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Research Article

SKELETAL DYNAMICS IN MAN MEASURED BY NONRADIOACTIVE STRONTIUM *

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A great deal of useful information about calcium metabolism in man has been obtained by balance technics. Balance studies give only net changes in total body calcium and do not indicate whether changes in balance result from alterations of rates of movement into or out of bone. For example, positive balance could result from increased bone deposition or decreased bone resorption. Similarly, balance could be unchanged if increased resorption were matched by increased deposition. Rates of bone deposition have been measured in man using Ca^{45} and Ca^{47} as tracers (1–11). Isotopes of strontium have been similarly used (5, 6, 8, 11–16), since strontium is a bone-seeking element whose distribution in the body is similar to that of calcium. Accumulated experience suggests that cautious use of these bone-seeking radionuclides in human subjects is without demonstrable risk. Nevertheless, this experience is still limited both in numbers of subjects and length of observation. In a study of Sr^{90} toxicity in mice, a direct linear relationship was noted between total internal radiation dose from Sr^{90} and decrease in survival time and tumor production (17). Even small doses of radiation may not be without danger, for this analysis showed no lower threshold.

A recently developed flame photometric method (18) for measurement of calcium was adapted to measure strontium. If stable strontium could be used as a tracer it would be valuable for safely studying various types of patients in statistically valid numbers and for repeated tests in the same individual under varied conditions. This possibility is the subject of the present investigation. The results indicate that nonradioactive strontium can be used to detect alterations of skeletal metabolism in various defined physiological and pathological states.

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METHODS

The following subjects were studied: 25 healthy persons at ordinary activity (including 11 inmates of San Quentin Prison; 31 studies); 14 athletes (all members of the San Quentin Prison football team); 11 patients with idiopathic nephrolithiasis; 28 with primary hyperparathyroidism (4 with skeletal disease shown by elevated serum alkaline phosphatase levels or roentgenographic evidence of skeletal involvement or both; 17 with normal phosphatase and X-ray appearance but with microscopic foci of resorption seen in bone biopsy; and 7 with normal phosphatase, X-ray appearance and bone biopsy); 7 with hyperthyroidism; 8 with acromegaly; 3 with hyperadrenocorticism; 26 with advanced, unequivocal postmenopausal or senile osteoporosis (40 studies); 5 with Paget's disease of bone; and 1 with chronic vitamin D overdose. The reproducibility of the method was tested by 21 duplicate tests in osteoporotic and normal subjects. All subjects were on diets free of milk and cheese except the prisoners, whose fare was unrestricted. All subjects were ambulatory.

Significant dietary strontium was excluded by checking initial blood and urine specimens. Then 10.0 mEq of strontium gluconate [1] was infused intravenously over a period of 10 minutes. Blood samples were taken every 24 hours and 24-hour urine specimens were collected for 4 to 6 days.

All specimens were collected in acid-washed glassware. All determinations were done in duplicate. Serum and urine calcium levels were determined on a flame spectrophotometer by the method of MacIntyre (18). Serum strontium was measured by diluting 1.0 ml of serum with 3 ml of an aqueous solution of 3 per cent perchloric acid and 0.5 mM monopotassium phosphate. The supernatant was read at 461 mμ in the flame spectrophotometer between standards in a 0.25 dilution of serum containing concentrations of sodium, potassium, and calcium which

[1] Strontium gluconate was generously supplied by Dr. A. Cerletti and Mr. H. Althouse of Sandoz, Inc.

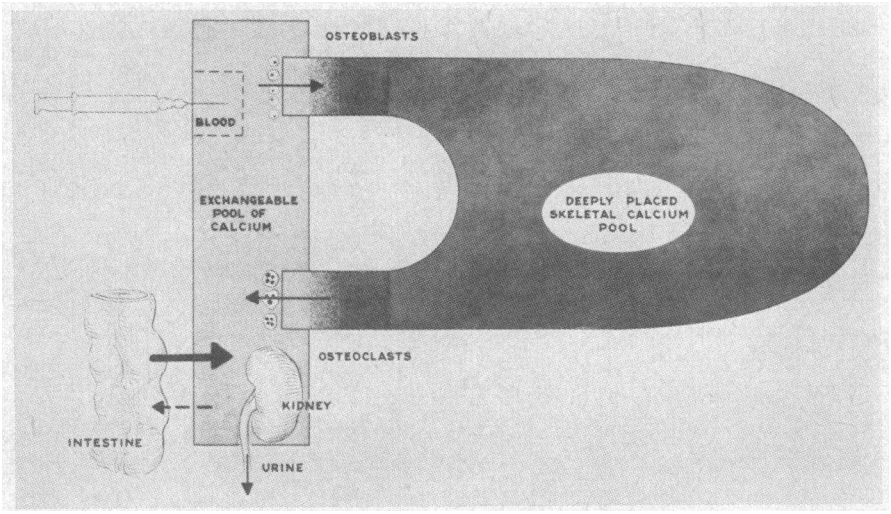

FIG. 1. MODEL FOR ANALYSIS OF SKELETAL DYNAMICS.

are in the plateau area of their effect in enhancing strontium emission (19). Complete recovery of urinary strontium required co-precipitation with calcium as follows. Three ml of saturated ammonium oxalate was added to 15 to 30 ml of urine, pH was adjusted to between 5.5 and 6.0; then 0.25 ml of 10 per cent calcium gluconate was added and the urine heated in a boiling water bath for a few minutes until the precipitate became flocculent. The urine was cooled at 4° C for 2 or more hours, then centrifuged at 2,500 rpm for 10 minutes. After the supernatant was decanted, the precipitate was dissolved in 5.0 ml of 2 N hydrochloric acid and made up to a total volume of 15.0 ml with distilled water. This solution was analyzed in the flame spectrophotometer, always by reading between adjacent standards. When this precipitation technic was checked with radioactive strontium tracer, recovery varied from 97 to 101 per cent.

TABLE I

Strontium/calcium observed ratios between serum and body tissues and fluids after intravenous infusion of strontium gluconate

Time after infusion		Source	$\frac{Sr}{Ca}_{source}/\frac{Sr}{Ca}_{serum}$
hrs	*min*		
9	5	Ascitic fluid	0.99
9	5	Ascitic fluid	0.89
9	5	Ascitic fluid	0.97
20	30	Ascitic ffuid	0.94
21	0	Ascitic fluid	0.90
22	45	Ascitic fluid	0.82
22	45	Ascitic fluid	0.94
22	45	Ascitic fluid	0.84
32	15	Ascitic fluid	0.73
32	15	Ascitic fluid	0.81
32	15	Ascitic fluid	1.02
40	0	Spinal fluid	1.04
4	20	Gall bladder	0.47
4	20	Breast fat	0.48
4	35	Rectus abdominis	0.44
5	0	Strap muscle	0.49
14	35	Strap muscle	0.60
20	0	Strap muscle	0.45

Analysis of data. The model for analysis of calcium movement is similar to that proposed by others (4, 7, 14, 15). This model (Figure 1) is based on studies which suggest that body calcium is divided into two pools (1, 3, 20–22). One is a very small pool of rapidly exchangeable calcium in the extracellular fluid, soft tissues, and surface crystal of bone. The other is a very large pool of less readily available calcium in the deeper layers of bone. Calcium is added to the exchangeable pool by intestinal absorption and bone resorption. It leaves the exchangeable pool by excretion and bone deposition. Thus, if one can introduce a tracer into the exchangeable pool and then measure the rate of loss of tracer from the pool and the rate of excretion, one can calculate the rate of bone deposition as the difference between the two. Such analysis can be done by using the usual formulas for measuring pool size and pool turnover rates. The calculations shown require the assumptions that there be no change in pool size, that mixing in the exchangeable pool is complete (or almost so) at the time that observations used for the calculations are made, that there is no continuing concentration (sequestration) of tracer in tissues other than bone during the period of observation, and that there is no return of tracer to the pool from bone.

