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 (Pi) reabsorption was studied during Pi 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 Pi reabsorption between the high- and low-phosphorus dietary groups. After chronic TPTX, the rats stabilized on the low-phosphorus diet exhibited nearly complete Pi reabsorption at every plasma Pi level, while the animals receiving the high-phosphorus diet manifested a marked phosphaturic response to Pi infusion. In addition, Pi reabsorption was significantly increased in the chronic TPTX low-phosphorus rats which achieved the highest filtered Pi loads, while their urine remained essentially phosphate-free. Dietary phosphorus-dependent alterations in Pi reabsorption may play a significant role in establishing the rate of Pi excretion per nephron under certain circumstances and should be considered in the interpretation of studies investigating renal Pi handling. The ability of phosphorus-depleted animals to maintain a phosphate-free urine during Pi loading would favor the rapid repletion of body phosphate stores.

INTRODUCTION

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

Recent studies in the phosphorus-depleted vitamin D-deficient rat (4), as well as older observations in the rat (3) and man (6, 7), have suggested that Pi reabsorption may be accentuated during phosphorus depletion. Presumably, the excretion of a Pi-free urin during phosphorus depletion has been attributed to hypophosphatemia and the resulting decrease in filtered Pi, both of which are known to decrease the urinary Pi (1, 2). Our results indicate that renal Pi reabsorption is enhanced substantially in the chronically thyroparathyroidectomized phosphorus-depleted rat, independently of the plasma Pi 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.
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

(Fromonta, 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·min 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

**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.
TABLE I
Dietary Phosphorus and \( P_i \) Excretion in Acute and Chronic TPTX Rats

<table>
<thead>
<tr>
<th></th>
<th>Control</th>
<th>Early Infusion</th>
<th>Late Infusion</th>
<th>Control</th>
<th>Early Infusion</th>
<th>Late Infusion</th>
<th>Control</th>
<th>Early Infusion</th>
<th>Late Infusion</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>GFR</td>
<td>早</td>
<td>晚</td>
<td>PO_{4} (1%)</td>
<td>早</td>
<td>晚</td>
<td>PO_{4} (1%)</td>
<td>早</td>
<td>晚</td>
</tr>
<tr>
<td>Acute TPTX</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>High-phosphorus (1%) P_i diet (n = 8)</td>
<td>0.80±0.03</td>
<td>0.77±0.12</td>
<td>0.91±0.12</td>
<td>0.83±0.03</td>
<td>13.6±1.1</td>
<td>17.6±1.1</td>
<td>1.24±0.03</td>
<td>3.34±1.1</td>
<td>23.3±1.1</td>
</tr>
<tr>
<td>Low-phosphorus (0.02%) P_i diet (n = 8)</td>
<td>1.07±0.06</td>
<td>0.98±0.04</td>
<td>0.84±0.04</td>
<td>4.6±0.06</td>
<td>10.9±1.5</td>
<td>17.5±1.5</td>
<td>0.16±0.06</td>
<td>0.10±0.8</td>
<td>9.29±1.5</td>
</tr>
<tr>
<td>Chronic (48-h) TPTX</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>High-phosphorus (1%) P_i diet (n = 7)</td>
<td>1.19±0.01</td>
<td>1.15±0.10</td>
<td>1.08±0.10</td>
<td>9.9±0.01</td>
<td>15.1±0.6</td>
<td>18.9±0.6</td>
<td>10.1±0.01</td>
<td>20.8±1.0</td>
<td>30.6±1.0</td>
</tr>
<tr>
<td>Low-phosphorus (0.02%) P_i diet (n = 13)</td>
<td>1.11±0.08</td>
<td>0.86±0.09</td>
<td>0.97±0.09</td>
<td>4.3±0.08</td>
<td>10.0±0.5</td>
<td>17.5±0.5</td>
<td>0.19±0.08</td>
<td>0.15±0.05</td>
<td>0.20±0.05</td>
</tr>
<tr>
<td>Acute vs. chronic</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>High-phosphorus ( P &lt; 0.01 )</td>
<td>( P &lt; 0.01 )</td>
<td>0.05±0.05</td>
<td>NS</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Low-phosphorus</td>
<td>NS</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Values are mean±SEM. Symbols indicate significant paired changes from control within the same experimental group: * \( P < 0.05 \); † \( P < 0.02 \); ‡ \( P < 0.001 \). 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 20.20±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.

Dietary \( P \) and \( P_i \) Reabsorption
Eight rats of the low-phosphorus chronic TPTX group and all the high-phosphorus chronic TPTX rats achieved filtered Pi values greater than 150 μg/min·100 g body wt. At these high filtered Pi loads, which averaged 204±16 and 189±9 μg/min·100 g body wt in the low- and high-dietary phosphorus groups, respectively, the simultaneous absolute Pi reabsorption values averaged 203±16 and 138±7 μg/min·100 g body wt, respectively (P < .001). Also, when filtered Pi was greater than 150 μg/min·100 g body wt, Pi 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 Pi reabsorption was enhanced significantly in the phosphorus-depleted chronic TPTX rats with the largest filtered Pi loads.

