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Influence of Dietary Stable Strontium and Calcium on the Turnover of Bone-Fixed Sr^{85} in Man.* (27570)

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Use of orally administered stable Sr and Ca to alter the distribution and retention of administered doses of radiostrontium has been studied by several investigators(1-5). These studies have indicated that retention of radiostrontium (Sr*) soon after administration is generally decreased by stable Sr or Ca given immediately prior to or immediately following Sr* administration. In this situation, the stable Sr or Ca atoms compete with the radioactive atoms being taken up by the slowly exchanging bone from the calcium pool available in blood, the soft tissues and exchangeable bone (the carrier effect).

In the almost steady-state condition which follows the transient response, the metabolic pattern changes considerably. Over 99% of the Sr* atoms which remain in the body are firmly fixed in the crystal lattice of the skeletal tissue(6). This bound Sr is henceforth subject only to radiological decay and to a slow biological turnover, resulting either from extremely slow exchange by the so-called "non-exchangeable" areas of bone, or from the bone-remodeling process (resorption).

It is thus of interest to study the effects of daily ingestion of Sr for a long period on the long-term turnover of the "fixed" Sr*, as the results cannot be predicted from the metabolic behavior of Sr* observed at early times. Such a study of the biological loss of Sr in man requires that highly sensitive measurements of the internally-deposited Sr* be made over a relatively long period, since the changes in turnover rate may be very subtle. It is difficult, if not impossible, to conduct such a study utilizing the conventional technic of radiochemical analysis. However, whole-body counting is very well suited to the purpose, as an independent, rapid and sensitive measurement of the internally-deposited gamma-emitting isotopes can easily be made, and the subjects followed for long periods.

Method. Four female patients (37 to 73 years of age) received 10 μc $Sr^{85}Cl_2$ intravenously. The patients were ambulatory and in good condition throughout the study. Diagnosis and degree of skeletal involvement in each patient are shown in Table I.

Retention of Sr^{85} was measured by *in vivo* counting with a whole-body gamma scintillation counter. The patients were positioned at a fixed geometry under an 8" × 4" NaI (T1) crystal detector as has been previously described(7). The radioactivity of the patients was determined by counting gamma-rays 4 hours after administration of the isotope and then at weekly intervals.

From 130 to 240 days following administration of Sr*, 2 patients received 1100 mg of Ca daily as gluconate, and 2 received 570 mg of Sr daily as lactate. These supplements were taken orally with meals.

Results. The biological loss of Sr^{85} in pa-

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TABLE I. Clinical Description of Patients.

Patient	Age	Sex	Wt (lb)	Urinary Ca (mg/day)*	Diagnosis	Skeletal involvement
KIR	73	♀	186	91	Ca of breast, 10 yr post-op. no recurrence	No metastases, osteoarthritis, spondylosis deformans
BRO	61	♀	133	140	Ca of thyroid, mild cong. heart failure	No abnormalities
KLE	61	♀	265	514	Pseudomyxoma peritonei, diabetes mellitus	Osteoarthritis, spondylosis, deformans, osteoporosis
MOS	57	♀	186	192	Osteoporosis	Moderate osteoporosis

* Avg urinary calcium excretion.

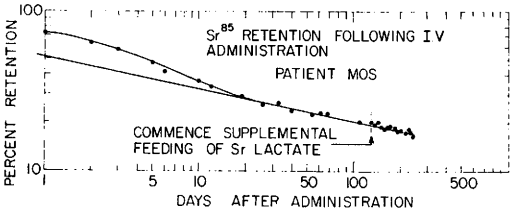

FIG. 1. Retention of Sr^{85} expressed as a power function.

tient MOS is shown in Fig. 1. Both retention and time are plotted as log transforms. After 30 days, retention followed a straight line on the log-log plot. The equations of all the straight lines were obtained with an IBM-610 computer by the method of least squares. Standard errors of the estimate of the regression coefficients were also obtained with the computer. Such a straight line for the log-log plot of the data corresponds to a power function of the Form $R = At^{-b}$, where R is the retention, A the intercept at 1 day on the log-log plot, and b the slope of the straight line. Values for the constants A and b obtained for the 4 patients for the period 30-130 days are listed in Table II. Whole-body retention during the period of dietary supplementation (130-240 days) was likewise characterized by a power function which was calculated similarly. The constants for this period are listed in the last 2 columns of Table II.