Important alterations in the size of the exchangeable pool are not likely in 4 to 6 days and could not occur imperceptibly because such an alteration requires excessive diuresis or loss of soft tissue or skeleton. (No such fluctuation in body weight, urine volume, or urinary calcium excretion occurred during these studies.) That mixing of strontium through the various compartments of the exchangeable pool actually occurs within 24 hours after injection was tested in a few patients by comparing Sr to Ca ratios of available fluids and tissues with Sr to

Ca ratio of serum at varying time intervals after injection (Table I). These figures confirm that intravenously injected strontium is largely equilibrated through body fluids and soft tissues by 24 hours, as is calcium (20, 23–25). The slightly longer mixing time indicated by the serum curves suggests that skeletal equilibration is a little slower. This is borne out by external counting over soft tissue and bone (8). After distribution of intravenously injected calcium and strontium, most of the retained dose moves into the skeleton, and there is no continued accumulation in other tissues (8, 23, 26, 27). Continued concentration of tracer in tissue other than bone would add an additional route of tracer loss from the pool. The studies of Heaney and Whedon (7) indicate that in most subjects tracer does not re-enter the pool until 6 to 8 days after its injection, and it may be assumed that bone growth and bone resorption do not occur simultaneously in the same sites. Hence the major assumptions for the analysis seem reasonable. Accordingly, serum strontium concentrations were plotted as in Figure 2 and the following calculations were made:

$$k = 0.693/t_{\frac{1}{2}} \qquad [1]$$

where k = fractional rate constant and $t_{\frac{1}{2}}$ = "half-time" derived by plotting serum specific activities.

$$E = D/s_0 \qquad [2]$$

where E = exchangeable pool (volume of strontium distribution), D = corrected dose of tracer and s_0 = serum specific activity at time zero.

$$T = kE \qquad [3]$$

where T = total turnover rate.

$$U = \int_{t_1}^{t_2} dU \; s_0 \int_{t_1}^{t_2} e^{-kt} dt = (U_{t_2-t_1})k/(s_{t_1} - s_{t_2}) \qquad [4]$$

where U = urinary excretion rate, $U_{t_2-t_1}$ = urinary content of tracer between time 1 and time 2 (usually the interval from 24 to 120 hours) and s_{t_1}, s_{t_2} = serum strontium concentration at time 1 and time 2.

$$B = T - U \qquad [5]$$

where B = rate of bone deposition.

During the 24 hours required for mixing, the strontium concentration in some parts of the pool will be greater than in others. Since the high concentration areas include blood, renal excretion will be temporarily enhanced. The excess excretion due to this inequality in distribution during mixing can be corrected by subtracting theoretical from actual urinary strontium measured during this interval. The theoretical urinary excretion during the mixing period was calculated from Equation 4 by letting t_1 and t_2 be the times at the beginning and end of mixing. The amount of excess excreted was usually 5 to 15 per cent of the dose. The injected dose was corrected for this amount in calculation of pool size. Examination of serum strontium curves indicated 24 hours as an average mixing time, with individual variations between 20 and 30 hours. The error introduced by using the initial 24 hours as a standard mixing time is small, since the steep portion of the mixing curve was always included in the correction.

To make the method widely applicable clinically, two routes of tracer excretion were not usually measured—sweat and feces. While some authors (28, 29) have suggested that sweat is normally an important route of calcium loss, our measurements of sweat calcium and strontium concentrations during physical exercise (Table II) showed that even at maximal rates, sweat accounted for only a small portion of calcium or strontium loss. The sweat glands, like the intestine and kidney, discriminate against strontium. Fecal losses were not measured

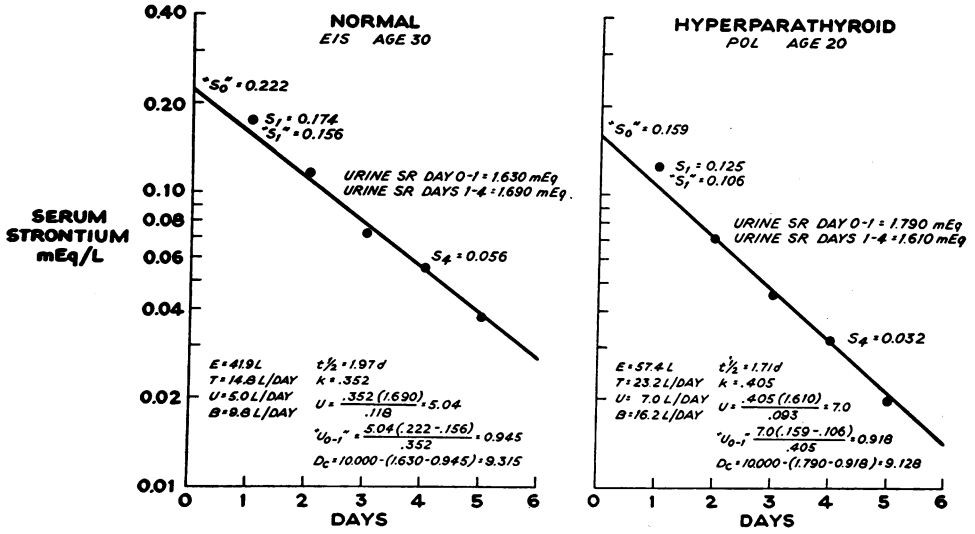

FIG. 2. REPRESENTATIVE PLOTS OF SERUM STRONTIUM CONCENTRATIONS AND CALCULATIONS OF SKELETAL DYNAMICS IN A NORMAL AND A HYPERPARATHYROID SUBJECT.

TABLE II

Sweat calcium and strontium content

Name	Period*	Serum			Sweat		
		Ca	Sr	Sr/Ca	Ca	Sr	Sr/Ca
		mEq/L			*mEq/L*		
EIS	1	5.40	0.243	0.045	1.86	0.103	0.055
	2		0.235		1.24	0.114	0.092
	3	5.65	0.216	0.038	1.78	0.089	0.050
WHI	1	5.65	0.216	0.038	1.75	0.085	0.049
	2		0.206		1.44	0.063	0.044
	3	6.10	0.197	0.032	1.83	0.071	0.039
LUB	1	5.35	0.215	0.040	1.92	0.110	0.057
	2		0.197		0.99	0.085	0.086
	3	6.10	0.178	0.029	1.48	0.105	0.071

* Periods 1, 2, and 3 are three consecutive 30-minute periods commencing 16 hours after infusion of strontium and during which subjects exercised. Sweat was collected on covered patches of ash-free filter paper from previously washed areas of skin. Filter paper was eluted with 2 N HCl. Calcium and strontium were determined flame spectrophotometrically as for urine.

in our routine studies. Harrison, Raymond and Tretheway (12) reported 5-day cumulative fecal excretion of 3 per cent of an intravenous dose of strontium. Spencer and her co-workers (13) reported approximately 9 per cent in 6 days (1 patient) and from 8 to 17 per cent in 12 days (7 patients) (30), and concluded that the major route of excretion is through the kidney. Dow and Stanbury (11) found from 2.5 to 19 per cent fecal excretion of Sr^{85} in 6 days in various disease states. Fraser, Harrison and Ibbertson (15) found that fecal excretion of intravenously injected stable strontium is 8 to 16 per cent of the administered dose in 6 days in the absence of diarrhea or steatorrhea. Calculation of the portion of pool lost daily through fecal excretion by our subjects based on the published range of values for fecal excretion shows that bone deposition is overestimated by 9 to 16 per cent in all groups by ignoring fecal excretion. This discrepancy does not appear to affect comparison between our groups but will affect, by this amount, comparison with data in which fecal excretion has been measured.

RESULTS

The size of the exchangeable strontium pool in 25 healthy subjects at ordinary activity was 42.7 L, of which 30.9 per cent was turning over daily (Table III).[2] Urinary excretion from the pool as measured by strontium was 3.9 L per 24 hours, and the rate of deposition in bone was 9.6 L per 24 hours. In 11 patients with a history of urinary tract stones but without hypercalcemia, the pool size was comparable to that of the control subjects, but more mineral went to urine and less to bone. In the 14 athletes the pool was larger, and 35.7 per cent was turning over daily. The rates of urinary excretion and deposition in bone were 50 per cent greater than in healthy people at normal activity.

Hyperparathyroidism with X-ray or phosphatase evidence of osteitis also enlarged the pool, and both urinary excretion and bone deposition were increased. When only microscopic evidence of osteitis could be found the pool was only very

[2] The individual data from which Table III has been compiled appear in Tables I through IX in the Appendix.

