FROM THE DEPARTMENT OF PHARMACOLOGY AND THE ORTOPEDIC CLINIC (MALMÖ), UNIVERSITY OF LUND, AND THE PEDIATRIC CLINIC, UNIVERSITY OF GOTHENBURG, SWEDEN

METABOLISM OF Ba^{140} IN MAN

By

GÖRAN C. H. BAUER, ARVID CARLSSON and BERTIL LINDQUIST

During recent years the metabolism of bone salt has been extensively studied in animals with the aid of radioactive isotopes and it has been shown that this technique permits accurate determination of the rates of formation (accretion) and resorption of bone salt (*Bauer, Carlsson* and *Lindquist* 1955 a). Tracer studies have also opened new pathways for investigations in man of skeletal metabolism under normal and pathological conditions (*Bauer, Carlsson* and *Lindquist* 1955 b, 1956 a; *Krane, Brownell, Stanbury* and *Corrigan* 1956; *Bronner, Harris, Maletskos* and *Benda* 1956, *Bauer* and *Ray* 1957).

In order to find suitable isotopes for skeletal metabolic studies, we have investigated the metabolism of Ba^{140} (half life 12.8 days) in rats (*Bauer, Carlsson* and *Lindquist* 1956 b). It was shown that Ba^{140} was irreversibly deposited in the skeleton and that the clearance rate of Ba^{140} from the plasma by skeletal accretion was about twice that of Ca^{45}. Although Ba^{140} and Ca^{45} thus were not handled by the skeleton in an identical manner, the behaviour of the two elements was sufficiently similar to suggest use of Ba^{140} as a tool for studying skeletal metabolism in humans.

The present communication is concerned with the application of Ba^{140} for determination of the accretion rate of bone salt in humans. The experimental series comprised seven individuals with clinically normal skeletons and one case of vitamin D resistant rickets. In some of the normal subjects the accretion rate was simultaneously studied with Ca^{45} and Ba^{140}.

EXPERIMENTAL

The experimental series comprised six children—five children with clinically normal skeletal metabolism (Cases 3, 4, 13, 14, 15) and one

child with primary vitamin D resistant rickets (Case 16)—and two adults with clinically normal skeletal metabolism (Cases 17 and 18). Cases 13 to 18 are described in the case histories below. Cases 3 and 4 have been described in a previous publication (*Bauer, Carlsson* and *Lindquist* 1955 b).

Administration of Ba^{140} *and* Ca^{45}. $Ca^{45}Cl_2$ and/or $Ba^{140}Cl_2$ (obtained from Harwell) were added at a high specific activity to a suitable amount of physiological saline. Each child received an intramuscular injection in the gluteal region of 2 ml. of this solution, and each adult an intravenous injection of 3 ml, the dose in each case being 2–3 μC Ba^{140} per kg body weight. Four patients (Cases 13, 14, 15 and 17) were in addition given 10μC Ca^{45} per kg body weight in the same injection. This high Ca^{45} dosage was given only to cases with a limited life expectancy.

The injection of the isotopes was always performed at 8.00 a.m. The children were fasting up to one hour after the isotope injection, and the adults up to the time of injection. Then the patients were allowed to eat and drink ad libitum during the whole experimental period.

Collection of samples. Blood samples were taken at the following intervals after the isotope injection: ½, 3, 6, 8, 12, 24, 48, 96 and 144 hours, from the children by finger puncture (capillary blood) and from the adults by vein puncture. In three of the cases (Cases 3, 4 and 18), however, blood samples were only taken for the first 48 hours. Immediately after each puncture, 1 ml serum in the children and 2 ml in the adults was mixed with 3 ml and 6 ml, respectively, of 10 % tricholoroacetic acid and centrifuged. The supernatant was examined for radioactivity (see below).

