

# Assessment of Urinary Phosphate Excretion in Normal and Abnormal Children

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There is no unanimity about the best way to express renal phosphate excretion for clinical use. Several methods are in use; phosphate clearance; the quotient of the clearances of phosphate and creatinine, which also gives an approximation of tubular phosphate resorption; the quotient of renal phosphate and creatinine concentrations in urine. Nordin and Fraser (1956, 1960) have added the phosphate excretion index (PEI), which relates the phosphate and creatinine clearances ratio to serum phosphate. They thought that the PEI would give better insight into the tubular handling of phosphate, because they had demonstrated that in normal persons the ratio of the clearances of phosphate and creatinine regularly increased with increasing serum phosphates. The PEI is the difference between the ratio found and the normal ratio at the same serum phosphate level.

Calculating the PEI in patients in this hospital we found that, at the same serum phosphate levels, the phosphate and creatinine clearances ratio was lower in children than in adults, using Nordin's data. The same trend has been reported by Taitz and de Lacy (1962). Furthermore, we felt that there were statistical objections to the method used by Nordin and Fraser for calculating the PEI.

Therefore we decided to collect normal values in children; the results are given in the first part of this paper. In the second part, different methods of expressing phosphate excretion are compared in patients with several illnesses leading to abnormal phosphate excretion.

## Material and Methods

To eliminate the daily fluctuation of phosphate excretion, only 24-hour clearances have been performed. Fasting serum phosphate levels have been determined at 9 a.m. in all cases. All children were on an unrestricted hospital diet. Phosphate was determined according to the method of Briggs (1924), creatinine according to de Vries and Daatselaar, quoted by Gorter and de Graaff

(1955). Clearances have been corrected for size to ml./min.  $1.73 \text{ sq. m.}$

Table I shows the results in 32 normal children, i.e. with normal renal function, no diseases of the urinary tract, and no signs of disturbance of calcium and phosphate metabolism. Only children above the age of 1 year have been included in this study. In infants the clearance ratio of phosphate and creatinine ( $C_p/C_{cr}$ ) is higher.

Table II describes the patients discussed in the second part of this paper.

## Results in Normal Children

From the values obtained in the 32 normal children the regression of  $C_p/C_{cr}$ \* upon serum phosphate has been calculated, resulting in the equation  $C_p/C_{cr} = 0.114 + 0.00001 \text{ serum P}$  (Fig. 1). This of course is a horizontal line and the coefficient of correlation is virtually zero. Within the range of serum P levels studied ( $3.8\text{--}5.9 \text{ mg./100 ml.}$ ) no relation exists between this level and the  $C_p/C_{cr}$ .

Nordin and Fraser also have studied the relation between  $U_p/U_{cr}$ † and serum P and demonstrated a positive correlation. In our normal children however, we found no relation either between  $U_p/U_{cr}$  and serum P, with a regression equation  $U_p/U_{cr} = -1.241 + 0.0546 \text{ serum P}$ , coefficient of correlation less than 0.001 (Fig. 2).

## Discussion

The results of the calculations of correlation between  $C_p/C_{cr}$  and  $U_p/U_{cr}$  on the one hand and serum P levels on the other are not in agreement with those of Nordin and Fraser. The difference cannot be explained by the fact that our results were in children while their data were from adults. As

\*  $\frac{\text{Phosphate clearance (ml./min. } 1.73 \text{ sq. m.)}}{\text{Creatinine clearance (ml./min. } 1.73 \text{ sq. m.)}}$

†  $\frac{\text{Phosphate in urine (mg./100 ml.)}}{\text{Creatinine in urine (mg./100 ml.)}}$