TABLE III

Strontium dynamics in various conditions *

Condition	No. of studies	No. of subjects	k	E	T	U	B
				L	*L/24 hrs*	*L/24 hrs*	*L/24 hrs*
Healthy; ordinary activity	31	25	0.309±0.010	42.7± 1.1	13.5± 0.6	3.9±0.2	9.6±0.4
Athletes	14	14	0.357±0.014	56.9± 2.3	20.7± 1.0	5.8±0.2	15.0±1.0
Nephrolithiasis	11	11	0.340±0.017	39.3± 2.3	13.3± 0.9	5.7±0.8	7.6±0.6
Hyperparathyroidism:							
with X-ray osteitis or increased alk. phosphatase;	4†	4	0.407 (0.269–0.517)	64.4 (50.8–73.7)	26.2 (18.4–33.6)	7.3 (4.7–8.8)	18.9 (12.8–24.8)
normal X-ray appearance and alk. phosphatase, microscopic osteitis on iliac crest biopsy;	18	17	0.396±0.025	49.1± 2.8	18.5± 0.8	6.9±0.5	11.5±0.6
no evidence of osteitis by X-ray exam., phosphatase, or bone biopsy	7	7	0.309±0.023	38.8± 3.2	11.8± 1.1	4.3±0.5	7.5±0.9
Hyperthyroidism	7	7	0.475±0.051	48.9± 3.6	23.8± 3.5	7.0±2.2	16.7±2.0
Acromegaly	9	8	0.332±0.022	73.8± 6.2	23.7±2.6	5.7±0.5	18.2±2.3
Osteoporosis, postmenopausal	40	26	0.263±0.007	33.0± 0.9	8.7± 0.3	2.3±0.2	6.4±0.3
Adrenocortical hyperplasia	2‡	2	0.413–0.537	19.8–28.2	8.2–15.2	5.8–8.6	2.4–6.6
Paget's disease	5†	5	0.508 (0.336–1.040)	95.4 (41.5–175.5)	58.7 (16.4–182.5)	4.7 (2.3–6.8)	54.0 (14.1–175.7)
Chronic vitamin D overdose	1	1	0.330	376.0	124	0.5	123.5

* k =Serum disappearance rate constant, E =exchangeable pool, T =total turnover, U =urinary excretion, B =bone deposition. Values are given as mean ± standard error.

† Mean and range.

‡ Individual values of 2 subjects are given.

TABLE IV

Strontium dynamics, before and after cure of hyperparathyroidism *

Patients	Status	Serum Ca	k	E	T	U	B
		mEq/L		*L*	*L/24 hrs*	*L/24 hrs*	*L/24 hrs*
NOR	Pre-op.	7.00	0.359	49.9	17.9	6.3	11.6
	4 days post-op.	4.85	0.328	51.0	16.7	5.9	10.8
POL	Pre-op.	7.35	0.502	58.2	29.2	10.0	19.2
	3 mos after 1st test	7.05	0.405	57.4	23.2	7.0	16.2
	1 week post-op.	5.26	0.563	43.2	24.3	2.8	21.5
TUR	Pre-op.	6.15	0.389	43.4	16.9	5.8	11.1
	9 mos post-op.	5.55	0.269	46.0	12.4	2.9	9.5
LAM	Pre-op.	6.10	0.359	31.7	11.4	5.5	5.9
	14 mos post-op.	5.50	0.225	44.4	10.0	2.6	7.4
SWE	Pre-op.	7.30	0.245	35.8	8.8	2.7	6.1
	2 mos post-op.	4.75	0.213	35.7	7.6	0.7	6.9
	8 mos post-op.	5.20	0.259	29.3	7.6	1.4	6.2

* For abbreviations, see Table III.

slightly enlarged, and there was a similar small increase in bone deposition rate ($p < 0.01$). When even the histological appearance of the bone biopsy specimen was normal, the exchangeable pool size and urinary excretion were normal and the bone deposition rate tended to be low. In five patients without clinical evidence of osteitis fibrosa, cure of hyperparathyroidism did not change bone deposition rates, but urinary excretion rates fell in four and exchangeable pool size decreased in two (Table IV).

Calcium dynamics in the four conditions associated with osteopenia differed widely. In senile osteoporosis the mean values for exchangeable pool size and bone deposition rate were significantly less (− 23 and − 33 per cent, respectively) than in the normal group, although there was some overlap (Figure 3). After correction for body weight or surface area, exchangeable pool and bone deposition rates were still significantly lower in osteoporotics than in normal subjects (Table V). The two patients with osteoporosis due to long-standing Cushing's disease (bilateral adrenal cortical hyperplasia) had the smallest miscible pools in the series. A large portion of the pool was excreted daily by the kidney and only a small portion was deposited in bone. A third patient with Cushing's syndrome (adrenal cortical adenoma) of 15 months' duration had moderate skeletal demineralization but no fractures. Her miscible pool was normal but the rate of urinary excretion was greatly increased and the bone deposition rate was a little above normal (Appendix Table VIII). After removal of the adrenal cortical adenoma, the urinary excretion rate was normal and bone deposition increased slightly.

In contrast to the osteoporosis of Cushing's disease and old age, hyperthyroidism and acromegaly both enlarged the exchangeable pool. In patients with hyperthyroidism the fraction of the pool turning over was also greater, but in the nine acromegalics it was the same as in the controls. Hyperthyroidism without hypercalcemia increased bone deposition without increasing urinary excretion. With hypercalcemia and normal renal function, bone deposition was increased and urinary excretion greatly augmented. In acromegalics the mineral went rapidly to bone and the urinary excretion rate was only slightly accelerated. No difference was found between the data of four

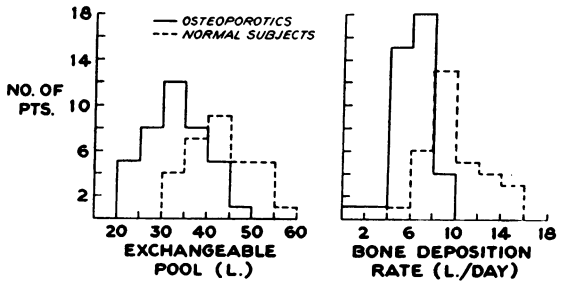

FIG. 3. FREQUENCY DISTRIBUTION CURVES FOR EXCHANGEABLE POOL SIZE AND BONE DEPOSITION RATES OF NORMAL SUBJECTS AND PATIENTS WITH POSTMENOPAUSAL OSTEOPOROSIS.

TABLE V

Effect of body size and weight on strontium dynamics

Condition	*E*	*T*	*U*	*B*
Body wt*				
Normals, average activity	0.602 ± 0023	0.196 ± 0.010	0.055 ± 0.004	0.140 ± 0.007
Normal athletes	0.758 ± 0.029	0.278 ± 0.014	0.077 ± 0.004	0.206 ± 0.014
Osteoporotics	0.542 ± 0.016	0.149 ± 0.007	0.041 ± 0.003	0.108 ± 0.006
Body size†				
Normals, average activity	23.2 ± 0.7	7.5 ± 0.3	2.1 ± 0.2	5.4 ± 0.2
Normal athletes	29.8 ± 1.2	10.9 ± 0.6	3.0 ± 0.1	7.9 ± 0.5
Osteoporotics	20.1 ± 0.6	5.6 ± 0.3	1.5 ± 0.1	4.0 ± 0.2

* Measurements of *T*, *U* and *B* are given as L/kg body weight/24 hrs; *E* is in L/kg.
† Measurements of *T*, *U* and *B* are given as L/m² BSA/24 hrs; *E* is in L/m².

acromegalics with roentgenographic evidence of osteoporosis and five without. In patients with Paget's disease of bone, the exchangeable pool and bone deposition rate were increased. The massive calcium deposits in one patient with chronic vitamin D overdosage increased the exchangeable pool almost tenfold; serum strontium values declined too rapidly to permit accurate measurement of bone deposition rate.

The reproducibility of the method is shown in Figure 4 where the results of a first test are plotted against a second test 21 times. For most subjects the values cluster fairly close to the theoretical slope of unity with a mean variation of 8 per cent.

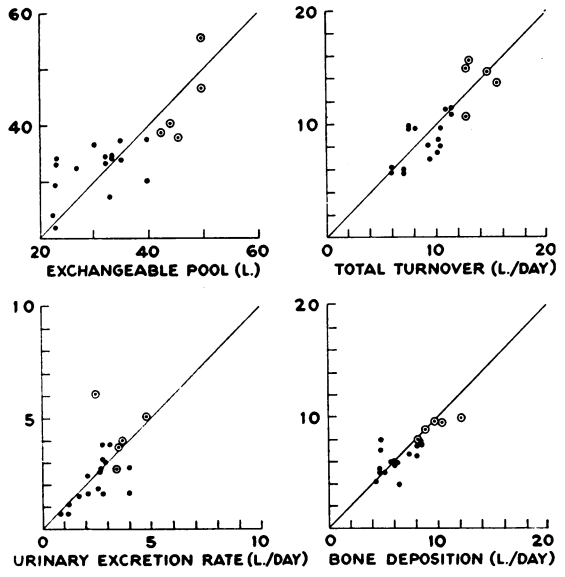

FIG. 4. REPRODUCIBILITY OF SKELETAL DYNAMICS MEASURED BY STABLE STRONTIUM. Duplicate (and occasionally triplicate) tests were performed 16 times in osteoporotic patients (dots) and in 5 normal subjects (circled dots). First results are plotted on abscissa and second (and third) tests on ordinate.

