosphorus diet, more than 99% of the filtered P_i was reabsorbed. In contrast, rats on the high-phosphorus diet did not increase P_i reabsorption significantly during phosphate loading.

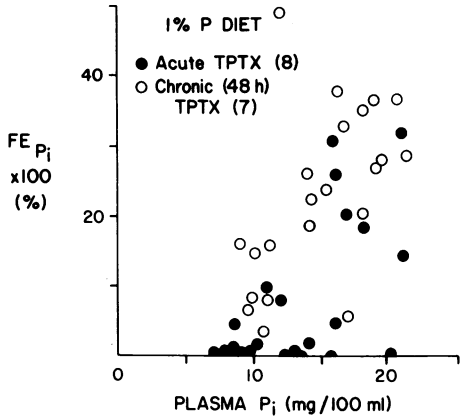

FIGURE 4 Effect of duration of TPTX on FE_{P_i} in the high-phosphorus rats. Because studies commenced at lower plasma P_i values in the acute TPTX rats, FE_{P_i} values tended to be low in many of those animals. After phosphate infusion, FE_{P_i} values in the acute TPTX group did not differ significantly from the corresponding chronic TPTX animals.

respectively, the simultaneous absolute P_i reabsorption values averaged 203±16 and 138±7 μg/min·100 g body wt, respectively ($P < .001$). Also, when filtered P_i was greater than 150 μg/min·100 g body wt, P_i reabsorption per unit GFR averaged 172±12 and 118±6 μg/ml, respectively, in the low- and high-dietary phosphorus chronic TPTX groups ($P < 0.001$). Therefore, absolute P_i reabsorption was enhanced significantly in the phosphorus-depleted chronic TPTX rats with the largest filtered P_i loads.

Fractional sodium excretion (FE_{Na}) was variable, but did not change in any consistent manner during phosphate infusion in the four groups of rats (Table I). FE_{Na} was correlated significantly with FE_{P_i} in the low phosphorus acute ($r = 0.51$) and chronic TPTX ($r = 0.31$) groups ($P < 0.05$ for both), but not in the high-phosphorus groups.

Control plasma calcium did not differ significantly between the two acute TPTX groups, but plasma calcium decreased significantly during late phosphate infusion in the low-phosphorus acute TPTX group (Table III). Conversely, control plasma calcium was increased in the chronic TPTX low-phosphorus group ($P < 0.001$), although not when compared to the acute TPTX groups. During phosphate infusion, plasma calcium values decreased in the low-phosphorus chronic TPTX group and increased in the high-phosphorus chronic TPTX group ($P < 0.001$ in both) so that, by late phosphate infusion, they were similar (Table III).

Substantive differences in renal P_i handling between corresponding acute and chronic TPTX groups were not present (Table I). Although the degree of variation was wide, FE_{P_i} values tended to be similar in magnitude, at any plasma P_i level in the high-phosphorus

TABLE II

Effect of Dietary Phosphorus on P_i Reabsorption

	Filtered P_i			Absolute P_i reabsorption			P_i reabsorption per unit GFR		
	Control	Early P_i infusion	Late P_i infusion	Control	Early P_i infusion	Late P_i infusion	Control	Early P_i infusion	Late P_i infusion
	μg/min·100 g			*μg/min·100 g*			*μg/ml*		
Acute TPTX									
High-phosphorus (1% P)	65	103§	154‡	64	99§	119	82	132‖	138
diet (n = 8)	±10	±13	±19	±10	±12	±17	±3	±6	±6
Low-phosphorus (0.02% P)	49	103§	145*	49	102§	130	46	109‖	161
diet (n = 8)	±4	±13	±19	±4	±13	±18	±2	±8	±9
	NS	NS	NS	NS	NS	NS	$P < 0.001$	$P < 0.05$	$P < 0.05$
Chronic (48 h) TPTX									
High-phosphorus (1% P)	126	171‡	201*	121	135	143	89	120§	132
diet (n = 7)	±9	±16	±13	±12	±12	±9	±3	±7	±7
Low-phosphorus (0.02% P)	48	84§	169‖	47	84§	169‖	42	100‖	174‖
diet (n = 13)	±4	±10	±16	±4	±10	±16	±2	±5	±9
	$P < 0.001$	$P < 0.001$	NS	$P < 0.001$	$P < 0.01$	NS	$P < 0.001$	$P < 0.05$	$P < 0.005$
Acute vs. chronic TPTX									
High-phosphorus	$P < 0.005$	$P < 0.01$	NS	$P < 0.01$	$P < 0.05$	NS	NS	NS	NS
Low-phosphorus	NS	NS	NS	NS	NS	NS	NS	NS	NS

