EVALUATION OF THEORETICAL RENAL PHOSPHORUS THRESHOLD AS AN INDEX OF RENAL PHOSPHORUS HANDLING

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SUMMARY

1. A simple phosphate infusion technique was employed to produce a linear elevation of plasma phosphorus levels with time. Using this technique theoretical renal phosphorus threshold (TRPT) was determined from sixty-seven infusions performed in fifty subjects in order to evaluate this measure of the renal excretion of phosphorus.

2. Glomerular filtration rate (GFR) was determined from phosphate data, and the maximum tubular reabsorptive capacity for phosphate (TmP) was obtained as the product of TRPT and GFR. Results obtained by simple graphic derivation of TRPT and GFR compared well with those obtained by regression analysis.

3. The normal adult range of TRPT was 2.7-4.1 mg/100 ml with a mean of 3.4 ± 0.4 (SD) mg/100 ml while adolescents had higher values. Results were compared in subjects with various disturbances of calcium and phosphorus metabolism. In primary hyperparathyroidism with and without bone disease the range of TRPT was 0.5-2.8 mg/100 ml with a mean of 2.0 ± 0.7 (SD) mg/100 ml (difference from normals P<0.0125); in osteomalacia before and during treatment the range of TRPT was 0.3-1.9 mg/100 ml with a mean of 1.0 ± 0.6 (SD) mg/100 ml (difference from normals P<0.0005). The standard deviation in repeated tests in the same individual was ±0.28 mg/100 ml.

4. There was a significant positive correlation between TRPT (TmP/GFR) and GFR. Changes in GFR of 10 ml/min were associated with absolute changes in TRPT of 0.08-0.19 mg/100 ml. Thus TRPT showed very much less dependence on GFR than TmP and appeared the more consistent index of renal phosphate handling.

5. The technique has proved valuable in monitoring the response to treatment in different forms of osteomalacia. It has provided evidence of increased urinary phosphate excretion in some patients with idiopathic osteoporosis. Lysine and probably...
certain other amino acids may be infused by the same technique for the more precise study of the renal excretion of these compounds.

Any assessment of renal excretion of phosphorus which involves the measurement of basal phosphate clearance (Kyle, Schaaf & Canary, 1958) suffers the twin disadvantages of primary dependence on glomerular filtration rate and on prevailing concentration of plasma phosphorus. Attempts to correct for one or both of these variables have included the measurement of phosphate/creatinine clearance ratio (McGeown, 1957), percentage tubular reabsorption of phosphate (Goldman, Gordan & Chambers, 1957; Thomas, Connor & Morgan, 1958), and the phosphorus excretion index (Nordin & Fraser, 1960). All these methods depend on the fact that the kidney excretes phosphate at normal plasma concentrations in the presence of an active tubular transport mechanism for phosphate reabsorption. More theoretically precise methods such as the measurement of maximum tubular reabsorptive capacity ($T_m^p$) (Smith, 1956; Thompson & Hiatt, 1957) have been hampered by greater technical difficulties, the need for an independent estimate of GFR and the quite large errors inherent in calculations based on the difficult chemical determination of inulin clearance (Bartter, 1961).

Anderson (1955) described a method for $T_m^p$ determination using a technique of phosphate infusion alone which produced a linear rise in plasma phosphorus levels. In this way urine phosphorus excretion in successive collection periods could be plotted against a number of true average plasma phosphorus levels, obtained at the midpoint of each urine collection. At the raised plasma phosphorus levels required to reach $T_m^p$, the rise in urinary phosphorus excretion relative to the rise in plasma phosphorus levels becomes a straight line, the slope of which is determined by GFR. Extrapolation of this straight line to the point of zero urine phosphorus excretion gives the concentration of plasma phosphorus corresponding to the theoretical renal phosphorus threshold (TRPT). TRPT is thus the ratio $T_m^p$/GFR.

Anderson's method while theoretically sound is technically tedious and a less cumbersome modification was introduced by Hyde, Jones, McSwiney & Prunty (1960). The recent availability of a mechanical peristaltic pump, in which increasing dial settings were shown to give constant increments in delivery rates, simplified the procedure still further and the test can now be performed without difficulty by a single attendant.

The purpose of this paper is to describe the method, to delineate the normal range and reproducibility of TRPT obtained, to discuss the relationship between TRPT, GFR, and $T_m^p$ and to indicate the value of the determination in clinical investigation.