DISCUSSION

The data indicate that strontium can be used as a tracer to detect alterations in skeletal metabolism. In order to relate changes in bone deposition of strontium to those of calcium, any major difference in their metabolism must be accounted for. Major differences do occur in absorption and excretion and there are minor differences in distribution. The intestine discriminates greatly against *orally* administered strontium (30) but fecal losses of intravenously injected Ca^{45} and Sr^{85} are not widely divergent (11, 30). Renal clearance of strontium is three to five times that of calcium (12) and renal discrimination appears responsible for the difference in total retention of the two elements when they are given intravenously. Skeletal accumulation of radioactive Ca and Sr was equal in rabbits whose kidneys had been poisoned with mercuric chloride (31) and in nephrectomized rats (32). The distribution of strontium is quite similar to that of calcium. Double tracer experiments in man with Ca^{45} and Sr^{85} gave similar "pool" sizes and disappearance rate constants for the two elements (11). Most of an injected dose of either element is deposited in bone (23, 26, 27, 33), and radioactive isotopes of the two elements produce the same radioautographic patterns in bone (27, 34). Their passage from blood into extracellular fluid and spinal fluid are the same (24, 25), but intracellular penetration of strontium appears limited (Table I). Differences in protein binding of strontium and calcium have

been reported for man (35) but not for the rat (36).

Many studies suggest that bone discriminates but little between calcium and strontium *in vivo*. From a study in which Sr^{87} and Ca^{45} were given orally, it was inferred that in man the ratio of Sr^{87} to Ca^{45} was the same in bone and blood (37). Changes in Sr metabolism paralleled those for Ca in various diseases affecting skeletal metabolism (5, 11). When differences in urinary excretion were taken into account, Sr^{90} and Ca^{45} had no marked difference in bone deposition rates after their simultaneous administration to rats (38). Their skeletal accumulation is the same in anuric animals (31, 32) and in short-term experiments in intact animals (36). The two are also taken up to almost the same extent *in vitro* by surviving embryonic chick bone (39), bone powder (31) and synthetic apatite crystals (36). Equimolar exchange of strontium for the calcium of bone crystal has been shown (40). However, bone does not appear to handle the two elements identically in all respects. Preferential release of strontium from bone has been noted both *in vivo* (32, 36) and *in vitro* (36, 39, 41, 42). In the present method gastrointestinal discrimination was minimized by administering the strontium intravenously, and differences in renal excretion were accounted for by direct measurement of the urinary strontium excretion rate. Since the major differences in their metabolism are accounted for, the calculated bone deposition rates for strontium probably closely reflect those of calcium. Although the present method overestimates the deposition rates by approximately 12 per cent because fecal excretion is not subtracted, changes in skeletal metabolism in the conditions studied are similar to those found when radiocalcium was used as a tracer.

The 10 mEq dose of strontium used in these studies is larger than usual tracer doses but was the minimal quantity that produced serum levels that could be accurately measured by flame spectrophotometry for 4 to 6 days after injection. Fraser and his associates (15) studied the problem of whether such large doses act as a true tracer by repeating tests at several dosage levels in the same subjects. They found no effect of varying the amount of strontium. Harrison and co-workers (12) have shown that renal clearance of strontium is the same over a wide range of serum concentrations. The percentage of dose excreted in the feces appears to be in the same range when large doses of stable strontium and small doses of Sr^{85} (11, 12, 15, 30) are given.

The use of tracers to measure bone accretion rates or osteogenesis has been challenged because bone-seeking radioisotopes are concentrated in "hot spots," where new bone is being formed, and are deposited diffusely in dense, previously well mineralized bone (43–45). Hence, part of the tracer transferred from the pool to bone may be accounted for by new bone formation, and part by another process which has not been fully characterized. This process may represent a slow exchange, intracrystalline rearrangement, or diffuse accretion, and is included in the measurement of what is variously termed bone formation rate, accretion rate, and rate of osteogenesis. The extent to which this process affects the exponential disappearance of tracer from the rapidly exchangeable calcium pool is a matter of conjecture. While the diffuse label may not represent new bone growth, it does involve deposition of mineral ions which are important in maintaining the supporting function of the skeleton. For this reason, we have called the entire movement of tracer from the exchangeable pool to deeper layers of bone, the bone deposition rate.

Some authors have proposed correcting bone deposition rates for body weight. Since part of the exchangeable calcium is in extracellular fluid, it is possible that pool size is partly related to body size. To determine whether the smaller exchangeable pool of senile osteoporotics could result from their smaller size, we calculated the effect of correction for weight and surface area in these patients (Table V). The decreased pool size of osteoporosis is partly explained by the smaller size of the patients, but the difference in the rate of bone deposition between the controls and the osteoporotics was only slightly reduced by correcting the figures. Since weight and surface area of the athletes were the same as those of the control subjects at average activity, body size could not be responsible for the increased values seen in the athletes. Perhaps correction for lean body mass would be more appropriate. Fraser and his associates (15) expressed the volume of tracer distribution and rate of osteogenesis in "total body

plasma units." They calculated plasma volume as a constant fraction of body weight, so this unit is merely the volume of distribution corrected for body weight. Since plasma contains only part of the exchangeable pool and plasma volume is not known to affect calcium turnover, we have preferred to express the results in apparent liters of tracer distribution based on sampling the exchangeable pool via the serum.

It is difficult to correlate our results quantitatively with most reported studies of skeletal dynamics because of variation in experimental design, methods of calculation, and selection of patients. The study most comparable in experimental design is that of Fraser and co-workers (15) who used a similar model of calcium movement and nonradioactive strontium as a tracer. However, they employed a weight correction and expressed the results in "total plasma units." Their results may be recalculated to our terminology if the weight of each subject is known. Individual weights are given only for their normal subjects, who had exchangeable pools about 10 per cent lower and bone deposition rates approximately 30 per cent lower than ours. These discrepancies might be accounted for by the different method used to correct for loss of tracer during the mixing period and to integrate urine excretion rate. In making this correction for initial loss of tracer, Fraser and associates assumed that total body retention of strontium was linear on a semilogarithmic plot, but Norris, Tyler and Brues (46) have shown that total body retention of bone-seeking elements is a linear function only when plotted on log-log coordinates. Nordin (9), using a modification of Fraser's method, reported data on seven normal subjects. He included data from the first 24 hours in plotting the rate of fall of urine specific activity over a 7-day period. Plots of serum concentration of bone-seeking tracers do not indicate first order rate processes until after 24 hours. Inclusion of these values from the first 24 hours, failure to correct for urinary loss of tracer during mixing, and the method of calculating fecal loss in this period operate in different directions to various degrees and make his results difficult to interpret. Bauer, Carlsson and Lindquist (6), using a method of calculation analagous to ours, calculated exchangeable pool space and bone accretion rates in normal subjects from data provided by their own and other published studies. In only one group are the figures expressed in liters of serum. Four normal subjects in this group had exchangeable pools and bone accretion rates higher than our normal subjects but these four were in various stages of convalescence from fracture or nerve injury. The results from the other groups were calculated from specific activities and are expressed in grams of calcium. Since the serum calcium of each subject is not given, one can convert their figures to liters of serum only by assuming an average normal serum calcium of 5.0 mEq per L of serum. Since the high and low extremes of normal serum calcium in most laboratories are about 18 per cent apart, such an assumption would not lead to valid comparison. Conversely, if one assumes the ratio of Sr/Ca to be the same in all parts of the exchangeable pool and the rate of movement into bone to be the same for the two elements, one can convert the results of the present study to milliequivalents of calcium by multiplying the result for each subject by his serum calcium value. Such conversion gives our group of normal adult subjects slightly smaller exchangeable space and faster bone deposition rates than those recalculated by Bauer and associates (6) from the Ca^{45} data of Bronner, Harris, Maletskos and Benda (2) (1 patient), Krane, Brownell, Stanbury and Corrigan (3) (4 subjects) and the figures reported by Heaney and Whedon (7) for 1 normal adult. Some of these variances might result from the lower intracellular penetration of strontium (viz. Table I) and our overestimation of bone deposition by not measuring fecal excretion.