Values are mean±SEM. Symbols reflect paired statistical comparisons *with the preceding phase*, within the same group (i.e., between "early" and "control" phases, and between "late" and "early" phases) as follows: * $P < 0.05$; ‡ $P < 0.02$; § $P < 0.01$; ‖ $P < 0.001$; otherwise, $P > 0.1$. P values given within the table reflect unpaired statistical comparisons, for the same phase, between high- and low-phosphorus dietary groups and between corresponding acute and chronic TPTX groups. NS, not significant ($P > 0.05$).

acute and chronic TPTX groups (Fig. 4). Similarly, at any filtered P_i value, P_i reabsorption was not significantly enhanced in the acute TPTX high-phosphorus group (Fig. 5).

Because all the rats were studied at body weights of 150–250 g, the high-phosphorus groups were younger at the time of study because of impaired growth within the phosphorus-deficient groups. To determine if age differences were important in the control of P_i reabsorption, four older chronic TPTX rats were studied after stabilization on the 1% phosphorus diet. These animals weighed 395–398 g, and their GFR averaged 1.11±0.09 ml/min·100 g. Control plasma P_i, 48 h after TPTX, averaged 8.8±0.3 mg/100 ml and the corresponding FE_{P_i} was 10.9±2.3%. During early phosphate infusion, plasma P_i averaged 13.5±0.9 mg/100 ml and FE_{P_i} was 22.6±2.2%. During late phosphate infusion, plasma P_i was 19.0±0.9 mg/100 ml and FE_{P_i} averaged 42.8±2.5%. Thus, P_i reabsorption was not accentuated in these older rats.

DISCUSSION

These experiments suggest that the dietary phosphorus content directly or indirectly influences P_i transport

TABLE III

Plasma Calcium during P_i Infusion

	Control periods		Late P_i infusion	
	mg/100 ml			
Acute TPTX				
High-phosphorus diet (n = 8)	7.2±0.3		7.7±0.3*	
		NS		$P < 0.005$
Low-phosphorus diet (n = 8)	6.9±0.5		5.6±0.3*	
Chronic TPTX				
High-phosphorus diet (n = 7)	4.1±0.4		5.3±0.4‡	
		$P < 0.001$		NS
Low-phosphorus diet (n = 13)	7.4±0.3		5.7±0.2‡	

Values are mean±SEM. Symbols indicate paired comparisons within the same group: * $P < 0.01$; ‡ $P < 0.001$. P values indicate unpaired statistical comparisons between high- and low-phosphorus groups. NS, not significant ($P > 0.05$).

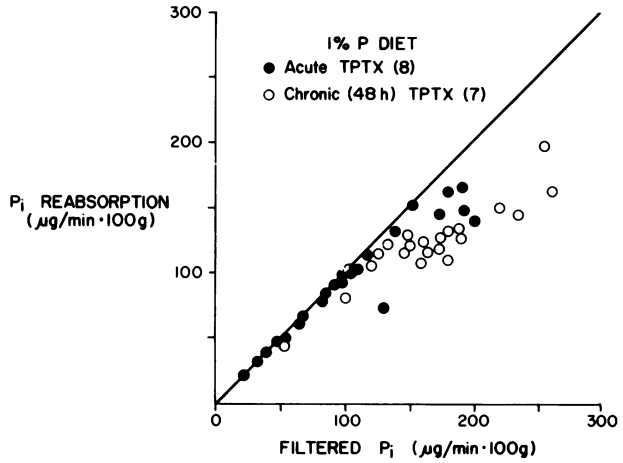

FIGURE 5 Absolute P_i reabsorption in acute and chronic TPTX rats receiving the high-phosphorus diet. Filtered P_i was lower in many acute TPTX studies, and the corresponding P_i reabsorption was nearly complete. After phosphate infusion, P_i reabsorption in the acute and chronic TPTX groups did not differ significantly.

