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Urinary excretion of calcium and magnesium in children

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Ghazali, S., and Barratt, T. M. (1974). *Archives of Disease in Childhood*, **49**, 97. **Urinary excretion of calcium and magnesium in children.** Urine calcium excretion in healthy children was $2 \cdot 38 \pm 0 \cdot 66$ (SD; no. = 52) mg/kg per 24 hr and urinary magnesium excretion was $2 \cdot 82 \pm 0 \cdot 79$ (SD; no. = 23). The 24-hour urine calcium excretion could be predicted with reasonable confidence from the calcium/creatinine concentration ratio of the second urine specimen passed in the morning. In this specimen the urine calcium/creatinine concentration ratio was $0 \cdot 14 \pm 0 \cdot 06$ (SD; no. = 60) mg/mg and the magnesium/creatinine concentration ratio was $0 \cdot 21 \pm 0 \cdot 10$ (SD; no. = 29) mg/mg.

The upper limit of the urine calcium excretion is taken to be 4 mg/kg per 24 hr and that of the calcium/creatinine concentration ratio in the second morning urine is 0·25 mg/mg. After a milk load of 700 ml/1·73 m^2 the urinary calcium/creatinine concentration ratio rose in the first two hours, but in no sample exceeded 0·25 mg/mg.

During a study of children with urolithiasis (Ghazali, Barratt, and Williams, 1973), we detected several individuals with apparent hypercalciuria. We were dissatsified, however, with the available data on calcium excretion in healthy children in England and expressed the view that data collected on children in other countries or in other decades were not satisfactory, because, for example, habits of diet and prescription of vitamin D vary. We therefore decided to measure the urinary excretion of calcium and magnesium in healthy children.

The collection of 24-hour urine samples from children is notoriously prone to error. We have therefore also examined the use of the calcium/creatinine concentration ratio of random urine samples, as first suggested by Nordin (1959). As it also seemed possible to us that the parameter of calcium excretion relevant to the genesis of urinary calculi was not the total 24-hour excretion but rather the peak calcium excretion after an oral calcium load, we measured the calciuretic response to a standardized intake of milk.

Patients and methods

Urine collections were obtained 24-hourly from 54 apparently healthy children aged 1 to 15 years. 13 children were at home; in the remainder the urine was collected during the first 24 hours of admission to hospital for elective minor operation. The children were fed a normal diet and their activity was not restricted. In 15 of these children, aged 4 to 15 years, each voided urine specimen was collected separately for the determination of diurnal rhythm of calcium and magnesium excretion.

The second urine sample passed in the morning (designated morning urine), i.e. the first specimen voided after the overnight urine had been passed, was collected in the hydrated but fasted state. Separate morning urine specimens were obtained during the 24-hour collection from 30 of the above healthy children and from 18 postoperative children, some of whom had hypercalciuria; morning urine specimens were also collected in a further 30 healthy children.

A standardized milk load was administered to 10 healthy children, aged 3 to 10 years, as follows. After the overnight urine had been voided, water 700 ml/1·73 m^2 was given to initiate diuresis, and two urine specimens were collected. 700 ml/1·73 m^2 cow's milk was then consumed over a 30-minute period, and urine was collected over the next 4 hours with hourly voiding whenever possible. 700 ml cow's milk contains about 840 mg calcium and about 32 g lactose.

Urine was collected with thiomersalyl 1:10,000 preservative. Aliquots for creatinine were centrifuged and deep frozen until assayed by an automated alkaline picrate method (Technicon Autoanalyser Methodology N-IIb). Aliquots for calcium and magnesium determination were diluted on the day of collection with

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1% lanthanum chloride and analysed by atomic absorption spectrophotometry.

Results

24-Hour excretion of calcium and magnesium. The 24-hour urinary excretions of calcium and magnesium (mg/24 hr) as a function of body weight (kg) are illustrated in Fig. 1 and 2. Data from 2 children are considered as outliers and have been excluded from the calculations.* The