Because of the moderate variation in values for normal subjects reported by different authors it is apparent that any comparison of changes in abnormal states must be in reference to normal figures obtained by each group. Because of the expected biological variation within any group, the small number of normal subjects reported by most authors makes such comparison liable to reservation except in those abnormal states associated with dramatic alteration in skeletal metabolism, such as Paget's disease. In this condition only greatly increased exchangeable pool size and bone deposition rates have been reported (7, 8, 11). This is true by our method also, and is

in keeping with previous concepts of bone metabolism in this disease.

Hyperthyroidism is associated with negative balance of calcium and phosphorus, which in extreme cases may lead to roentgenographically evident osteoporosis and pathological fractures. It has recently been proposed that the osteoporosis of acromegaly and hyperthyroidism may be related to the unavailability of protein for the production of bone matrix and a resulting decrease in bone formation (47). Our data are not compatible with this proposal and confirm the enlarged pool of exchangeable calcium and rapid turnover rate found in hyperthyroidism by Krane and his associates (3), Heaney and Whedon (7), Dow and Stanbury (11), and Fraser and colleagues (15). Since bone is forming rapidly in these conditions, the development of osteoporosis must be due to even more rapid rates of osteolysis.

Osteoporosis is a common feature of hyperadrenocorticism. Elevation of the urinary excretion rate despite the reduced size of the pool in two patients with Cushing's disease suggests that bone dissolution is responsible for the demineralization. The patient with adrenocortical adenoma and symptoms of short duration had a very rapid urinary excretion rate and an apparent effort (unsuccessful) to compensate for increased bone dissolution by a slight increase in bone deposition rate. A similar rapid rate of urinary excretion and 15 per cent increase in bone deposition is an early feature of corticoid overdose in normal subjects (48).

Albright's hypothesis that bone formation is decreased in postmenopausal osteoporosis has recently been challenged (49–51). Patients with postmenopausal osteoporosis have been reported to have calcium (7, 9, 11) and strontium (11, 15) kinetics indistinguishable from those of normal subjects. Our data show that the rate of bone formation is decreased in osteoporosis and that this difference persists after correction for body size. The histograms for exchangeable pool size and bone deposition rate for the control subjects and osteoporotics show moderate overlap between the two groups, but the groups clearly comprise two populations. Our values for osteoporotics are similar to those reported by others. Hence, interpretation of these values as "low" depends on the relatively high values of our normal subjects compared with the published normal values discussed above. Lower than normal values for strontium retention by osteoporotics have been reported by others (6, 13, 16). Bone accretion rate of P^{32} is also decreased in osteoporosis (52). These data are in harmony with Albright's hypothesis that postmenopausal osteoporosis is due to decreased osteogenesis, but do not prove it, since the low rate of bone formation could reflect a decrease in skeletal mass, as in the two cases of advanced Cushing's disease. However, if the decreased skeletal mass of postmenopausal osteoporosis is due to an increased rate of bone resorption, calcium and strontium metabolism might resemble that of Cushing's disease, in which the urinary excretion rate is rapid in spite of skeletal depletion manifested by osteoporosis and decreased exchangeable pool size. In our experience, long-standing postmenopausal osteoporosis is rarely associated with increased calciuria. If postmenopausal osteoporosis is associated with increased bone resorption, as suggested by others, the urinary excretion rate might be normal if exogenous calcium was curtailed and bone deposition rate was normal. Hypercalciuria might result from normal bone resorption with decreased rate of bone deposition. This situation occurs in the osteoporosis of disuse or immobilization, which is regularly accompanied by marked hypercalciuria. Physical strain is considered to be a normal osteoblastic stimulus and its loss results in decreased osteogenesis. This concept is supported by the decreased bone accretion rate in an immobilized subject (6) and by the greatly increased bone deposition rates in our group of hard-playing athletes. The decreased bone deposition rate in postmenopausal osteoporosis, as in immobilization osteoporosis, probably reflects impaired osteogenesis, but it is not yet clear whether this is due to abnormal bone mineral metabolism or bone matrix formation.

Unlike patients with osteoporosis, all reported hyperparathyroid patients have had enlarged exchangeable calcium pools and rapid bone turnover rates (11, 15). This is not surprising, since there is more exchange surface in the actively metabolizing bone. Secondary increase in osteoblastic activity is thought to occur in hyperparathyroidism only when bone involvement is well developed and changes are roentgenographically

evident. In our four patients with hyperparathyroidism who had roentgenographic changes or rise in serum alkaline phosphatase or both, the exchangeable pools were large and bone deposition rates rapid. The 17 patients who had normal bones by X-ray and alkaline phosphatase tests but showed microscopic evidence of bone involvement had small but significant increases in strontium space and turnover. Seven patients with no microscopic foci of bone resorption had normal values for pool size and decreased rates of bone deposition. Thus, the degree of bone involvement in hyperparathyroidism measured by strontium movement correlates well with that found histologically. In 11 patients with recurrent nephrolithiasis who were distinguishable from patients with hyperparathyroidism only by their lack of hypercalcemia, the pool size and total turnover rate were normal, but more mineral was being channeled to urine than in normal subjects and bone formation was slightly decreased. Four patients studied by Fraser and co-workers (15) before and after cure of hyperparathyroid bone disease showed continued avidity for strontium for several months. One of our patients with a rapid initial bone deposition rate still had high values 1 week after operation. Four other patients had normal or low bone deposition rates before operation and these did not change after removal of parathyroid adenomas (Table IV). Although the number of liters of exchangeable pool being deposited daily in bone does not change, the fall in calcium concentration throughout the pool postoperatively results in less actual calcium being deposited in bone. The decrease in urinary excretion rate of strontium postoperatively parallels the decrease in hypercalciuria usually seen when hypercalcemia is corrected.

SUMMARY

1. Skeletal dynamics were calculated by usual dilution formulas, using stable strontium as a tracer, in 25 normal subjects, 14 athletes, 26 patients with postmenopausal osteoporosis, 28 with primary hyperparathyroidism, 3 with hyperadrenocorticism 8 with acromegaly, 7 with thyrotoxicosis, 11 with urolithiasis, 5 with Paget's disease of bone, and 1 with vitamin D poisoning. The technic requires that 10 mEq of strontium gluconate be injected intravenously and blood and urine concentrations be measured for 4 to 6 days.

2. In normal subjects the rapidly miscible pool was equivalent to 42.7 ± 1.1 L of serum, turning over at a rate of 13.5 ± 0.6 L daily, of which 3.9 ± 0.2 L was excreted by the kidney and 9.6 ± 0.4 L went to bone. Since only approximately 2.5 per cent of the pool is excreted in the feces daily, fecal excretion was not measured routinely. Good reproducibility was found in 21 duplicate studies.

3. Intense muscular exercise (athletes) was found to expand the pool greatly and to accelerate the rate of deposition in bone.

4. Kinetically, two divergent types of osteoporosis were differentiated. A small pool and low rate of bone deposition were found in postmenopausal osteoporosis and Cushing's disease of long duration. The large pool and rapid rate of bone deposition in thyrotoxicosis was confirmed and also found in acromegaly. In these two, excessive bone resorption is postulated. Urinary excretion rate was excessive in Cushing's disease, thyrotoxicosis, and acromegaly.

5. In hyperparathyroidism with clinically evident osteitis, expanded pools, greatly increased turnover, urinary excretion, and bone deposition rates were confirmed. In patients with normal roentgenographic appearance and phosphatase, bone involvement was shown by slight increase in bone deposition rate and microscopic foci of resorption on iliac crest biopsy. In seven patients without histological foci of resorption, the bone deposition rate was not increased.

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APPENDIX

Tables I through IX give clinical and experimental data on individual subjects. In each table % TRP = per cent renal tubular resorption of phosphate, k = serum strontium disappearance rate constant per day, E = exchangeable pool size in liters, T = exchangeable pool turnover in liters per day, U = urinary excretion rate in liters per day and B = bone deposition rate in liters per day.