**SUBJECTS AND METHODS**

The fifty subjects tested included a normal group of thirteen volunteer medical students and laboratory staff (twenty-one tests), ten patients with primary hyperparathyroidism, eight patients with osteomalacia of various origins both before and during treatment (thirteen tests), four patients with hypoparathyroidism (five tests), two with idiopathic hypercalciuria, and two with osteoporosis. The remaining eleven patients (fourteen tests) had a wide range of diagnoses (Table 1, nos. 7–17).

Tests were begun at about 09.00 hours after a 12–14 h fast. Subjects were given 2–3 l. of water to drink over a total 3-h period. After a control urine collection period of 30–60 min the phosphate infusion consisting of a 0.1 M solution of sodium phosphate buffered at pH 7.4
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### TABLE 1. Values for TRPT, GFR and $T_m^P$ in the determination of individual reproducibility (nos. 1–7) and in the investigation of certain patients (correlation coefficient between plasma phosphorus concentration and urine phosphorus excretion $r > 0.99$ except where indicated)

<table>
<thead>
<tr>
<th>Subject no.</th>
<th>Diagnosis</th>
<th>TRPT (mg/100 ml)</th>
<th>GFR (ml/min)</th>
<th>$T_m^P$ (mg min$^{-1}1.73$ m$^{-2}$)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Normal</td>
<td>3.5</td>
<td>175</td>
<td>5.0</td>
</tr>
<tr>
<td></td>
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<td>147</td>
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<td>4.1</td>
<td>160</td>
<td>5.3</td>
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<td></td>
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<td>3.8</td>
<td>142</td>
<td>4.3</td>
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<td></td>
<td></td>
<td>2.9</td>
<td>87</td>
<td>2.8</td>
</tr>
<tr>
<td>3</td>
<td>Normal</td>
<td>3.8†</td>
<td>95</td>
<td>3.9</td>
</tr>
<tr>
<td></td>
<td></td>
<td>2.9†</td>
<td>83</td>
<td>2.6</td>
</tr>
<tr>
<td>4</td>
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<td>5</td>
<td>Primary hypophosphataemia</td>
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<td>53</td>
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<td></td>
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<td>38</td>
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<td>105</td>
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<td></td>
<td></td>
<td>1.7</td>
<td>105</td>
<td>1.8</td>
</tr>
<tr>
<td>7</td>
<td>Treated tropical sprue</td>
<td>4.4</td>
<td>77</td>
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<td></td>
<td></td>
<td>4.6</td>
<td>103</td>
<td>4.9</td>
</tr>
<tr>
<td>8</td>
<td>Treated malabsorption syndrome; partial gastrectomy, lactase and sucrase deficiency, colitis</td>
<td>4.4</td>
<td>44</td>
<td>2.6</td>
</tr>
<tr>
<td>9</td>
<td>Isolated hypophosphataemia 2.5 mg/100 ml; healthy mother of child with hereditary vitamin D-resistant rickets</td>
<td>2.8</td>
<td>88</td>
<td>2.6</td>
</tr>
<tr>
<td>10</td>
<td>Spontaneous resolution of vitamin D-resistant osteomalacia; no treatment 10 years but persistent hypophosphataemia 2.3 mg/100 ml</td>
<td>2.8</td>
<td>88</td>
<td>2.5</td>
</tr>
<tr>
<td>11</td>
<td>Nutritional osteomalacia, tertiary hyperparathyroidism, osteitis fibrosa; post-operative treatment:</td>
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<td></td>
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<tr>
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<td>DHT 1 mg daily 2 months</td>
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<tr>
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<td>65</td>
<td>4.7</td>
</tr>
<tr>
<td></td>
<td>Vitamin D$_2$ 1 mg daily substituted 4 months</td>
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<td>81</td>
<td>3.5</td>
</tr>
<tr>
<td>12</td>
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<td>82</td>
<td>6.7</td>
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<td>Idiopathic juvenile osteoporosis; aged 13</td>
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<td>107</td>
<td>8.0</td>
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<td>Milk-alkali syndrome</td>
<td>NS*</td>
<td>19</td>
<td>—</td>
</tr>
<tr>
<td>15</td>
<td>Hypercalcaemic sarcoidosis</td>
<td>NS*</td>
<td>2</td>
<td>—</td>
</tr>
<tr>
<td>16</td>
<td>Hypoparathyroidism; vitamin D intoxication</td>
<td>1.0</td>
<td>28</td>
<td>0.3</td>
</tr>
<tr>
<td>17</td>
<td>Chronic pyelonephritis</td>
<td>1.6</td>
<td>39</td>
<td>0.6</td>
</tr>
</tbody>
</table>