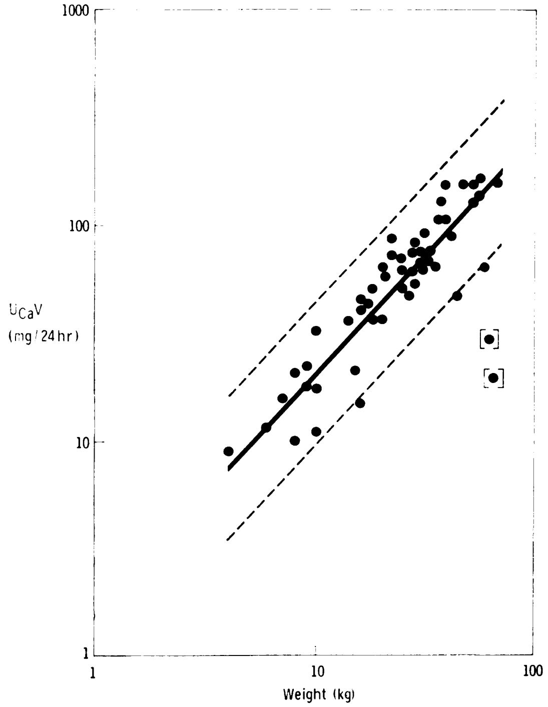

FIG. 1.—*24-hour urine calcium (mg/24 hr) plotted as a function of weight. 95% confidence limits are given. Two outliers are shown in brackets.*

data have been logarithmically transformed to stabilize variances and the 95% confidence limits are shown. The equations are

24 hr urine calcium $= 1 \cdot 8$ weight$^{1 \cdot 09}$
(r $= 0 \cdot 91$, no. $= 52$)

24 hr urine magnesium $= 17$ weight$^{0 \cdot 54}$
(r $= 0 \cdot 73$, no. $= 23$).

*In 2 apparently healthy sibs urine calcium was 0·31 and 0·50 mg/kg per 24 hr; these values are more than 4 SD below the mean calculated for the remaining 52 children (Fig. 1). The discrepancies are not due to inadequate urine collection, for the urine creatinine excretion rates fall within the normal range. The results from these two individuals have been regarded as outliers and have not been included in subsequent calculations.

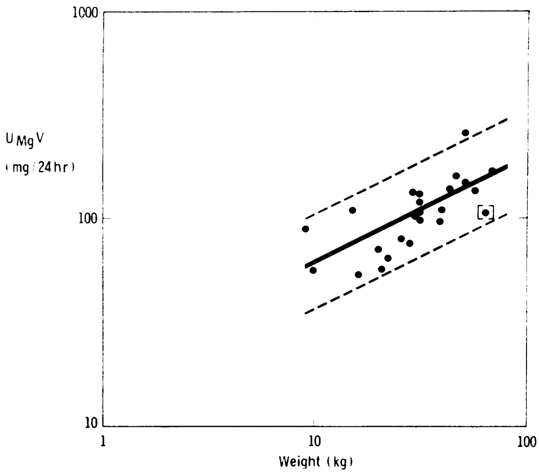

FIG. 2.—*24-hour urine magnesium (mg/24 hr) plotted as a function of body weight. 95% confidence limits are given. One individual whose calcium excretion was considered to be an outlier is shown in brackets.*

The slope of the regression line of the log of the 24-hour urine calcium plotted against the log of body weight (Fig. 1) does not differ significantly from unity and we have therefore related urine calcium excretion to body weight (mg/kg per 24 hr) in subsequent presentations. For convenience we have expressed the 24-hour magnesium excretion similarly, though it is in fact proportional to the square root of body weight.

The urine calcium excretion in 52 healthy children was $2 \cdot 38 \pm 0 \cdot 66$ (SD) mg/kg per 24 hr (Table I). It is convenient, therefore, to consider the upper limit to be 4 mg/kg per 24 hr. There was no correlation of urine calcium with age or sex, and no difference between the children in hospital and those at home.

The urine magnesium excretion was estimated in

TABLE I

Calcium and magnesium excretion in healthy children

	No.	Mean	SD
24-hour urine calcium (mg/kg per 24 hr)	52	2·38	0·66
Morning urine calcium/creatinine concentration ratio (mg/mg)	60	0·14	0·06
24-hour urine magnesium (mg/kg per 24 hr)	23	2·82	0·79
Morning urine magnesium/creatinine concentration ratio (mg/mg)	29	0·21	0·10
Morning urine magnesium/calcium concentration ratio (mg/mg)	29	1·6	0·7

23 of these children, and was found to be $2 \cdot 82 \pm 0 \cdot 79$ (SD) mg/kg per 24 hr. The concentration ratio of magnesium to calcium in these samples was $1 \cdot 3 \pm 0 \cdot 5$ (SD) mg/mg.

There was a significant positive correlation ($r = 0 \cdot 62$, $P < 0 \cdot 05$) between the 24-hour urinary calcium and magnesium. However, this may in part be an artefact of urine collection errors for the correlation between the calcium/creatinine and magnesium/creatinine concentration ratios in the 24-hour urine samples did not reach significance at the 5% level ($r = 0 \cdot 35$).

Adequacy of urine collection was confirmed as far as possible by estimation of urinary creatinine excretion rate (mg/kg per 24 hr)

24 hr urine creatinine $= 15 \cdot 4 + 0 \cdot 46 \times$ age (yr) $\pm 3 \cdot 4$* ($r = 0 \cdot 50$).