In the infants, 24-hour specimens of *urine* were collected in special bottles for about 10 days following the administration of the isotopes. In addition some of the urine was collected in paper tissue. In this way it was possible to collect the urine quantitatively. In the adults, 2-hour specimens of urine were collected during the first 12 hours, 6-hour specimens during the following 12 hours, and 12- or 24-hour specimens for about 10 days. The urine was examined for radioactivity and in case 17 also for calcium content (see below). The paper tissue was ashed in an electrically heated muffle, and examined for radioactivity (see below).

Twenty-four-hour specimens of *faeces* were collected for 10 to 18 days. The specimens were placed in porcelain crucibles, dried and then ashed in an electrically heated muffle at 800° C for about 6 hours before they were examined for radioactivity (see below).

In cases 13, 14 and 15 a *bone* biopsy was made in the upper part of the tibia at the junction of the proximal ¼ and next proximal ¼ of the bone, where the antero-medial bone surface lies immediately beneath the subcutis (see Fig. 1 in *Bauer, Carlsson* and *Lindquist*, 1955 b). The bone specimens were taken 8 to 12 days after the isotope administration. The specimens were taken with borers, which had an inner diameter of 3 mm. By this technique a piece of mainly compact bone was generally obtained. Any adherent spongy bone was removed. The specimens were carefully dissected free from adherent soft tissue and were then shaken several times with physiological saline solution, in order to remove as much as possible of blood and bone marrow. The specimens were ashed in an electrically heated muffle at 500° C for 2 hours, were weighed (accuracy ± 0.1 mg), and examined for radioactivity and content of Ca and P.

Determinations of radioactivity. In order to re-establish equilibrium between Ba^{140} and its daughter isotope La^{140} (half life 40 hours), the samples were not counted until at least 12 days after they had been collected. Counting was made on liquid samples after suitable dilutions with HNO_3 (density 1.10). The technique used was that of *Carlsson* (1951). Each sample was counted with and without an aluminium absorber, which absorbed all the Ca^{45} radiation and 61 per cent of the Ba^{140}, La^{140} radiation. The activity emanating from Ca^{45} and Ba^{140}, La^{140}, respectively, was calculated and compared with the activity of standard solutions of either of the two isotopes. The values obtained were expressed as per cent of the dose administered.

Determinations of the radioactivity of the *serum* were carried out on the trichloroacetic acid supernatant. In the *urine*, the determinations of activity were made directly on the urine specimens, acidified to pH 4 to 5 by means of glacial acetic acid, and on the ash from the paper tissue samples, dissolved in dilute HNO_3. The ash from the *faeces* samples were dissolved in dilute HNO_3 before the activity determination. The *bone* ash was dissolved in 1 ml 1-N HCl, and the activity determinations were made on these liquid samples.

Determinations of calcium in serum and urine were carried out by the method of *Clark* and *Collip*. The urine was first acidified to pH 4 to 5 by means of glacial acetic acid and filtered.

Determinations of calcium and phosphorus in the bone specimens were made on the HCl solutions of the bone ash. The methods used were those of *Clark* and *Collip*, and *Youngburg* and *Youngburg*, respectively.

CASE HISTORIES

Case 13. (Myelomeningocele).—Girl, one month old, weight 4.3 kg; birth weight 3.5 kg; only child to healthy parents. Immediately after birth she was transferred from the maternity hospital to the pediatric clinic. In the clinic she received citric acid milk. The infant had multiple malformations: myelomeningocele, spina bifida, hydrocephalus and clubfeet. She gained, however, normally in weight. At the time of the experiment her serum calcium and phosphorus values were within normal limits.

Case 14. (Hydrocephalus).—Boy, 5 months old, weight 6.9 kg; birth weight 3.5 kg; only child to healthy parents. The child was delivered by cesarian section. He was immediately transferred from the maternity hospital to the pediatric clinic. In the clinic he was given citric acid milk. His general condition was good. Ventriculography showed a marked hydrocephalus with only minimal amounts of cerebral tissue. Furthermore, the infant had microphtalmus and catarrhacta congenita. At the time of the experiment his serum calcium and phosphorus values were within normal limits.