TABLE I  
Normal Subjects

Name	Age (yr.)	S <sub>p</sub>	C <sub>p</sub> /C <sub>cr</sub>	U <sub>p</sub> /U <sub>cr</sub>	Diagnosis
F.M.	12	4.4	0.154	0.73	Precocious puberty
A.L.	12	3.8	0.074	0.35	Sigmoiditis
G.V.	12½	3.9	0.126	1.05	Dwarfism
J.H.	6½	4.9	0.120	1.33	Constipation
D.S.	6½	4.7	0.114	0.96	Precocious puberty
F.V.	7	4.9	0.094	0.85	Normal
C.B.	14	4.1	0.085	0.51	Psych. abdominal pain
J.E.	6	4.6	0.115	1.09	Hypertension
W.G.	6	4.5	0.110	0.96	Henoch-Schönlein's disease
I.M.	13½	4.2	0.122	1.04	Mental retardation
E.D.	9	5.2	0.078	0.67	Normal
W.K.	6	5.7	0.107	1.16	Mental retardation
J.B.	12	4.8	0.118	0.97	Headache
R.Z.	12½	3.9	0.136	0.95	Nervous heart complaints
R.O.	9½	4.5	0.126	1.14	Rheumatic fever (convalescent)
M.W.	7	4.8	0.064	0.70	Coeliac disease
J.C.	12½	5.4	0.148	1.43	Rheumatic fever (convalescent)
H.V.	2	5.1	0.114	2.78	Mental retardation
S.S.	4	4.6	0.093	1.06	Constipation
W.W.	2½	4.6	0.143	1.94	Tonsillitis
J.B.	4	4.9	0.100	1.17	Meningitis (convalescent)
A.D.	5½	4.8	0.112	1.30	Meningitis (convalescent)
E.B.	3½	5.2	0.109	1.58	Pneumonia (convalescent)
K.R.	2½	5.9	0.127	1.74	Thrombocytopenia
J.S.	5½	5.5	0.083	1.20	Mental retardation
J.B.	3	4.9	0.127	1.53	Pneumonia
M.K.	2½	4.4	0.161	2.08	Mental retardation
"	"	5.8	0.130	0.21	"
M.S.	1½	5.4	0.130	0.27	Achondroplasia
L.L.	1	5.8	0.106	2.54	Mental retardation
M.K.	1½	4.9	0.123	1.77	Pyoderma
F.K.	1½	5.4	0.144	2.05	Pyoderma
T.K.	1	5.2	0.079	2.28	Febrile convulsion

Note: S<sub>p</sub>, serum phosphate (mg./100 ml.); C<sub>p</sub>, phosphate clearance; C<sub>cr</sub>, creatinine clearance; U<sub>p</sub>, urinary phosphate; U<sub>cr</sub>, urinary creatinine.

some doubt may arise as to the normality of the children with growth retardation or mental deficiency, we have compared the values of such children with those of the other children (C<sub>p</sub>, C<sub>cr</sub>, and serum P) but there was no difference (p < 0.01, Wilcoxon).

Moreover, the correlation between C<sub>p</sub>/C<sub>cr</sub> and serum P reported by Nordin and Fraser does not follow from their data. They calculated their regression line partly from heterogeneous data, viz. the values for C<sub>p</sub>/C<sub>cr</sub> of 2-hour clearances assembled by Milne, Stanburry, and Thomson (1952) during phosphate-infusion experiments. Within the range of serum P levels from their own normal subjects however, the correlation is not at all apparent; their values cluster rather than scatter around only one

part of the regression line. It seems from this that increase of phosphate clearance is only demonstrable when very high serum phosphate levels are reached, as in infusion experiments.

On the basis of our own results and of the

TABLE II  
Patients

Diagnosis	Total No. of Cases	Total No. of Observations	
		C <sub>p</sub>	C <sub>p</sub> /C <sub>cr</sub>
Vitamin D resistant rickets	6	62	66
Vitamin D deficient rickets	5	4	4
(Pseudo)-hypoparathyroidism	2	7	7
Renal disease	24	29	29

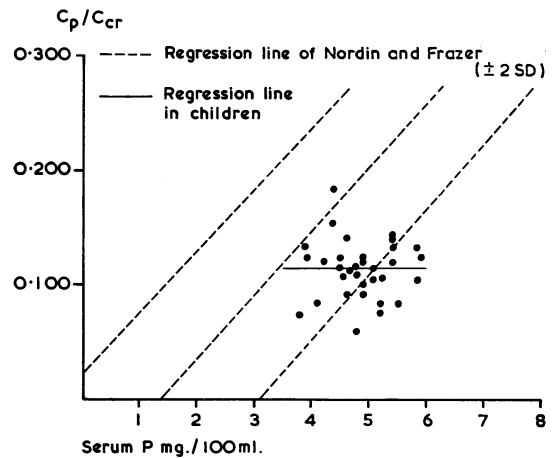


FIG. 1.—Serum phosphate and phosphate clearance/creatinine clearance ratio of 32 normal children (33 observations).  $C_p/C_{cr} = 0.114 + 0.00001 \text{ serum P.}$