* NS = no significant correlation between plasma and urinary phosphorus ($r = 0.57$ and 0.55 respectively).
† $0.97 < r < 0.99$. 
(Na$_2$HPO$_4$.2H$_2$O, 13.8 g; NaH$_2$PO$_4$.2H$_2$O, 3.6 g, water to 1 l.) was begun into a forearm vein. The Buchler Polystaltic pump (Buchler Instrument Co., Fort Lee, New Jersey, U.S.A.) was used, with silicone rubber tubing (Escorubber) of either 2.5 mm or 3.2 mm internal diameter which could be repeatedly sterilized. A linear rise in plasma phosphorus levels over the subsequent period of approximately 150 min was obtained simply by increasing the pump dial setting by $\frac{1}{2}$-division every 15 min. Typical calibration lines of delivery rate versus dial setting, together with the initial pilot study of plasma phosphorus levels obtained as above, are shown in Fig. 1. Bladder catheterization was unjustifiable and all but a very small number of patients could void on request and time the start of the urinary stream to within 5 or 10 s.

Six urine samples each of approximately 24 min duration were collected in the course of an infusion. Blood samples at the planned midpoint of each urine period were collected via an indwelling disposable cannula inserted into an opposite forearm vein and fitted with a two-way tap. In those very few patients who could not void on time more frequent blood samples were collected and the midpoint plasma phosphorus levels were determined by interpolation. It can be easily shown that errors due to delay time in urine excretion are negligible (McSwiney & de Wardener, 1950).

The total phosphate infused over 2$\frac{1}{2}$ h was planned to vary between 60 and 90 mmol (600-900 ml) depending on the size of the patient and the degree of any urea retention, by varying the size of the pump tubing and the initial dial setting. In all subjects the average rise of plasma phosphorus levels to the final midpoint was 8.6±2.4 (SD) mg/100 ml, and no significant symptoms developed in patients achieving the highest plasma levels.
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Since the straight-line relationship between plasma phosphorus levels and urine phosphorus excretion only holds at levels of $T_m$, the control and first infusion periods were not used in the regression analysis for TRPT and GFR and all calculations were thus based on the last five urine collection periods.

The accuracy of GFR determinations from the phosphate data was verified by an independent estimate of GFR in almost every test using either $[^{51}Cr]$ EDTA or inulin, or both, infused after a priming dose at a constant rate through a second pump. The simultaneous infusions entered the same intravenous cannula via an open two-way tap. Phosphorus was estimated in plasma and urine by the method of Gomori (1942) adapted for use with an AutoAnalyzer. Determinations were performed in duplicate, or triplicate where necessary to obtain agreement to the nearest 0.05 mg/100 ml.

**RESULTS**

Typical plots of urine phosphorus excretion against the concentration of plasma phosphorus are shown in Fig. 2 for three subjects, a patient with primary hyperparathyroidism, a patient with hypoparathyroidism and a normal subject. Out of sixty-seven tests, in fifty the correlation coefficient ($r$) between plasma phosphorus concentration and urine phosphorus excretion was greater than 0.99, in sixty-two $r$ was greater than 0.97, and in the remaining five less than 0.97. TRPT and GFR were determined graphically by a single observer before calculation.
A very small but significant overestimation of TRPT by a mean of 0.06 mg/100 ml resulted \((P<0.025)\); sixty values differed by not more than 0.2 mg/100 ml and fifty-five values by not more than 0.1 mg/100 ml from those calculated. A similarly small overestimation of GFR by a mean of 0.7±2.6 (SD) ml/min \((P<0.025)\) resulted. The ratio of phosphate-GFR/mean inulin clearance in thirty-eight simultaneous infusions was 1.00±0.03 (SEM). In thirty-three simultaneous infusions the ratio mean \(\text{[}^{51}\text{Cr}]EDTA\text{ clearance/phosphate-GFR = 0.94±0.03 (SEM).}

![Graph showing comparison between TRPT (○ or △) and respective TmP (○ or △) in normal subjects and patients with various disorders of calcium and phosphorus metabolism.](image)

**Fig. 3.** Comparison between TRPT (○ or △) and respective TmP (○ or △) in normal subjects and patients with various disorders of calcium and phosphorus metabolism.