Case 15. (Hypotrophia cerebri).—Girl, 1½ years old; weight 12.9 kg; birth weight 3.6 kg; only child to healthy parents. After birth the child was breast-fed for 6 months and then received a diet containing cow's milk and ordinary dietary supplements including vitamins A and D in prophylactic dosage. In the clinic she had received citric acid milk. From birth the child showed signs of retarded mental development with occasional convulsive seizures. She was apathetic and had weak muscular power; encephalography showed atrophy of the brain. At the time of the experiment her serum calcium and serum phosphorus values were within normal limits.

Case 16. (Primary vitamin D resistant rickets).—Girl, 8 years old; weight 19.9 kg; birth weight 3.9 kg; only child of healthy parents. The child was breast-fed for 9 months. From 6 months of age she received about 1,000 I.U. vitamin D daily. Her mother consulted the doctor *for the first time* when the girl was 1½ year old because her legs were bent, and because she did not walk without support. X-ray showed active rickets. Vitamin D was given in doses of 30,000 I.U. daily. When this dose had been given for about 2 months, the mother noted that the girl walked without trouble and therefore ceased to administer vitamin D in the high dosage prescribed.—The girl was admitted to the clinic *for the second time* when she was 2 years old because she refused to stand on her legs. She had marked epiphyseal enlargements at her wrists and ankles. X-ray showed large rachitic metaphyses with cupping and fraying of the shafts and with periosteal deposits along the shafts. Liver and renal function tests were normal. The rickets symptoms did not disappear until vitamin D was given in a dose of 500,000 I.U. per day, partly by i.m. injections. She then was given a maintainance dose of 15,000 I.U. per day.—When 5 years old the girl was admitted to the clinic *for the third time,* because of recurrence of her rickets, noted at a control examination at the out-patient department of the clinic. There was reason to assume that she had not received her prophylactic vitamin D treatment regularly. X-ray showed wide and frayed metaphyses, but these signs of rickets were less severe than before treatment at the age of 2 years.

After vitamin D had been given in a dosage of about 100,000 I.U. per day for some months the symptoms of rickets disappeared She was then given the same maintainance dosage as before. After ½–1 year the mother again ceased to give this dose of vitamin D, and instead cod liver oil was given in ordinary prophylactic dosage.—At 8 years of age the girl was admitted to the clinic *for the fourth time* because of pains in her legs. The examination showed marked deformation of both legs, and she was unwilling to stand on her legs. X-ray showed marked rickets. Her serum phosphorus was 3.6 mg per 100 ml, serum calcium 8.0 and alkaline phosphatases more than 50 King-Armstrong U. These values did not normalize and healing was not observed on X-ray before the dosage of vitamin D had been increased to 2,000,000 I.U. per day. This dose was, however, only given for a short time. The serum phosphorus then rose to 5.7 mg per 100 ml and serum calcium to 12.0 and the alkaline phosphatases decreased to 12 units. One Ba^{140} test was performed when the girl received 15,000 I.U. per day, and another during treatment with 2,000,000 I.U. vitamin D per day.

Case 17. (Cerebral tumor).—Woman, 25 years old, weight 60 kg, had always enjoyed good health. For 6 months before admittance she had been feeling tired and generally unwell. She then got headache, and developed parestesias in the right side of her body. X-ray revealed a hydrocephalus, caused by a tumor to the left of the posterior part of the third ventricle. There were no signs of skeletal engagement. The general condition of the patient was good during her stay at the clinic. Serum calcium and phosphorus values were within normal limits.

Case 18. (Normal adult).—Man, 32 years old, weight 80 kg. He has always been healthy and was in a good general condition at the time of the study. (This subject was one of the authors, G.B.).

PRINCIPLES OF COMPUTATION

See *Bauer, Carlsson* and *Lindquist* 1955 a for a detailed analysis of the principles involved.