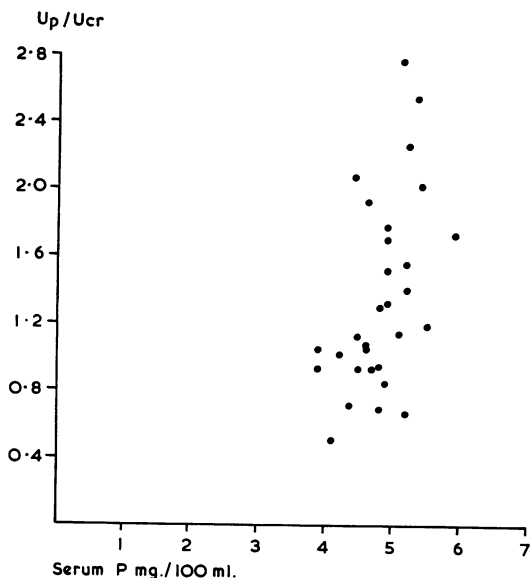


FIG. 2.—Serum phosphate and phosphate/creatinine ratio in urine of 30 normal children.  $U_p/U_{cr} = -1.241 + 0.0546 \text{ serum P.}$

statistical objections to Nordin and Fraser's studies, therefore, it is concluded that there is no correlation between  $C_p/C_{cr}$  and serum P, at least within the serum P levels usually encountered in paediatric patients.

Other authors (Hodgkinson, 1961; Hyde, Vaughan Jones, McSwiney, and Prunty, 1960; McGeown, 1957; Reiss and Alexander, 1959; Reynolds, Lanman, and Tupikova, 1960) have also expressed doubts about the value of the PEI as a measure of phosphate excretion, usually because a normal PEI does not exclude a diagnosis of hyperparathyroidism, and a high PEI does not prove it.

The  $U_p/U_{cr}$  ratio did not correlate with serum P in our normal children, while Nordin and Fraser reported a positive correlation.

We conclude that there is no reason to use the PEI, or to relate  $U_p/U_{cr}$  to serum P, when studying 24-hour phosphate excretion in children.

### Results in Pathological Cases

The mean normal value of the 24-hour phosphate clearance was 12.7 ml./min. 1.73 sq. m., with a 2 SD range of  $\pm 4.8$ . Fig. 3 shows the mean and 2 SD limits, as well as the values for  $C_p$  in a number of patients, mentioned in Table II. Fig. 4 shows the values for  $C_p/C_{cr}$  in the same way. The mean normal value of  $C_p/C_{cr}$  was 0.114 with a 2 SD range of 0.048.