Seven subjects were tested on a total of eighteen occasions at intervals of up to 1 year in order to determine the individual reproducibility of TRPT and TmP (Table 1, nos. 1–7). Analysis of variance gave a SD for TRPT of ±0.28 mg/100 ml, while the SD of TmP was ±0.55 mg/min. The SD of GFR was ±11 ml/min. Thus it was apparent that the variance of TmP was proportionately much greater than the variance of TRPT, as might be expected when two variables (TRPT and GFR) are multiplied to obtain a third \(T_mP\).

Fig. 3 shows the calculated respective values of TRPT and TmP in each major group of
Theoretical renal phosphorus threshold

subjects. In thirteen normal subjects the mean TRPT was 3.4±0.4 (SD) mg/100 ml (range 2.7–4.1 mg/100 ml), and the mean $T_m^P$ was 3.8±0.9 (SD) mg min$^{-1}$ 1.73 m$^{-2}$ (range 2.6–5.3).

In ten patients with subsequently proven primary hyperparathyroidism the mean TRPT was 2.0±0.7 (SD) mg/100 ml (difference from normals $P<0.0125$, range 0.5–2.8) and the mean $T_m^P$ was 1.8±0.9 (SD) mg min$^{-1}$ 1.73 m$^{-2}$ (difference from normals $P<0.025$, range 0.3–3.3). In eight patients with osteomalacia from several different causes the mean TRPT was 1.0±0.6 (SD) mg/100 ml (difference from normals $P<0.0005$, difference from primary hyperparathyroidism 0.05 $P<0.1$, range 0.3–1.9) and the mean $T_m^P$ was 0.9±0.8 (SD) mg min$^{-1}$ 1.73 m$^{-2}$ (difference from normals $P<0.0025$, range 0.3–2.3). In each group it was again apparent that the variance in TRPT was appreciably smaller than the variance in $T_m^P$. Fig. 3 also illustrates the rather wide range of TRPT in patients with hypoparathyroidism, from clinically marginal, e.g. post-thyroidectomy, to florid states, e.g. idiopathic. In two patients with idiopathic hypercalciuria and renal stone formation, low values of TRPT and $T_m^P$ occurred, while of two patients with idiopathic osteoporosis one had TRPT above and one had TRPT below the normal range (Fig. 3).

Results obtained in eleven other subjects tested are given in the Table (nos. 7–17). Mildly elevated levels of TRPT were found in two patients with treated malabsorption syndromes (nos. 7 and 8). Two healthy subjects with evidence of a primary renal phosphate-losing defect had borderline low normal values (nos. 9 and 10). Two adolescent patients (nos. 12 and 13) had values of TRPT well above the normal adult range. One unusual patient (no. 11) with severe nutritional osteomalacia underwent parathyroidectomy for tertiary hyperparathyroidism and was tested repeatedly in the postoperative period; substitution of vitamin D$_2$ for dihydrotachysterol (DHT) was associated with a marked temporary rise in TRPT. Of seven patients in the series with chronic renal failure arbitrarily defined as GFR below 40 ml/min, three had primary hypophosphataemia and the remainder are listed in the Table (nos. 14–17).

The possible relationship between TRPT and GFR was studied and Fig. 4 shows the correlation between TRPT and GFR corrected for body surface area in two groups, normal subjects and patients with primary hyperparathyroidism. The correlation in twenty-one tests on thirteen normal subjects was highly significant, $r = 0.66$ ($P<0.0025$). In ten hyperparathyroid patients the correlation coefficient $r$ was 0.52 and this just failed to reach levels of significance ($0.1 > P > 0.05$). The relationship between low GFR and TRPT in five of the seven patients with chronic renal failure, omitting cases no. 14 and 15 (see Table 1), is also illustrated in Fig. 4. Regression analysis for TRPT on GFR (corrected for body surface area) gave the equations:

\[
TRPT = 1.26 + 0.019 \times GFR \text{ in normal subjects, and}
\]
\[
TRPT = 0.37 + 0.019 \times GFR \text{ in patients with hyperparathyroidism.}
\]