The rate of bone salt formation (the accretion rate) and the size of the exchangeable fraction of the skeletal calcium were computed according to equation

$Ca^{45}_{Obs} = E \times S + A \times T \times S_M$, where

Ca^{45}_{Obs} = Total amount of Ca^{45} present in a calcified tissue;

E = Amount of Ca (Ca^{40} + Ca^{45}) in the exchangeable fraction of the bone salt;

S = specific activity of the serum (plasma) Ca;

A = Rate of Ca accretion;

T = interval of time between administration of Ca^{45} and observation;

S_M = average specific activity of serum Ca during this interval of time.

The equation can be used for calculating the accretion rate not only in different calcified tissues but also in the whole skeleton. In this calculation the whole body is treated in the same manner as a calcified tissue. Ca^{45}_{Obs} is then equal to retention of Ca^{45} in the body, *i.e.* 100 *minus* the percentage of dose lost via the kidneys and the gastrointestinal tract, and E is the amount of Ca present in the exchangeable fraction of the bone salt *plus* the amount of Ca of the fluid phase of the body.

The computation of the accretion rate was also carried out from data of the bone biopsy specimens according to *Bauer, Carlsson* and *Lindquist* (1955 b).

If in the equations used S is expressed in term of per cent of dose per gm calcium, and T in days, E will be expressed in grams of calcium and A in grams of calcium per day.

The Ba^{140} results were treated in exactly the same way as the Ca^{45} results. For both isotopes the blood activities were thus expressed as percentage of dose/gm of calcium.

Treatment of the data.

The serum specific activity values (S) necessary for solving the equations were obtained in the following way. In each patient the observed serum specific activity and the urine activity values (per cent of dose excreted per day) were plotted on a logarithmic coordinate against time (T) which was plotted on a Cartesian coordinate. It was found that the Ba^{140} serum specific activity values fitted a straight line from about 16 hours following administration of the isotope. Similarly the Ba^{140} urine activity values fitted a straight line from the 24 hour interval on. A curve was now drawn through the Ba^{140} serum specific activity values. The final slope of this curve (from about 18 hours following administration of the isotope) was chosen to fit as well as possible both urine and serum activity values. The S values used in the equations were then taken from this curve. Integration of this curve (determination of $T \times S_M$) was made by estimating the area under this curve.

The Ca^{45} data were treated in the same way. It was found that a final exponential was reached after about 30 hours following administration of the isotope. The Ca^{45} urinary specific activity values could be used for determinations of both slope and amplitude of the final exponential of the S curve.

In each patient the S curve was graphically analysed into three exponentials according to usual methods (*Sheppard* and *Householder,*

TABLE I

Accretion rate (A) and exchangeable fraction (E) of calcium in the entire body as computed from Ba^{140} data.

Subject	Age (years)	Body weight (kgm)	Rate constants (fraction/day)			Coefficients (% dose/Gm)			Exchangeable fraction (E) (Gm Ca)	Accretion rate (A) (Gm Ca/day)	Excretion (U) (Gm Ca/day)	Route of administration
			k_3	k_2	k_1	S_3	S_2	S_1				
13	1/12	4.3	0.898	9.23		46.5	305		1.10	0.37	0.615	i.m.
14	5/12	6.9	0.479	5.01		24.3	108	240	2.58	0.65	0.585	i.m.
3	9/12	10.0	0.659	5.21	41.5	33.3	73.0	520	2.18	0.94	0.452	i.m.
4	1 3/12	10.5	0.554	4.88	23.7	18.4	47.0	105	3.79	0.72	1.28	i.m.
15	1 6/12	12.9	0.445	4.87		7.75	54.0		6.92	1.06	2.02	i.m.
16	8	19.9	0.167	5.04	24.5	8.10	51.0	71.0	9.81	1.20	0.502	i.m.
„	„	„	0.308	5.04	26.6	2.98	14.5	55.0	21.8	5.67	1.05	i.m.
17	25	60	0.554	5.13		9.5	20.8		7.60	0.57	3.64	i.v.
18*	32	80	0.461	5.16	43.0	3.41	16.7	44.8	18.5	1.88	8.65	i.v.