Urine calcium/creatinine and magnesium/creatinine concentration ratio. The diurnal variation of the urine calcium/creatinine concentration ratio (mg/mg) is shown in Fig. 3. The ratio in each voided sample is expressed as a percentage of the measured calcium/creatinine concentration ratio of the pooled 24-hour sample, and is plotted at the midpoint of each collection period. The values obtained in the second morning urine samples showed the smallest scatter and were most representative of the 24-hour period. A similar diurnal variation of magnesium/creatinine concentration ratio was observed.

In 30 normal and 18 postoperative children the morning urine calcium/creatinine concentration ratio was estimated on a specimen obtained during the collection of the 24-hour urine. The relation between the morning calcium/creatinine concentration ratio and the 24-hour calcium excretion (mg/kg per 24 hr) is illustrated in Fig. 4 and was found to be

24 hr urine calcium $= 19 \cdot 4 \times$ morning calcium/creatinine $-0 \cdot 17 \pm 1 \cdot 35$* ($r = 0 \cdot 88$).

The morning urine calcium/creatinine concentration ratio in 60 normal children aged 1 to 15 years was $0 \cdot 14 \pm 0 \cdot 06$ (SD); the upper limit of normal is taken to be $0 \cdot 25$ mg/mg. There was no significant correlation with age ($r = -0 \cdot 22$) and no significant difference between the sexes.

The magnesium/creatinine concentration ratio in the morning urine in 29 of these children was $0 \cdot 21 \pm 0 \cdot 10$ (SD) mg/mg. There was a significant correlation between the calcium/creatinine and magnesium/creatinine concentration ratios in these samples ($r = 0 \cdot 71$). The calcium/magnesium concentration ratio was $1 \cdot 6 \pm 0 \cdot 7$ (SD) (mg/mg).

Urine calcium/creatinine concentration ratio after milk load. After the milk load, the calcium/creatinine ratio rose from $0 \cdot 10$ to $0 \cdot 13$ mg/mg in the 2nd hour (Table II). The mean urinary calcium/creatinine concentration ratio after the milk load, expressed for each individual as a percentage of his pre-milk value, was 158 ± 19% (SEM) in the first 3 hours after milk.

Discussion

Available data on 24-hour urinary calcium excretion in healthy children are sparse. Macy

*Standard error of the estimate of y from x.

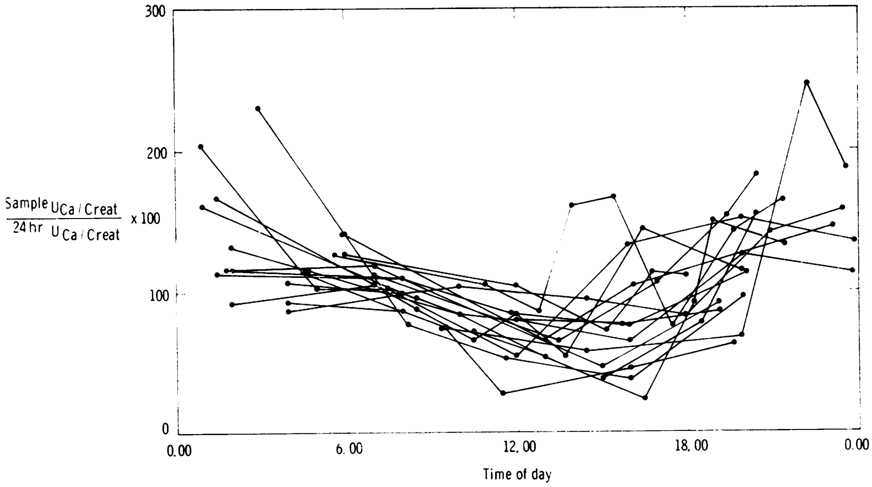

FIG. 3.—*Diurnal variation of the urinary calcium/creatinine concentration ratio.*

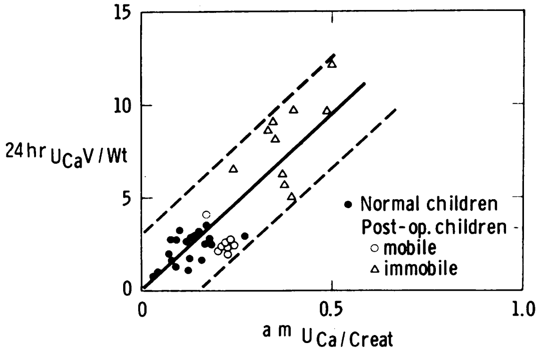

FIG. 4.—*Relation between the morning (see text for definition) urine calcium/creatinine concentration ratio and the 24-hour urine calcium excretion (mg/kg per 24 hr).*