Thus at theoretical zero GFR, in normal subjects TRPT would become 1.26 mg/100 ml, while in patients with primary hyperparathyroidism TRPT would become 0.37 mg/100 ml. The slopes of both regressions however were identical. The correlation between TRPT and GFR was also determined from fifteen tests in ten subjects with hypophosphataemia of renal tubular origin not due to primary hyperparathyroidism. Eight either had active osteomalacia or were on long-term treatment for renal tubular defects including hereditary vitamin D resistant rickets, Wilson's disease, and adult-presenting hypophosphataemic osteomalacia. Two were healthy (Table 1, nos. 9 and 10). The correlation in these fifteen tests was again
significant, \( r = 0.49 \) (\( P < 0.05 \)) and regression analysis gave the equation:

\[
\text{TRPT} = 0.07 + 0.014 \times \text{GFR}
\]

In order to exclude the possibility of a false correlation between TRPT and GFR introduced by the body surface area correction, the regression of TRPT on GFR without correction of the latter for body surface area was analysed in normal subjects and gave the equation:

\[
\text{TRPT} = 2.4 + 0.008 \times \text{GFR}
\]

The slope of this regression was thus more shallow than that obtained using the corrected GFR but the correlation coefficient \( (r = 0.55) \) remained highly significant \( (P < 0.005) \).

The reverse regressions of GFR on TRPT were also analysed. At theoretical zero TRPT, GFR would become 36, 57 and 60 ml/min in normal subjects, hyperparathyroid patients, and the ten ‘renal tubular’ patients respectively. This illustrates from the opposite standpoint the excessive renal phosphate loss relative to GFR in these conditions.

The important relationship between TRPT and pre-infusion plasma phosphorus levels was determined, and this more complex correlation is illustrated in Fig. 5. The correlation coefficient \( r \) was 0.62 \( (P < 0.0001) \) and was derived from sixty-three tests. At values of TRPT of 2.0 mg/100 ml and above the appearances are those of a straight-line relationship. Below this value however plasma phosphorus levels tend to be higher again, due presumably to phosphate retention from the increasingly low glomerular filtration rates associated with the lower levels of TRPT.
DISCUSSION

Determination of the physiological response to a load or stress may be useful in situations where resting or basal measurements show considerable variability between normal and abnormal ranges, as with renal phosphate clearance (McGeown, 1957; Hodgkinson, 1961). This principle is involved in the determination of maximum tubular reabsorptive capacity.

Early measurements of phosphate $T_m$ were performed in the presence of rapidly falling plasma levels following a single intravenous injection (Ollayos & Winkler, 1943), or at variably raised plasma phosphorus levels during a constant infusion, or in the presence of PAH which itself affected phosphate transport (Thompson & Hiatt, 1957). These studies thus all contained sources of error.

Anderson (1955) showed that a simultaneous accurate determination of $T_mP$, GFR, and the mean phosphorus threshold ($T_mP$/GFR ratio) could be obtained by a technique of phosphate infusion alone, using a method aimed to achieve a linear increase in plasma phosphorus levels. He derived the following equation to express the relationship between phosphate infusion rate and plasma phosphorus level:

$$R = F K t + F c + S K - T_m$$

Where $R$ = rate of phosphate infusion (mg/min); $F$ = GFR (ml/min); $S$ = phosphate 'space

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**FIG. 5.** Relationship between TRPT and fasting plasma phosphorus level; ● = normal subjects, ○ = patients.
(ml); $K$ = rate of rise of plasma phosphorus concentration ($\text{mg ml}^{-1} \text{min}^{-1}$); $t$ = time (min); $c$ = plasma phosphorus concentration at zero time (mg/ml) and $T_m = T_m P$ (mg/min). The relevance of this equation to the present study is that if GFR, phosphate space, and $T_m P$ are all constants as expected, then achievement of a linear increase in infusion rate with time should produce a linear rise in plasma phosphorus levels; it is therefore unnecessary to calculate first the amounts of phosphate to be infused as was done in earlier studies since the final extent of plasma phosphorus rise and therefore the total amount of phosphate infused is unimportant within fairly broad limits.

The method described here is relatively simple to perform, is easily left in the hands of a single attendant and a linear rise in plasma phosphorus level can be achieved by no more arduous means than altering a simple dial setting every 15 min. In most instances simple graphic derivation of results appears adequate. Employing a different technique McSwiney & Prunty (1961) found that the determination of $T_m P$/GFR ratio, called by them the theoretical renal phosphorus threshold (TRPT), proved a more reliable method than the other standard indices of renal phosphorus handling. We have also confirmed the accuracy of GFR determination by the present method by simultaneous comparison with both inulin and $^{51}\text{Cr}$ EDTA clearances (Stamp, Stacey & Rose, 1970). The infusion technique described here provides a way to study also the renal handling of other substances such as amino acids; thus linear increments in plasma lysine levels can be achieved by the same technique for the study of $T_m$ and threshold values for this amino acid (Cusworth, Lester & Stamp, unpublished).