APPENDIX TABLE I

Healthy subjects, average activity

Name	Sex	Age	Wt	Ht	Clinical notes	Serum Ca	Serum P	Serum Phos-pha-tase	Urine Ca	% TRP	*k*	*E*	*T*	*U*	*B*
		yrs	*kg*	*cm*		*mEq/L*	*mg/ 100 ml*	*SJR units*	*mEq/ 24 hrs*						
JES	M	24	78.2	185	Normal San Quentin	5.25	3.7		7.4	78	0.319	51.2	16.3	3.9	12.4
SUL	F	25	79.9	175	Familial hirsutism; normal bones by X-ray	4.95	4.0	4.8	6.6	86	0.286	35.8	10.2	3.5	6.7
DYK	M	26	77.8	173	Normal San Quentin	5.15	2.7		8.0	81	0.415	38.3	15.9	4.3	11.6
FIL	M	27	76.4	170	Normal San Quentin	5.10	2.9		6.6	88	0.280	50.6	14.2	4.1	10.1
DEL	M	27	86.3	188	Normal	5.70	3.2	5.4	6.4	81	0.359	45.3	15.5	3.5	12.2
						5.85	3.6		7.5	82	0.255	37.8	13.6	3.7	9.9
STA	M	27	65.5	183	Normal San Quentin	5.35	4.2		7.7	79	0.336	51.4	17.3	5.4	11.9
WYA	F	29	51.6	155	Dermatitis, hands	5.05	3.4		8.7	76	0.262	32.9	8.6	3.1	5.5
EIS	M	29	65.9	146	Normal	5.35	3.2	4.9	7.9	81	0.330	43.8	14.5	4.8	9.7
		30	69.1			5.00	2.7		8.2	87	0.352	41.9	14.8	5.0	9.8
CAM	M	30	81.9	180	Normal San Quentin	5.30	4.1		6.9	85	0.304	45.0	13.7	4.0	9.7
HUT	M	33	81.9	183	Normal San Quentin	5.10	4.4		8.2	88	0.276	46.2	18.1	4.0	14.1
ZEK	M	33	68.3	178	Normal San Quentin	5.55	3.4		7.2	79	0.259	49.6	12.9	2.5	10.4
						5.25	4.0		8.2	83	0.335	46.4	15.6	6.1	9.5
BLA	M	34	80.5	183	Normal San Quentin	5.30	2.8		23.1	77	0.380	51.4	23.4	9.2	14.2
KIN	M	37	99.6	185	Normal San Quentin	5.00	3.5		4.4	83	0.238	40.8	9.7	3.0	6.7
STO	M	40	91.9	183	Normal San Quentin	4.90	4.2		4.7	93	0.289	42.2	10.6	2.4	8.2
						5.25	4.2		4.1	91	0.252	44.6	12.9	3.2	9.7
GOR	M	41	84.1	181	Normal	5.10	3.8	6.1	3.5	79	0.254	49.4	12.6	3.7	8.9
						5.25	4.1		8.9	87	0.232	55.4	12.9	4.0	8.9
TOR	F	42	53.6	171	Juvenile epiphysitis	5.00	3.5	5.6	8.2	88	0.285	43.4	12.4	4.1	8.3
REY	F	43	53.6	163	Contact dermatitis	5.10	3.5	3.4	8.8	78	0.347	31.0	10.7	3.1	7.6
ARB	F	48	53.2	163	Psoriasis	4.75	3.6	4.6	3.5	84	0.256	34.0	8.5	1.9	6.6
AND	F	49	65.0	165	Psoriasis	5.30	3.4		11.1	77	0.447	35.6	15.9	3.5	12.4
HOLC	F	52	64.1	170	Normal	5.10	3.9	3.8	9.1	84	0.336	40.9	13.7	3.5	10.2
CRO	F	53	62.0	161	Normal	5.10		4.7	11.9		0.333	50.4	16.6	4.2	12.4
SOO	F	61	75.0	153	Normal	5.20	3.3	5.0	6.8	90	0.281	39.0	11.0	2.7	8.3
MYE	F	71	68.8	151	Hypertension	5.80	2.7	2.0	12.7	79	0.385	36.0	13.8	5.5	8.3
HOLM	F	73	60.4	165	Osteoarthritis, mild	5.05	2.9	3.4	6.7		0.299	42.1	12.6	3.4	9.2
						5.30	3.0	3.8	5.9		0.274	38.7	10.6	2.7	7.9
TUC	F	80	50.9	160	Osteoarthritis, mild	5.00	3.6	6.2	7.4		0.318	35.0	11.1	3.4	7.7

APPENDIX TABLE II

San Quentin athletes *

Name	Sex	Age	Wt	Ht	Serum Ca	Serum P	Serum Phos-pha-tase	Urine Ca	% TRP	*k*	*E*	*T*	*U*	*B*
		yrs	*kg*	*cm*	*mEq/L*	*mg/ 100 ml*	*SJR units*†	*mEq/ 24 hrs*						
STA	M	26	70.0	174	5.10	3.7		8.9	82	0.412	43.8	16.1	5.6	17.0
					5.40	2.9		7.0	75	0.367	54.8	22.6	4.6	11.5
REE	M	34	71.9	185	5.40	3.2		10.4	80	0.325	44.4	14.4	5.2	9.2
ROL	M	28	68.7	171	5.45	4.5		11.9	78	0.383	56.4	21.6	7.4	14.2
MAS	M	25	67.8	175	5.50	3.2		11.1	81	0.361	47.2	17.0	5.2	11.8
THO	M	28	74.2	175	5.40	4.0		13.7	85	0.347	50.0	17.4	5.8	11.6
WAT	M	25	81.0	180	5.35	3.9		11.7	83	0.425	58.6	24.9	7.3	17.6
YOU	M	33	73.7	173	5.05	3.3		11.1	81	0.398	61.6	24.6	5.8	18.8
DEL	M	28	69.6	170	5.15	4.2		11.3	87	0.425	49.5	21.1	5.2	15.9
NEA	M	25	73.4	182	5.20	3.4		11.2	82	0.286	71.8	28.6	4.9	23.7
BEL	M	30	79.4	177	5.15	2.5		10.2	76	0.318	68.2	21.7	5.7	16.0
LEE	M	31	67.9	170	5.15	2.9		12.6	75	0.368	60.2	22.2	6.5	15.7
BAR	M	30	91.8	177	5.45	4.6		11.9	83	0.265	64.3	17.1	4.9	12.2
					5.10	3.3		16.5	83	0.315	65.4	20.7	5.5	14.1

* All subjects were normal. † No data.

APPENDIX TABLE III

Multiple urinary tract stones

Name	Sex	Age	Wt	Ht	Clinical notes	Serum Ca	Serum P	Serum Phos-phatase	Urine Ca	% TRP	*k*	*E*	*T*	*U*	*B*
		yrs	*kg*	*cm*		*mEq/L*	*mg/ 100 ml*	*SJR units*	*mEq/ 24 hrs*						
BLI	M	43	80.0	169	Stones, 8 yrs	5.30	3.2	3.0	6.5	83	0.266	48.4	12.9	3.1	9.8
COR	M	46	73.9	162	Familial history of stones; stones, 14 yrs	5.45	2.8	6.0	17.0	81	0.382	29.5	11.3	5.9	5.4
GEN	M	39	71.9	179	Recurrent stones, 8 yrs; pyelonephritis	5.65	2.9	6.0	11.1	83	0.269	34.8	9.4	5.2	4.2
FRI	M	40	76.2	182	Immobilized 13 yrs before; asymptomatic renal calculi	5.45	2.9	5.8	7.8	72	0.316	43.1	13.6	4.6	9.0
HOP	M	55	80.0	171	Recurrent stones, 12 yrs; rheumatic heart disease	5.30	2.8	6.0	9.4	64	0.279	41.7	11.6	3.9	7.7
LEO	M	29	68.7	170	Recurrent stones, 2 yrs	5.50	2.6	3.0	9.0	77	0.382	34.3	13.1	4.5	8.6
PAL	M	58	76.0	170	Ca oxalate stones, 7 yrs	5.55	3.2	8.0	11.8	81	0.305	36.6	11.2	6.2	5.0
RAG	M	53	73.0	176	Stones, 14 yrs	5.30	2.4	7.0	11.1	60	0.360	40.4	14.5	6.2	8.3
SCH	M	32	69.0	173	Ca oxalate and phosphate stones; chronic pyelonephritis, 5 yrs	5.40	3.3	5.6	12.4	86	0.415	45.4	18.8	11.6	7.2
KNI	M	59	59.6	167	Bilat. stones, 6 yrs; arteriosclerosis	5.35	2.4	4.8	16.1	79	0.370	49.8	18.4	8.5	9.9
MOR	M	32	66.2	148	Renal tbc; stones, 9 yrs	5.00	3.0	10.0	4.5	70	0.396	28.6	11.3	2.8	8.5