after prolonged absence of PTH, and independently of the plasma P_i and filtered P_i. Chronic TPTX animals receiving the 0.02% phosphorus diet manifested a markedly elevated renal P_i threshold as demonstrated by FE_{P_i} values consistently less than 1%, even when the plasma was as great as 20 mg/100 ml. In the acute TPTX rats, only three of the *low*-phosphorus group manifested FE_{P_i} values greater than 5% during late phosphate loading. In contrast, several *high*-phosphorus acute TPTX rats manifested very low FE_{P_i} values during hyperphosphatemia (Fig. 4). Amiel and his collaborators reported that chronically parathyroidectomized rats had an FE_{P_i} of 10.9% at a plasma P_i of 10.9 mg/100 ml, while acutely parathyroidectomized rats had an FE_{P_i} of 2.5% at a plasma P_i of 9.2 mg/100 ml (11). Many investigators have reported low FE_{P_i} values in the rat after acute parathyroidectomy (11–16). Our results demonstrate that the acute TPTX rat on a high-phosphorus intake can readily increase FE_{P_i} during phosphate loading (Fig. 4).

The chronic TPTX *low*-phosphorus rats with the greatest filtered P_i loads demonstrated significantly increased absolute P_i reabsorption when compared to the corresponding high-phosphorus animals with filtered P_i loads in excess of 150 μg/min·100 g body wt. Indeed, the high-phosphorus chronic TPTX rats manifested a Tm_{P_i} of 120–140 μg/min·100 g (Table II), while no such tendency to develop a Tm_{P_i} could be discerned in the low-phosphorus group. Finally, during late phosphate infusion, P_i reabsorption per unit GFR was significantly greater in both the acute and chronic TPTX low-phosphorus rats than in their corresponding high-phosphorus counterparts.

Calcium infusion has been reported both to increase (17) and to decrease (18) P_i reabsorption, and hypercalcemia has been reported to reduce the phosphaturic response to volume expansion in the rat (19). In our two groups of *acute* TPTX rats, control plasma calcium values were similar, but plasma calcium decreased substantially during phosphate infusion in the low-phosphorus dietary group. If P_i reabsorption varies directionally with the plasma calcium (17, 19), then P_i reabsorption in the low-phosphorus acute TPTX rats might have been impaired secondary to hypocalcemia during late phosphate infusion. Within the *chronic* TPTX groups, plasma calcium was initially greater in the low-phosphorus rats, but values in the two groups became nearly equal by late phosphate infusion. Yet, P_i reabsorption remained virtually complete in the *low*-phosphorus group.

A correlative relationship between P_i and sodium reabsorption has been demonstrated for both the proximal tubule (20) and whole kidney (21, 22) of the dog during saline loading. Gradowska and co-workers could not elicit a phosphaturic response in the dog during saline loading after acute TPTX, but a brisk phosphaturic response *did* occur during volume expansion in the chronic TPTX dog (23). Hebert et al. demonstrated that P_i reabsorption could be diminished by saline loading in the acute TPTX dog when the plasma P_i was elevated by phosphate infusion (24). Our studies were performed after a moderate degree of saline loading, but the protocol was designed to diminish the amount of progressive volume expansion because sodium infusion during phosphate loading occurred at only half the previous rate. That this was relatively successful is suggested by the lack of a progressive increase in FE_{Na} (Table I). FE_{P_i} and FE_{Na} were correlated slightly in both low-phosphorus groups. However, a diminished sodium excretion was not required for the increased urinary P_i threshold and the relatively increased absolute P_i reabsorption accompanying the low-phosphorus intake.