(1946) reported the urine calcium excretion (determined by oxalate precipitation) to be 4·7±1·0 (SD; no. = 32) mg/kg per 24 hr and the magnesium excretion (determined by phosphate precipitation) to be 3·8±0·9 (SD; no. = 20) mg/kg per 24 hr* in healthy American children aged 4 to 12 years. Knapp (1947) summarized the published data on urinary calcium excretion in adults and children up to 1947. On a calcium intake of 0·7–1·0 g/24 hr, the urine calcium excretion (determined by oxalate precipitation) in children 1 to 4 years was 47±23; aged 5 to 9 years 79±39; and 10 to 14 years 94±49 (SD) mg/24 hr. Assuming average body weights, these figures are approximately equivalent to 3·4±1·6, 3·4±1·3, and 2·5±1·3 mg/kg per 24 hr. Royer (1961) reported the 24-hour urine calcium excretion (oxalate precipitation) to be less than 4 mg/kg per 24 hr in 66 of 74 children aged 0 to 18 years, and to exceed 6 mg/kg per 24 hr in only one. Paunier, Borgeaud, and Wyss (1970) reported the urinary excretion of calcium and magnesium measured by atomic absorption spectrophotometry in Swiss children to be calcium 3·6±2·4 (SD) mg/kg per 24 hr on an intake of 53±39 (SD) mg/kg per 24 hr, and magnesium to be 2·8±1·1 mg/kg per 24 hr on an intake of 10·5±3·7 (SD) mg/kg per 24 hr. In this series there were 38 children of whom 11 were under the age of 1 year; the infants had a significantly lower magnesium excretion and a higher (but not statistically significant) calcium excretion on a body weight standard. Excluding the infants, the urine calcium excretion in Paunier *et al.*'s (1970) report was 3·3±1·9 mg/kg per 24 hr and magnesium excretion was 2·0±1·2 (SD) mg/kg per 24 hr.

*Recalculated from Macy's (1946) original data using the first 24-hour urine observation in each individual.

In our children the urine calcium excretion at 2·4±0·7 (SD) mg/kg per 24 hr was thus somewhat lower than the other published data, but it agrees with the figure of 2 mg/kg per 24 hr in British children aged over 2 years estimated from the calcium/creatinine concentration ratio of random urine samples by Widdowson and McCance (1970). There are several possible explanations for these differences, of which variation in the dietary intake of sodium, calcium (Peacock, Hodgkinson, and Nordin, 1967), and vitamin D are probably the most important. The dietary calcium intake was not controlled in our children, as we were concerned to determine the normal range of urine calcium excretion under the usual conditions of clinical observation.

It was convenient to find that the calcium/creatinine concentration of the first urine specimen voided after the overnight specimen was passed was reasonably representative of the 24-hour calcium/creatinine concentration ratio found in adults (Nordin, 1959; Dauncey and Widdowson, 1972). Assuming that the upper limit of urine calcium excretion is 4 mg/kg per 24 hr, and that the average creatinine excretion in mid-childhood is 18 mg/kg per 24 hr, the upper limit of the calcium creatinine concentration would be expected to be 0·22; we found that the upper limit in the morning urine

TABLE II

Calciuretic response of healthy children to an oral intake of 700 ml/1·73 m² cow's milk

Hours	−2	−1	1	2	3	4
Urine calcium/creatinine concentration ratio (mg/mg)	0·09	0·10	0·13	0·13	0·11	0·09
SD	0·05	0·06	0·05	0·05	0·09	0·05
%rise above baseline	—	—	158	175	138	113
SEM	—	—	19	26	20	12
		↑ Milk load 700 ml/1·73 m²				

Note: The % rise above baseline is significant (P <0·05) in the first 3 hours after milk. However, in no specimen did the calcium/creatinine concentration ratio exceed 0·25 mg/mg.

specimen in healthy children was 0·25, which is slightly less than the upper limit in adults, suggested by Nordin (1959), of 0·28. This system provides a convenient screen for hypercalciuria.

Lactose is a known stimulant of calcium absorption (Wasserman, 1964), and some adult patients with recurrent calcium oxalate calculi have an exaggerated calciuretic response to oral carbohydrate (Lemann, Piering, and Lennon, 1969). It was, therefore, of interest to determine whether an oral load of milk (i.e. lactose+calcium) affected calcium excretion. The calcium/creatinine concentration ratio rose significantly above basal levels in the first 2 hours after the milk load and then returned towards the pre-milk value. These data will be used as standards against which to compare the response of stone-forming children (S. Ghazali and T. M. Barratt, in preparation).

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