APPENDIX TABLE IV

Postmenopausal osteoporosis

Name	Sex	Age	Wt	Ht	Clinical notes	Serum Ca	Serum P	Serum Phos-phatase	Urine Ca	% TRP	*k*	*E*	*T*	*U*	*B*
		yrs	*kg*	*cm*		*mEq/L*	*mg/ 100 ml*	*SJR units*	*mEq/ 24 hrs*						
MCD	F	57	57.7	155	Mult. compressions T and L spine; nontoxic nodular goiter	5.20	2.7	7.0	4.9	84	0.247	37.4	9.2	2.4	6.8
WAL	F	60	52.3	154	Guillain-Barre, 10 yrs; postmeno. fract. $T_{2,3,9,10}$ $L_{1,5}$	4.90	3.3	8.0	4.5	87	0.278	43.8	11.8	1.9	9.9
OLE	F	60	55.0	157	Fract. lumbar vertebrae and left hip	5.25	2.8		3.9	85	0.245	27.7	6.3	1.4	4.9
NEI	F	63	33.2	146	Multiple compressions; osteoporosis (biopsy); hysterectomy at 40	5.35	3.4	4.9	4.1	86	0.258	34.7	9.0	1.8	7.2
BER	F	65	69.5	155		5.10	3.0		6.9	84	0.319	35.6	11.4	2.7	8.7
BRI	F	67	76.4	156	Bilat. ovariectomy at 47; compression L_2	4.75	3.2	4.3	6.2	85	0.254	41.5	10.6	3.4	7.2
CAM	F	67	58.2	146	Generalized demineralization; Schmorl's nodes	5.25	3.2	6.0	1.8	84	0.245	29.0	7.1	0.9	6.2
JAC	F	67	70.0	160	Fract. $T_{10,12}$; urinary tract infection	5.20	4.0	6.0	3.9	95	0.295	34.8	10.3	2.1	8.2
						5.10			3.0		0.237	33.8	8.0	1.6	6.4
			69.6			5.10			4.6		0.261	37.2	9.7	2.4	7.3
KRU	F	68	48.6	153	Demineralized spine; fract. $T_{8,10}L_1$; thyrotoxic, 25 yrs previous	5.25	3.0		7.0	88	0.347	28.8	10.0	3.3	6.7
GIB	F	68	72.8	159	Femoral fract.; diabetes	5.05	3.5	3.3	2.5	91	0.181	40.4	7.3	2.0	5.3
AND	F	69	54.5	163	Osteoporosis (biopsy); demineralized spine; emphysema	5.40	4.3	7.2	5.0	95	0.199	35.1	7.0	5.4	1.6
BRU	F	70	54.1	145	Comp. fract. T_6-L_2; calcification in spleen and liver	5.15	4.2	5.2	6.6	82	0.316	32.1	10.1	4.0	6.1
			53.9			4.95	3.5		4.9		0.259	33.2	8.6	2.8	5.8
						5.05	3.2		4.1	87	0.219	34.4	7.5	1.6	5.9

APPENDIX TABLE IV—(*Continued*)

Postmenopausal osteoporosis

Name	Sex	Age	Wt	Ht	Clinical notes	Serum Ca	Serum P	Serum Phos-phatase	Urine Ca	% TRP	*k*	*E*	*T*	*U*	*B*
		yrs	*kg*	*cm*		*mEq/L*	*mg/100 ml*	*SJR units*	*mEq/24 hrs*						
DAD	F	70	52.3	158	Mod. demineralization; biconcave vertebrae	5.10	4.0	5.7	9.8	88	0.300	39.7	11.3	2.8	8.5
			53.4			5.00	3.4		7.0	91	0.359	30.2	10.8	3.1	7.7
			53.0			4.85			7.8		0.286	37.5	11.3	3.8	7.5
MEY	F	70	66.3	155		5.20			3.2		0.308	30.0	9.2	1.7	7.5
			66.5			5.10			2.6		0.223	36.5	8.1	1.5	6.6
VIC	F	72	67.3	157	Osteoarthritis; Schmorl's nodes; arteriosclerosis	5.35	3.5	5.0	6.1	79	0.286	32.8	9.4	2.9	6.5
			68.5			5.45			6.4		0.318	27.3	6.9	3.0	3.9
WAG	F	72	74.0	155	Compressions L_{1-4}; Parkinson's dis.; arterioscler.	5.05	3.7	7.6	8.1	86	0.267	36.2	9.7	5.0	4.7
COO	F	74	50.0	154	Osteoporosis (biopsy); treated lues	5.30	3.4	4.3	2.2	87	0.262	26.6	7.0	0.8	6.2
						5.25	2.7		1.7	80	0.172	32.3	5.6	0.7	4.9
WAT	F	75	38.1	144	Osteoporosis (biopsy); gastrectomy	4.55	3.4	6.0	0.8	90	0.187	45.2	8.5	0.8	7.7
MAN	F	75	53.2	165		5.15			4.1		0.208	34.7	7.2	1.5	5.7
WALK	F	76	46.8	158		5.10	3.4		3.8		0.248	28.8	7.2	1.4	4.8
STA	F	77	59.5	146	Collapsed $T_{10,12}$ $L_{2,4}$; scoliosis; osteoarthritis; arteriosclerosis	5.25	3.7		1.6		0.260	22.8	5.9	1.2	4.7
			60.4			5.10			1.7		0.282	22.0	6.2	1.1	5.1
		78	60.9			5.05			4.1		0.193	29.3	5.7	0.7	5.0
MCC	F	78	59.5	147	Thyrotoxic, 13 yrs prev.; compression T and L spine	4.80	3.6		4.1	89	0.328	21.3	7.0	2.6	4.4
			59.0			4.70	3.2		3.3	81	0.245	24.1	5.9	1.8	4.1
CHA	F	80	59.1	158	Compression T_{12},$L_{1,2}$	5.25	3.5		5.5	83	0.327	23.0	7.5	2.7	4.8
			60.3	157		5.20	3.0		5.7		0.290	33.2	9.6	2.6	7.0
			60.2			5.20			3.9		0.284	34.1	9.7	2.7	7.0
JAE	F	80	62.1	155	Compressed L vertebrae; emphysema	4.70	2.7	8.0	4.3	84	0.258	41.2	16.0	1.8	14.2
SCH	F	81	61.2	167	Anterior compression L_{2-4}, bromide rash	4.90	2.8	6.8	1.5	79	0.270	30.2	8.2	3.1	5.1
BRUS	F	85	56.6	151	Schmorl's nodes	5.35	3.4	4.0	3.4	82	0.215	40.7	8.8	2.2	6.6

APPENDIX TABLE V

Hyperthyroids

Name	Sex	Age	Wt	Ht	Clinical notes	Serum Ca	Serum P	Serum Phos-phatase	Urine Ca	% TRP	*k*	*E*	*T*	*U*	*B*
		yrs	*kg*	*cm*		*mEq/L*	*mg/100 ml*	*SJR units*	*mEq/24 hrs*						
CLE	F	33	50.0	168	Graves' disease	5.25	4.8	7.0	3.6	82	0.468	52.0	24.3	4.4	19.9
SYK	M	70	56.7	160	Toxic nodule	5.35			4.3		0.392	51.4	20.2	2.4	17.8
PAP	F	59	54.8	153	Menopause at 33; osteoporosis; toxic nodular goiter; comp. of T_{11-12}	5.20	3.3	3.0	2.4	82	0.292	41.1	12.0	1.5	10.5
SMI	F	46	60.7	167	Constipated; thirsty; Graves' disease	5.75	4.4	6.7	19.4	91	0.488	55.9	27.2	4.6	22.6
GIL	M	32	54.5	170	Graves' disease with myopathy; osteitis (biopsy)	6.22	4.2		40.7	76	0.693	48.7	33.7	16.2	17.5
SYA	F	53	42.2	160	Graves' disease; fract. T_9, L_1	5.75	5.0	6.0	16.9	88	0.592	61.2	36.2	14.0	21.8
MAR	F	58	57.1	160	Graves' dis.; uremia; comp. fract. $T_{7,11,12}$	6.71	3.7	4.7	20.0		0.401	32.2	12.9	6.0	6.9