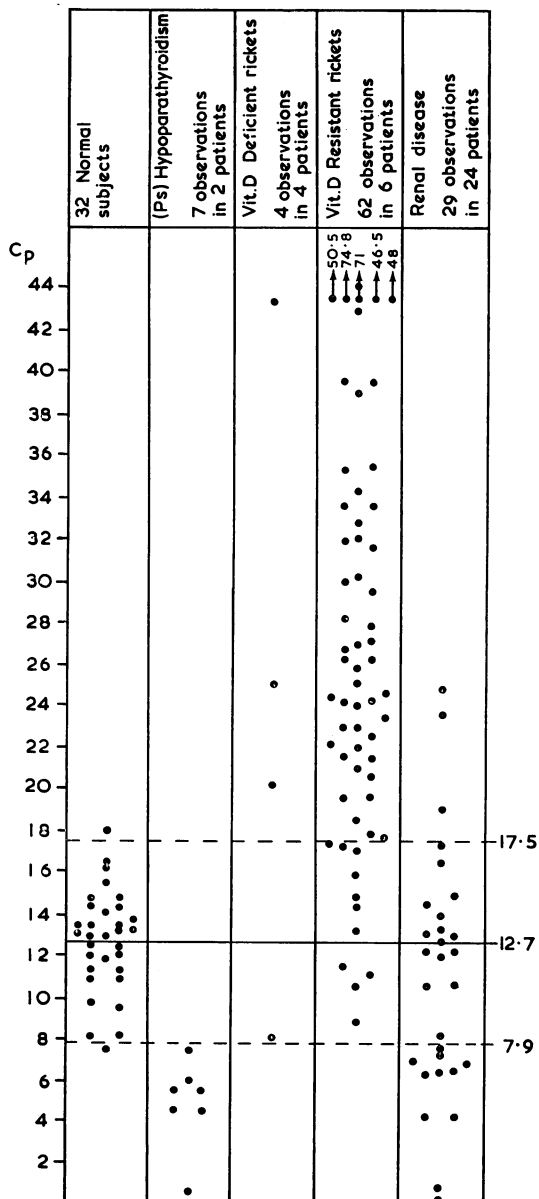


FIG. 3.—24-hour phosphate clearance values in 32 normal children (33 observations) and in the patients of Table II.

### Discussion

Fig. 3 shows that the 24-hour phosphate clearance is a satisfactory measure of tubular phosphate handling in the diseases shown. All values in the two patients with (pseudo)-hypoparathyroidism are below the normal range. Most of the rickets

patients also show distinctly pathological values. In resistant rickets the majority of  $C_p$  values are high; the observations were made both before and during treatment, which did not influence the  $C_p$  greatly. The patients with renal disease show a wide range of values.

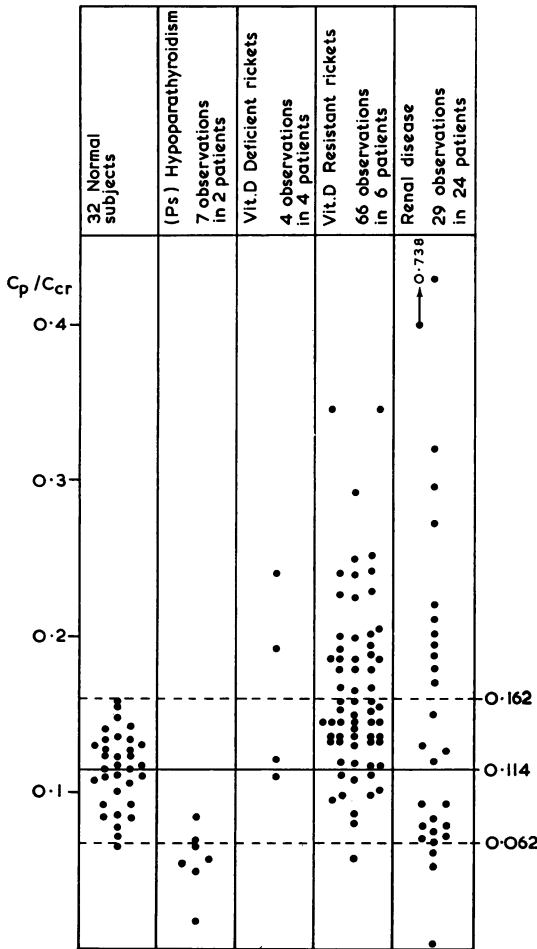


FIG. 4.— $C_p/C_{cr}$  ratio in 32 normal children (33 observations), and in the patients of Table II.

The  $C_p/C_{cr}$  ratio (Fig. 4) does not discriminate as well as the 24-hour phosphate clearance (Fig. 3) between normal and pathological. This may be the result of using a quotient of two variables, which

influenced particularly the results in patients with renal disease, as well as some of the measurements in other patients where creatinine clearances were unusually high.

In children without renal insufficiency 24-hour phosphate clearance is still the preferred method of expressing phosphate excretion. In practice it is desirable, however, to determine  $C_p/C_{cr}$  as well, because this may give some insight into tubular absorption of phosphate, may discover unexpected renal insufficiency, and obviates faults caused by inaccurate urine collection.

**Summary**

In children there is no relation between serum phosphate and either the phosphate clearance/creatinine clearance (24-hours) ratio, or the urinary phosphate/urinary creatinine ratio. The value of the phosphate excretion index of Nordin and Fraser is doubtful.

In children with abnormal phosphate metabolism (hypoparathyroidism, rickets and resistant rickets) the 24-hour phosphate clearance discriminated best between normal and abnormal. Phosphate clearance/creatinine clearance ratio should, however, preferably be determined as well.

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