* In case 18 the data permitted analysis of a fourth exponential ("K_0" = 474.0; "S_0" = 114) because of early sampling of serum.

Siri). This analysis makes for a convenient way of presenting the activity data (Table 1).

Owing to the rapid fall in blood activity over the comparatively long experimental periods studied, it was not deemed necessary to allow for individual variation in the intestinal lag in faecal output. This lag was therefore routinely regarded as two days, and the faecal output at Day T + 2 was considered to represent the intestinal excretion at Day T. The total excretion was therefore the sum of the urinary excretion at time T and the faecal excretion at time T + 2, T in these experiments usually being about 6–8 days. As excretion of activity is directly proportional to the value of $T \times S_M$, the values for total excretion at intervals before time T were computed from the corresponding value at time T.

When solving the equations usually two intervals between 5 and 10 days were used.

From the values for the excretion of urine and faeces ($Excr_{tot}$) and from the curve of the serum specific activity, the excretory rate (U) was calculated from the relation

$$U = \frac{Excr_{tot}}{T \times S_M}$$

In the equation T is expressed in days and S_M in per cent of dose per gm calcium. U will then be expressed in grams of calcium per day.

RESULT

In the present investigation Ca^{45} was given to four patients in addition to the Ba^{140} (Cases 13, 14, 15 and 17). The Ca^{45} results are described in detail in another publication (*Bauer, Carlsson* and *Lindquist* 1957 a).

Blood activities. In Fig. 1 the S values of serum of a representative case (Case 17) have been plotted against time on a semilogarithmic paper.

It is seen how the Ba^{140} values were lower than the Ca^{45} values. Consequently, $T \times S_M$ was constantly lower for Ba than for Ca. The blood activity curves of Ca^{45} and Ba^{140} are thus related to each other in a similar manner in man as has previously been found in rats (*Bauer, Carlsson* and *Lindquist* 1956 b).

Immediately following injection of the isotopes, the specific activity of both rapidly declined. After this rapid fall there was a slower exponential decline. For the Ba^{140} data this "final" exponential (k_3) adequately described the fall in blood activity from an interval of about

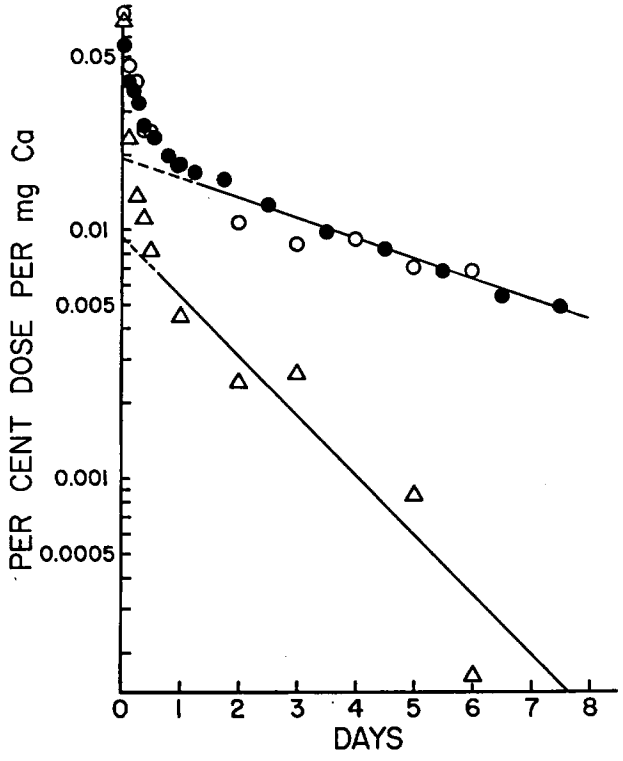

Fig. 1.