While the clinical determination of TRPT (and other indices of renal phosphorus excretion) has usually been applied to the study of hyperparathyroidism, this diagnosis still rests mainly on the accurate determination of plasma calcium corrected for plasma protein (Dent, 1962) rather than on renal studies (reviewed by Fourman & Royer, 1968). However, more important applications are to be found, particularly in the investigation of different forms of osteomalacia and their subsequent response to therapy (Dent & Stamp, 1970). In idiopathic osteoporosis we have found a small proportion of patients with low plasma phosphorus levels (unpublished results) in contrast to the normal tendency to raised values in this condition (reviewed by Dent & Watson, 1966). The present finding that TRPT may also be abnormally low requires further investigation. During the postoperative treatment of osteitis fibrosa with vitamin $D_2$ and dihydrotachysterol higher values of TRPT have been found than in simple hypoparathyroidism; treatment with vitamin $D_2$ may be associated with a significantly higher TRPT than treatment with the same amount of dihydrotachysterol.

The present study has shown that the measurement of TRPT is more accurate and reproducible and has narrower ranges of normal and abnormal values than the measurement of $T_m P$, primarily because of its much smaller dependence on GFR. Unlike $T_m P$ it therefore probably does not require correction in terms of body surface area. It is significant that adolescents may have high uncorrected values for TRPT, commensurate with their plasma phosphorus levels, despite their small stature; further upward correction of TRPT for body surface area would thus appear unnecessary. It was at first surprising however to find a significant positive correlation between TRPT and GFR. This correlation is such that changes in GFR of 10 ml/min are associated with absolute changes in TRPT of between 0·08-0·19 mg/100 ml. Moreover the slope of the regression is of very similar order in both normal subjects and patients with hyperparathyroidism or with osteomalacia. In such patients the
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mechanism is thus simply set at lower levels of TRPT throughout the studied ranges of GFR. The same relationship between changes in GFR and TRPT was also noticed in repeated studies among normal subjects and patients in whom individual reproducibility was studied. Thus $T_mP$ (i.e. TRPT × GFR) appears to be a function of the square of the GFR. The concept of this 'twice over' relationship involves, firstly, total kidney mass (total number and size of healthy nephrons, for which the body surface area correction allows), and, secondly, impaired renal function (either glomerulo-tubular disease or alterations, even physiological, in renal perfusion). The finding that TRPT becomes zero at a GFR of 36 ml/min in normal subjects agrees fairly well with the observation of Anderson & Parsons (1963), using classical methods, that $T_mP$ is zero when the GFR is 28 ml/min. The practical advantage of not requiring to correct TRPT for body surface area is the elimination of errors thus introduced in patients with skeletal deformities such as those found in rickets, or in other metabolic diseases associated with skeletal rarefaction and spinal shortening, or in those who may be obese.

The relationship of TRPT to fasting plasma phosphorus concentrations, and the possible controlling influence of the former, has recently been extensively discussed by Bijvoet (1969). The present study has confirmed the close correlation between TRPT and values for fasting plasma phosphorus. However it conflicts with the data of Bijvoet, Jansen, Prenen & Majoor (1964) who were unable to demonstrate a correlation between TRPT and GFR. Several of their normal values for TRPT were below the present normal range and well below the normal values found by Anderson (1955), and their GFR values appear uncorrected for surface area. The present findings thus also conflict with the conclusion (Bijvoet, 1969) that the contribution of GFR to the variation of $T_m$ can be removed by expressing the latter as the ratio $T_mP$/GFR. Whatever the reason for this discrepancy the present concept is perhaps a more logical one: since changes in GFR usually denote corresponding changes in overall renal tubular function, then a similar relationship might be expected between GFR and any individual measure of tubular function such as TRPT. This is regardless of whether an appreciable reduction in GFR may in addition be associated with secondary hyperparathyroidism.

The present method is of appreciably less value at low levels of GFR since the intercept which gives TRPT becomes more difficult to locate accurately. The inevitable small errors, such as in bladder emptying, become large relative to the slow rise in urine phosphorus during the infusion, and the correlation coefficient between plasma phosphorus levels and urine phosphorus excretion will necessarily fall. Similar difficulties are also encountered with other methods of measuring renal phosphorus handling by the kidney.

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REFERENCES