APPENDIX TABLE VI

Hyperparathyroidism

Name	Sex	Age	Wt	Ht	Clinical notes	Serum Ca	Serum P	Serum Phos-pha-tase	Urine Ca	% TRP	*k*	*E*	*T*	*U*	*B*
		yrs	*kg*	*cm*		*mEq/L*	*mg/ 100 ml*	*SJR units*	*mEq/ 24 hrs*						
					Hyperparathyroidism with high alkaline phosphatase level or osteitis by X-ray										
ABR	F	69	57.5	148	Stones-bilat.; Paget's disease of bone	6.05	2.8	15.0	10.7	72	0.269	68.2	18.4	4.7	13.7
OLD	M	50	76.3	174	Giant cell osteoclastoma; partial loss of lamina dura	7.15	1.1	11.0	19.6	58	0.413	50.8	21.0	8.2	12.8
DEL	M	29	60.9	161	Demineralized skeleton; no osteitis (biopsy); stones rt. side	7.00	2.2	11.9	16.4	75	0.517	65.0	33.6	8.8	24.8
LEV	M	40	70.5	171	Stones, left. Duodenal ulcer	6.90	2.4	10.1	24.1	70	0.430	73.7	31.7	7.3	24.4
					Hyperparathyroidism with normal X-ray appearance, normal alkaline phosphatase level, but positive bone biopsy										
BRO	M	52	78.8	180	Stones, bilateral	6.20	3.1	3.8	26.8	67	0.217	79.1	17.2	8.1	9.1
HOE	F	46	61.2	157	Stones, bilateral	6.75	1.7	7.7	13.1	70	0.357	40.7	14.5	4.8	9.7
JON	M	38	80.0	173	Kidney stones	6.05	2.3	5.2	21.6	75	0.359	61.5	22.0	8.3	13.7
MOO	F	50	75.0	165	Parathyroid cyst palpated in neck; no stones	6.35	3.0	5.0	18.8	71	0.375	54.6	20.6	8.4	12.2
NOR	M	40	61.4	178	Stones, bilateral	7.00	2.4	6.2	31.7	75	0.359	49.9	17.9	6.3	11.6
POL	M	20	69.2	182	Stones, bilateral	7.35	2.4	8.4	25.4	69	0.502	58.2	29.2	10.0	19.2
			69.0			7.05	2.4	6.0	25.0	70	0.405	57.4	23.2	7.0	16.2
PUR	F	54	62.5	167	Stones, bilateral	6.60	2.5	7.1	19.7	66	0.333	51.6	17.2	4.5	12.7
DAR	F	53	69.5	160	Renal stones, left	5.85	3.2	2.5	8.7	65	0.403	33.5	13.5	4.2	9.3
ALV	F	60	54.9	160	Constipation, nausea	6.25	3.3	5.6	11.4	72	0.335	48.5	14.5	5.0	9.5
NOR	M	56	68.4	164	Stones, bilateral	7.35	2.2	6.5	21.9	70	0.509	32.6	16.5	6.2	10.3
CAN	F	37	59.4	163	Inc. fatigue, 14 mos Stones, left, 18 mos	6.00	2.8		9.1	81	0.367	54.2	16.6	3.4	13.2
HYA	F	35	40.4	151	Stones, bilateral	7.20	2.9	6.2	25.3	75	0.722	24.6	17.8	8.0	9.8
NEL	M	34	71.2	171	Stones, bilateral	6.10	2.5	3.7	18.7	71	0.431	45.5	19.6	9.3	10.3
COR	M	55	85.6	177	Stones, bilat. ulcer hist.	6.30	2.3	6.1	10.1	82	0.415	43.2	17.9	10.0	7.9
WOL	F	52	56.0	160	Stones, bilat.; prev. hemorrhage into parathyroid cyst; ulcer	6.65	2.5	6.9	4.3		0.308	51.2	15.8	4.4	11.4
BRY	F	58	120.2	163	Weakness, nausea, emesis, no stones	6.05	2.2	4.3	17.6	62	0.324	55.2	17.9	8.7	9.2
HOD	F	32	57.7	169	Nephrolithiasis; nephrocalcinosis, bilat.	6.20	3.0	6.3	23.2	67	0.403	50.0	20.2	6.4	11.8
					Hyperparathyroidism with normal X-ray appearance, normal alkaline phosphatase level, and normal bone biopsy										
ALE	F	56	59.1	148	Back pain; gen. weakness and body aches, 5 yrs	6.25	1.4	5.7	8.0	70	0.350	28.7	10.0	2.9	7.1
DYM	F	56	86.5	162	Stones, bilateral	5.85	2.0	6.5	11.6	64	0.238	53.1	12.6	3.5	9.1
LAM	F	51	74.5	163	Stones, bilateral, 2 yrs	6.10	2.6	2.0	14.6	76	0.359	31.7	11.4	5.5	5.9
SWE	F	70	50.7	152	Radical mastectomy for cancer; constipation; fractured vertebrae with demineralization; osteoporosis (biopsy)	7.05	2.3	6.8	11.0	53	0.245	35.8	8.8	2.7	6.1
TUR	M	25	91.5	175	Back pain, juvenile epiphysitis	6.15	2.2	6.0	23.2	69	0.389	43.4	16.9	5.8	11.1
SAU	M	43	67.1	170	Stones, bilat.; serum Ca fell to normal on corticoids	6.10	1.9	5.9	12.3	71	0.308	45.2	13.9	5.2	8.7
MCB	M	50	75.6	169	Uremia; renal stones	6.55	2.5	6.5	12.1	74	0.276	33.5	9.2	4.6	4.6

APPENDIX TABLE VII

Acromegaly *

Name	Sex	Age	Wt	Ht	Serum Ca	Serum P	Serum Phos-pha-tase	Urine Ca	% TRP	*k*	*E*	*T*	*U*	*B*
		yrs	*kg*	*cm*	*mEq/L*	*mg/ 100 ml*	*SJR units*	*mEq/ 24 hrs*						
ODL	F	35	8.55	165	5.20	5.0		6.4	95	0.308	64.7	18.5	5.4	13.1
		36			5.35	4.8		9.4		0.286	72.4	19.2	7.5	11.7
BOL	F	30	56.3	155	5.20	4.7	5.5	7.9	94	0.425	39.7	16.9	5.8	11.1
WHI	F	38	72.7	163	5.25	4.1		10.6	82	0.322	66.2	21.3	5.4	15.9
LOH	M	29	100.0	203	5.20	4.4	6.6	13.8	89	0.425	103.5	41.0	7.7	33.3
SEG	M	47	85.8	118	5.35	4.6		11.9	83	0.401	73.2	29.3	5.2	24.1
THO	M	41	78.5	174	5.15	3.4		7.3		0.289	77.2	22.3	5.8	16.5
BAL	M	44	72.7	165	5.15	5.2		6.5	91	0.245	70.8	17.4	2.5	14.9
REE	M	55	78.7	171	5.30	3.8	6.0	15.8	80	0.284	96.8	27.5	6.0	21.5

* Clinically active in all patients.

APPENDIX TABLE VIII

Adrenocortical hyperfunction

Name	Sex	Age	Wt	Ht	Clinical notes	Serum Ca	Serum P	Serum Phos-pha-tase	Urine Ca	% TRP	*k*	*E*	*T*	*U*	*B*
		yrs	*kg*	*cm*		*mEq/L*	*mg/ 100 ml*	*SJR units*	*mEq/ 24 hrs*						
ARM	M	57	59.3	167	Bilateral hyperplasia	5.00	2.8	4.1	6.0	78	0.537	28.2	15.2	8.6	6.6
CHU	F	57	50.5	174	Bilateral hyperplasia	5.30	3.4	6.8	5.9	84	0.413	19.8	8.2	5.8	2.4
GIL	F	26	73.3	162	Left adrenal adenoma; diabetes; obesity; amenorrhea; demineralized spine, fract. T_5	5.35	2.7	3.4	23.3	80	0.846	41.1	34.8	20.2	14.6
	3 mos post op.		67.1	160	No remineralization; collapse T_{12}; on cortisol, 0.015 daily	5.25			2.9		0.430	46.1	19.8	2.4	17.4

APPENDIX TABLE IX

Pagel's disease

Name	Sex	Age	Wt	Ht	Clinical notes	Serum Ca	Serum P	Serum Phos-pha-tase	Urine Ca	% TRP	*k*	*E*	*T*	*U*	*B*
		yrs	*kg*	*cm*		*mEq/L*	*mg/ 100 ml*	*SJR units*	*mEq/ 24 hrs*						
SAN	M	54	56.5	164	Prog. muscular dystrophy, familial; pelvis, femora, calcanei	5.35	3.8	18.9	6.2	86	0.423	69.8	29.5	3.3	26.2
MAR	M	41	65.7	164	Marked widespread disease	5.05	3.6	178.0	3.6	87	1.04	175.5	182.5	6.8	175.7
SIM	M	46	81.5	118	L_3, rt. femur	5.00	4.1	3.0	7.4		0.336	65.0	21.8	5.5	16.3
MAC	M	74	81.0	181	L clavicle; rt. scapula; L tibia; skull; pelvis	5.45	2.9	32.5	7.8		0.347	125.0	43.4	5.8	37.6
MCK	M	76	44.0	172	Pelvis and lumbar spine	5.00	3.1	9.0	4.0	85	0.396	41.5	16.4	2.3	14.1

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