Specific activity of serum (urine) Ca and serum Ba in one of the subjects (Case 17) plotted on a logarithmic scale against time.

Note: For both curves the values are expressed in percentage of dose per mg of Ca.

Symbols: ○ serum Ca^{45} values
● urine „ „
△ serum Ba^{140} „

0.6 days, the interval being a little shorter for the smallest infants. The preceding exponential (k_2) was drawn from about 0.14 days. The brake between the exponentials computed from the Ca^{45} data was obtained at a longer time interval after the administration of the isotope, the corresponding values being 1.0 and 0.20 days.

The fractional rate constants were throughout higher for Ba^{140} than for Ca^{45}.

In the subject with resistant rickets (Case 16) the two initial rate constants (k_1 and k_2) were practically the same before and after treatment with vitamin D. These values were also in good agreement with corresponding values of the other subjects. Before treatment the slope of the "final" exponential (k_3) had the lowest value of the whole series

TABLE II

Accretion rate (A) of calcium in the entire skeleton and in a bone biopsy specimen measured by concurrent use of Ba^{140} and Ca^{45}.

Subject	Age (years)	Weight (kg)	Whole skeleton (Gm Ca per day)			Bone sample* (Gm Ca per day per Gm Ca of bone sample)		
			Calculated from		Ratio	Calculated from		Ratio
			Ca^{45}	Ba^{140}	Ba^{140}/Ca^{45}	Ca^{45}	Ba^{140}	Ba^{140}/Ca^{45}
13	1/12	4.3	0.28	0.37	1.3	.00444	.00727	1.6
14	5/12	6.9	0.37	0.65	1.8	.00777	.0126	1.6
						.0159**	.0233**	1.5
15	1 6/12	12.9	0.54	1.06	2.0	.00593	.0144	2.4
17	25	60	0.47	0.57	1.3	–	–	–

* The specimens consisted of compact bone except one of the specimens of Case 14.

** The specimen consisted of spongy bone.

(0.167). After treatment it increased to 0.308, even this a low value. It should be pointed out, however, that the slope of this final exponential is determined not only by the accretion rate but also by the excretory rate.

Excretion. The values for the excretion rate were considerably higher in the two adults than in the children. Furthermore, the values of the excretion rate were higher for Ba^{140} than for Ca^{45} which is in agreement with our earlier findings in rats.

Retention. As a consequence of the higher excretion of Ba^{140}, the retention of this isotope in the whole body and in the calcified tissues was lower than that of Ca^{45}.

Accretion rate. The values for the accretion rate are higher when calculated from the Ba^{140} than from the Ca^{45} data (cf. *Bauer, Carlsson* and *Lindquist* 1957 a), the values being about 0.75 for the smaller children and 0.57 and 1.88 for the two adults, expressed as grams of calcium per day. In Table II are presented the accretion values of the four subjects, who were concurrently given Ba^{140} and Ca^{45}. In three children (Cases 13 through 15) bone biopsy specimens were also analysed. The mean value of the accretion rate for the compact bone calculated from the Ca^{45} data of the bone samples was 0.006, expressed as gm calcium per day per gm calcium of bone sample. In case 14 an analysis was also carried out on spongy bone. The accretion rate computed from the Ca^{45} data as well as from the Ba^{140} data was about twice that of the compact bone.

The relation between the values for the accretion rate computed from the Ba^{140} and Ca^{45} data (Table II, ratio Ba^{140}/Ca^{45}) for the three abovementioned children (cases 13 through 15) was 1.3, 1.8 and 2.0, respectively, when calculated for the entire skeleton as compared to values of 1.6, 1.6, and 2.4, respectively, when calculated for the compact bone of the bone samples. The ratio Ba^{140}/Ca^{45} thus was about the same when determined with either of these techniques. In case 17 the ratio was 1.3. No bone sample was taken in this case.