Fractional sodium excretion (FENa) was variable, but did not change in any consistent manner during phosphate infusion in the four groups of rats (Table I). FENa was correlated significantly with FEPi 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 Pi handling between corresponding acute and chronic TPTX groups were not present (Table I). Although the degree of variation was wide, FEPi values tended to be similar in magnitude, at any plasma Pi level in the high-phosphorus
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 \( \text{FE}_{P_i} \) was 10.9±2.3%. During early phosphate infusion, plasma \( P_i \) averaged 13.5±0.9 mg/100 ml and \( \text{FE}_{P_i} \) was 22.6±2.2%. During late phosphate infusion, plasma \( P_i \) was 19.0±0.9 mg/100 ml and \( \text{FE}_{P_i} \) 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 II

**Effect of Dietary Phosphorus on \( P_i \) Reabsorption**

<table>
<thead>
<tr>
<th>Filtered ( P_i )</th>
<th>Absolute ( P_i ) reabsorption</th>
<th>( P_i ) reabsorption per unit GFR</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>( \mu g/\min \cdot 100 \text{ g} )</td>
<td>( \mu g/\min \cdot 100 \text{ g} )</td>
</tr>
<tr>
<td><strong>Acute TPTX</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>High-phosphorus (1% P)</td>
<td>65±10</td>
<td>103±13</td>
</tr>
<tr>
<td>diet (n = 8)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Low-phosphorus (0.02% P)</td>
<td>49±4</td>
<td>103±13</td>
</tr>
<tr>
<td>diet (n = 8)</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Chronic (48 h) TPTX</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>High-phosphorus (1% P)</td>
<td>126±9</td>
<td>171±12</td>
</tr>
<tr>
<td>diet (n = 7)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Low-phosphorus (0.02% P)</td>
<td>48±4</td>
<td>84±10</td>
</tr>
<tr>
<td>diet (n = 13)</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Acute vs. chronic TPTX</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>High-phosphorus</td>
<td>P &lt; 0.005</td>
<td>NS</td>
</tr>
<tr>
<td>Low-phosphorus</td>
<td>NS</td>
<td>NS</td>
</tr>
</tbody>
</table>

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).

### Table III

**Plasma Calcium during \( P_i \) Infusion**

<table>
<thead>
<tr>
<th></th>
<th>Control periods</th>
<th>Late ( P_i ) infusion</th>
</tr>
</thead>
<tbody>
<tr>
<td>( \mu g/100 \text{ ml} )</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Acute TPTX</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>High-phosphorus diet (n = 8)</td>
<td>7.2±0.3</td>
<td>7.7±0.3*</td>
</tr>
<tr>
<td>Low-phosphorus diet (n = 8)</td>
<td>6.9±0.5</td>
<td>5.6±0.3*</td>
</tr>
<tr>
<td><strong>Chronic TPTX</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>High-phosphorus diet (n = 7)</td>
<td>4.1±0.4</td>
<td>5.3±0.4†</td>
</tr>
<tr>
<td>Low-phosphorus diet (n = 13)</td>
<td>7.4±0.3</td>
<td>5.7±0.2‡</td>
</tr>
</tbody>
</table>

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).
REABSORPTION increased absolute during phosphate infusion. Our results demonstrate that the values in the greatest acute collaborators concerned in the loading. The plasma FEpi prolongs the phosphate Pi infusion, with several investigators reporting that. Pi reabsorption was as great in the acute and chronic TPTX groups as the chronic TPTX rats, control plasma calcium values were similar, but plasma calcium decreased substantially during phosphate infusion in the low-phosphorus dietary group. If Pi reabsorption varies directionally with the plasma calcium, then Pi reabsorption in the low-phosphorus acute TPTX rats might have been impaired secondary to hypo-calcemia 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, Pi reabsorption remained virtually complete in the low-phosphorus group.

A correlative relationship between Pi and sodium reabsorption has been demonstrated for both the proximal tubule (20) and whole kidney (21, 22) of the dog during saline loading. Gradovska 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 Pi reabsorption could be diminished by saline loading in the acute TPTX dog when the plasma Pi 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. This was relatively successful is suggested by the lack of a progressive increase in FENa (Table I). FEpi and FENa were correlated slightly in both low-phosphorus groups. However, a diminished sodium excretion was not required for the increased urinary Pi threshold and the relatively increased absolute Pi reabsorption accompanying the low-phosphorus intake.

Vitamin D (25, 26) and its metabolites (26, 27), when administered in pharmacologic doses, accelerate Pi 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 Pi levels during phosphate infusion, those animals reabsorbed essentially all the filtered Pi, similarly to the present chronic TPTX low-phosphorus animals which were not deficient in vitamin D. Thus, the avid reabsorption of Pi during phosphate infusion 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

---

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

---

Calcium infusion has been reported both to increase (17) and to decrease (18) Pi reabsorption, and hyper-calcemia 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 Pi reabsorption varies directionally with the plasma calcium (17, 19), then Pi reabsorption in the low-phosphorus acute TPTX rats might have been impaired secondary to hypo-calcemia 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, Pi reabsorption remained virtually complete in the low-phosphorus group.

---

872 T. H. Steele and H. F. DeLuca
Pi "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 \( FE_{\text{Pi}} \) 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 co-workers 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 \( FE_{\text{Pi}} \) 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.

ACKNOWLEDGMENTS

We gratefully acknowledge the highly capable assistance of Kathryn Dudgeon, Catherine Larmore, and Yoko Tanaka in the performance of these experiments.

This work was supported by U. S. Public Health Service grants AM-14881, AM-15512, and AM-15162.

REFERENCES