Vitamin D (25, 26) and its metabolites (26, 27), when administered in pharmacologic doses, accelerate P_i reabsorption, although the presence of PTH may be required for such an action in the rat (28). Recently, we have carried out phosphate loading studies in chronic TPTX phosphorus-depleted rats which were also vitamin D-deficient (4). Even at very high plasma P_i levels during phosphate infusion, those animals reabsorbed essentially all the filtered P_i, similarly to the present chronic TPTX low-phosphorus animals which were not deficient in vitamin D. Thus, the avid reabsorption of P_i during phosphorus depletion is not impaired during vitamin D deficiency, at least if PTH is absent. Costanzo et al., on the other hand, have reported the presence of a vitamin D-reversible urinary

P_i "leak" in *acutely* parathyroidectomized D-deficient rats (29). Vitamin D and its metabolites probably are not necessary for the development of phosphaturia during phosphate loading in rats stabilized on a high phosphorus intake. In acute TPTX rats stabilized on a vitamin D-deficient 1% phosphorus diet, both FE_{P_i} and absolute P_i reabsorption are similar to values encountered in animals receiving the same diet not deficient in vitamin D (T. H. Steele and H. F. DeLuca, unpublished observations). Therefore, vitamin D deficiency in high- and low-dietary phosphorus TPTX animals does not appear to measurably accelerate or impair P_i reabsorption.

Because the kidney provides a major route for the elimination of P_i from the body, the rate of P_i excretion per nephron must reflect phosphorus intake if balance is to be maintained. In the dog with experimental chronic renal disease, Slatopolsky and coworkers demonstrated that fractional P_i reabsorption was strikingly diminished, but increased to nearly normal values after TPTX (30). They postulated that PTH increases P_i excretion per nephron under those conditions where the dietary phosphorus intake per functioning nephron is disproportionately great (30). Indeed, studies in normal man have demonstrated that phosphate ingestion results in a decline in the ionized serum calcium and in an elevated serum PTH (31). Slatopolsky et al. also have shown that the reduction in fractional P_i reabsorption, normally accompanying a sequential reduction of the nephron population, can be prevented in dogs maintained on a low-phosphorus diet (32). Other studies from the same laboratory have demonstrated that a progressive reduction in the dietary phosphorus intake, proportionate to the degree of reduction in GFR, resulted in the maintenance of a normal fractional P_i reabsorption in dogs with reduced nephron populations (33). Furthermore, an inverse relationship between fractional P_i reabsorption and serum PTH levels suggested that the parathyroids were responsible for the adaptive increase in P_i excretion per nephron (32, 33).

On the other hand, Van Stone and Hano have reported that P_i excretion varies directly with the dietary phosphorus in parathyroidectomized rats receiving a constant amount of exogenous PTH (34). Although their experiments indicated that varying amounts of PTH were not necessary for the regulation of P_i excretion per nephron, the presence of PTH might have been necessary to promote P_i excretion. Also, their changes in P_i excretion could have resulted from alterations in plasma P_i. Recently, Swenson et al. have indicated that TPTX vitamin D-treated dogs subjected to partial renal ablation could increase FE_{P_i} and maintain plasma P_i values comparable to control non-TPTX animals with similar reductions in renal function (35). In those experiments, the role of vitamin D. the dietary phosphorus content, and the degree of extracellular fluid volume expansion can not be evaluated.

The data presented here indicate that the renal P_i threshold and P_i reabsorption can be modulated according to the dictates of the antecedent dietary phosphorus intake, independently of the plasma P_i and filtered P_i per se, even after PTH has been absent for nearly 48 h. Although the action of PTH is vitally important to the maintenance of normophosphatemia under usual circumstances, an additional phosphorus-dependent system for the regulation of P_i reabsorption also appears to exist. This system might function primarily to facilitate the rapid repletion of body phosphorus stores during the correction of phosphate depletion. At present, however, the physiologic importance of this putative PTH-independent system is not known. Nevertheless, the present results do emphasize the necessity of controlling the dietary phosphorus intake in studies of renal P_i reabsorption, especially if observations are made during the hypofunction or absence of the parathyroid glands.

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