In a previous paper on the metabolism of Ba^{140} and Ca^{45} in rats (*Bauer, Carlsson* and *Lindquist* 1956 b) the ratio Ba^{140}/Ca^{45} was 2.2 when calculated for the entire skeleton and 1.9 when calculated for the tibia shafts. The ratio would thus possibly be somewhat lower in humans than in rats. It seems certain, however, that even in humans Ba^{140} is incorporated into the skeleton at a faster rate than is Ca^{45}.

In the patient with resistant rickets (Case 16) the value of the accretion rate before treatment was 1.20 and after treatment 5.7 gm Ca

per day. Treament with massive doses of vitamin D thus enhanced the accretion rate about fivefold.

Exchangeable fraction. In the previous investigation in rats practically the same values for the size of the exchangeable fraction (E) of calcium were obtained from the Ba^{140} data as from the Ca^{45} data. In the four cases of the present series who received Ba^{140} and Ca^{45} simultaneously, the size of the exchangeable fraction appeared about twice as high when calculated from the Ba^{140} data as when calculated from the Ca^{45} data.

DISCUSSION

The results of the present investigation indicate that even in humans the skeletal metabolism of Ba^{140} closely parallells that of calcium. Ba^{140} may consequently be used as a tool for studies of skeletal metabolism. This is particularly evident in the case of resistant rickets (Case 16) in which the enhanced rate of bone salt formation induced by vitamin D was accompanied by a rise in the accretion rate value calculated from the Ba^{140} data. The values of the accretion rate are higher when computed from Ba^{140} data than when computed from Ca^{45} data. When using Ba^{140} in studies of skeletal metabolism it does not seem necessary, however, to transform the actual results to values corresponding to those which would have been obtained by calcium isotopes. Ba^{140} results would probably furnish information of i.a. clinical importance when eventually a large enough normal material will be available.

In earlier studies of bone salt metabolism in resistant rickets by means of P^{32} it was shown that the accretion rate was initially almost normal but rose after treatment with massive doses of vitamin D to values significantly higher than normal. The results obtained by Ba^{140} in the case of resistant rickets in the present investigation support this finding, the accretion rate before treatment being about the same as in the normal children (1.20 gm Ca per day), and after treatment with massive doses of vitamin D about five times this value.

SUMMARY

The metabolism of Ba^{140} has been studied in seven subjects with normal skeletal metabolism and in one subject with vitamin D resistant rickets by serial sampling of serum, urine and stools over a 7 to 14 day period following parenteral administration of Ba^{140} (half life 12.8 days).

The values of the accretion rate of bone salt calculated from Ba^{140}

data were higher than those calculated from Ca^{45} data under the same experimental conditions.

In the case with vitamin D resistant rickets the accretion rate of bone salt as calculated from the Ba^{140} data was probably normal. After treatment with massive doses of vitamin D the accretion rate rose to values significantly higher than normal.

Since there seems to be no fundamental difference in the metabolism of Ba^{140} and Ca^{45}, Ba^{140} should be suitable for use as an indicator of skeletal metabolism in humans.

RESUME

Le métabolisme de Ba^{140} a été étudié chez sept sujets dont le métabolisme osseux était normal et chez un sujet souffrant de rachitisme résistant aux vitamines D, au moyen d'examens d'une série d'échantillons de sang, d'urine et de selles sur une période variant entre 7 et 14 jours, après administration parentérale de Ba^{140}. On a constaté que la valeur du taux d'accrétion du sel osseux, calculé sur le base Ba^{140} était plus élevée que celle calculés sur la base Ca^{45}, dans les mêmes conditions expérimentales.

Dans le cas de rachitisme résistant aux vitamines D, le taux d'accrétion du sel osseux, calculé sur la base Ba^{140} était probablement normal. Après un traitement avec des doses massives de vitamines D, le taux d'accrétion s'est élevé à des valeurs sensiblement supérieures à la donnée normale.