Neither the 2 patients receiving calcium gluconate nor the 2 patients receiving strontium lactate had significant change in the slope and intercept of the time plot of retention during the period of dietary supplementation as compared to the earlier control period.

Discussion. On the basis of studies(3-5) which have shown that stable Sr or stable Ca given immediately following Sr^{85} administration decreases retention of the isotope, it was

TABLE II. Effect of Dietary Supplementation on Sr^{85} Retention. % Retention $(R) = At^{-b}$.

Patient	Route of admin.	Daily dietary supplement	Dose (mg)	Random urinary Ca (mg/day)	Control period 30-130 days A	Control period 30-130 days b	Supplemental feeding period 130-240 days A	Supplemental feeding period 130-240 days b
KIR	I.V.	Ca gluconate	1100	121, 145	53.5 + 4.7* − 4.3	.192 ±.020*	50.8 + 7.8 − 6.3	.154 ±.043
BRO	"	"	1100	145	50.5 + 3.5 − 2.9	.183 ±.015	48.6 + 7.8 − 6.1	.171 ±.034
KLE	"	Sr lactate	570	382, 385 657, 258 378	21.7 + 3.2 − 2.7	.226 ±.032	21.9 + 8.8 − 6.3	.235 ±.065
MOS	"	"	570	260	52.5 + 8.8 − 7.5	.204 ±.038	58.6 +13.0 −10.7	.222 ±.039

* Stand. error of estimate of coefficients of line of regression: Ref. Y. Beers, *Theory of Error*, Addison-Wesley Pub. Co., 1957.

$$S_A^2 = S^2xy \left(\frac{\Sigma x_i^2}{[n \Sigma x_i^2] - [\Sigma x_i]^2} \right) \qquad S_b = S^2xy \left(\frac{n}{[n \Sigma x_i^2] - [\Sigma x_i]^2} \right)$$

thought that a similar though lesser effect might be observed when the stable elements were administered at relatively long times after the isotope was given. Reference is made, from time to time, to a high Ca or Sr diet as a possible therapeutic procedure for Sr^{90} poisoning. The possibility of achieving this effect is made less likely, however, by the fact that at late times after administration, an almost steady-state condition obtains, in which almost all the Sr* atoms are firmly bound in the skeletal tissue.

Enhancement of the biological turnover of Sr* following oral ingestion of stable Sr or Ca at a late period following Sr* administration must come about by one or both of 2 means: an increase in the bone-remodeling rate, or an increased exchange of Sr* atoms for the stable Sr or Ca atoms. It would appear rather unlikely from theoretical considerations alone that increasing the level of Sr or Ca in the plasma or soft tissues would influence the first of these means: that of bone-remodeling. As for the second means, an increase in rate of exchange of Sr* from the crystal lattice of bone, recent studies have indicated that the turnover time for Sr in some of the "long-term" compartments of bone may range up to values exceeding 50 years(8). Thus it can be inferred that some of the bound Sr will not readily exchange. It would appear from the present study that the long-term exchange of bone-fixed Sr is not primarily influenced by the level of stable Sr or Ca available for exchange.

The technics employed in this study may be valuable in other similar studies. Whole-body counting of internally-deposited tracer doses of Sr* is simple, comfortable for the patient, and studies of low levels of the tracer can be carried out over long periods.

We also noted in this study that the technic of using each patient as his own control obviates the problem of comparison of Sr loss data in the different patients in which wide variations normally occur. Mathematical presentation of the data in the form of a log-log plot proved a very convenient method for presenting and comparing the data, as the slopes of the lines can be determined with precision and can readily be compared. It is felt, on the basis of this study, that influence on the deposition of Sr* by dietary supplementation of stable Sr and/or Ca can occur only when the stable elements are taken just prior to or immediately following administration of the isotope, *i.e.*, prior to the time when a significant amount of Sr* is fixed in the skeletal tissue.

Summary. The turnover of Sr^{85} was determined for four patients by wholebody counting for a period of 130 days following administration of the isotope. The data obtained were expressed as power functions. Two patients then received Sr lactate, and the other two Ca gluconate as dietary supplements for a period of 110 days. Sr^{85} turnover was determined for this period and again expressed as a power function for each patient. While the data suggested that the addition of Ca gluconate to the diet somewhat decreased Sr^{85} excretion and the addition of Sr lactate slightly enhanced excretion, no statistically significant changes in the long-term turnover rate of Sr^{85} were observed.

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