Etant donné qu'il ne paraît pas y avoir de différence fondamentale dans le métabolisme de Ba^{140} et Ca^{45}, Ba^{140} paraît susceptible d'être utilisé comme l'indicateur des données du métabolisme osseux chez l'homme.

ZUSAMMENFASSUNG

Der Stoffwechsel von Ba^{140} wurde in sieben Personen mit normalem Skelettstoffwechsel und in einer Person mit D-Vitamin resistenter Rachitis mittels Reihenproben von Serum, Urin und Stuhl für eine Periode von 7 bis 14 Tagen nach parenteraler Einverleibung von Ba^{140}, (Halbwertzeit 12.8 Tage) untersucht.

Die Werte der Einlagerungsgeschwindigkeit von Knochensalzen, errechnet auf Grund der Ba^{140} Daten waren grösser als diejenigen welche von den Ca^{45} Daten unter gleichen experimentellen Bedingungen erhalten wurden.

In dem Fall mit D-Vitamin resistenter Rachitis war die Einlagerungsgeschwindigkeit von Knochensalzen errechnet aus den Ba^{140} Daten

wahrscheinlich normal. Nach Behandlung mit massiven Dosen von Vitamin D stieg die Einlagerungsgeschwindigkeit zu Werten, die bedeutend höher als normal lagen.

Da keine wesentliche Verschiedenheit im Stoffwechsel von Ba^{140} und Ca^{45} zu bestehen scheint, sollte Ba^{140} als ein Indikator des Skelettstoffwechsels beim Menschen verwendbar sein.

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REFERENCES

Bauer, G. C. H., Carlsson, A. and *Lindquist, B.:* Evaluation of accretion, resorption, and exchange reactions in the skeleton.—Kungl. Fysiograf. Sällsk. Förhandl. (Lund) *25*: Nr. 1, 1955 a.

– – – Bone salt formation measured in infants by means of P^{32}.—Acta paediat. *44*: 477, 1955 b.

– – – Bone salt metabolism in human rickets studied with radioactive phosphorus.—Metabolism *5*: 573, 1956 a.

– – – A comparative study on the metabolism of Ba^{140} and Ca^{45} in rats. Biochem. J. *63*: 535, 1956 b.

– – – Bone salt metabolism in humans studied by means of Ca^{45}, 1957 a (to be published).

– – – Use of isotopes in clinical studies of skeletal metabolism, 1957 b (to be published).

Bauer, G. C. H. and *Ray, R.:* Kinetics of strontium metabolism in man.—J. Bone and Joint Surg. *39-A*, 1957 (in press).

Bronner, F., Harris, R. S., Maletskos, C. J. and *Benda, C. E.:* Studies in calcium metabolism. The fate of intravenously injected radiocalcium in human beings. —J. Clin. Invest. *35*: 78, 1956.

Carlsson, A.: Metabolism of radiocalcium in relation to calcium intake young rats.— Acta Pharmacol. et toxicol. *7*: suppl. 1, 1951.

Clark, E. P. and *Collip, J. B.:* A study of the Tisdall method for the determination of blood serum calcium with a suggested modification.—J. Biol. Crem. *63*: 461, 1925.

Krane, S. M., Brownell, G. L., Stanbury, J. B. and *Corrigan, H.:* The effect of thyroid disease on calcium metabolism in man.—J. Clin. Invest. *35*: 874, 1956.

Sheppard, C. W. and *Householder, A. S.:* The mathematical bases of the interpretation of tracer experiments in closed steady-state systems.—J. Appl. Physics *22*: 510, 1951.

Siri, W. E.: Theory of tracer methods *in* Isotopic Tracers and Nuclear Reactions. York, Pa. 1949, p. 392.

Youngburg, C. E. and *Youngburg, M. V.:* Phosphorus metabolism. I. A system of blood phosphorus analysis.—J. Lab. & Clin. Med. *16*: 156, 1930.