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Biochem. J. (1963) **87**, 612

Comparative Studies of the Metabolism of Strontium and Barium in the Rat

BY P. H. BLIGH AND D. M. TAYLOR

Department of Physics, Institute of Cancer Research: Royal Cancer Hospital, London, S.W. 3

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Although the alkaline-earth metals calcium, strontium and barium follow, in general, similar metabolic pathways, there are important quantitative differences in their metabolic behaviour. In recent years the comparative metabolism of calcium and strontium has been widely studied but relatively little attention has been paid to barium.

Bauer, Carlsson & Lindquist (1956) have studied the comparative metabolism of ^{45}Ca and ^{140}Ba in rats during the first 48 hr. after intraperitoneal injection, and have shown that the clearance of ^{140}Ba from the plasma by skeletal accretion is about twice that of ^{45}Ca , but that the overall re-

tention of ^{140}Ba in the skeleton is less than that of ^{45}Ca . Similar observations have also been made in human subjects (Bauer, Carlsson & Lindquist, 1957). In contrast with bone, however, there is little information available on the turnover of barium in soft tissues.

In the present paper the results of some comparative studies of the metabolism of strontium and barium in the femur, teeth and some soft tissues of young and old rats are reported. To reduce biological variation as far as possible the behaviour of ^{85}Sr and ^{140}Ba has been directly compared in the same animal after the simultaneous administration of ^{85}Sr and ^{140}Ba .

EXPERIMENTAL

Animals. The animals used were female rats of the highly-inbred brown-hooded August strain, maintained throughout on M.R.C. diet no. 41B, both food and water being allowed *ad libitum*. The rats were aged either 6–8 weeks or 13–15 months at the beginning of each experiment. The older animals had borne several litters of young before being used in the experiment.

Radioactive material. Carrier-free $^{140}\text{BaCl}_2$ in dilute HCl was obtained from The Radiochemical Centre, Amersham, Bucks. $^{85}\text{SrCl}_2$ was prepared as a carrier-free solution in HCl from RbCl bombarded with deuterons in the M.R.C. cyclotron at Hammersmith Hospital (Overstreet, Jacobson, Scott & Hamilton, 1951).

Animal experiments. Fifty animals aged 6–8 weeks and 56 aged 13–15 months were each given 20–80 μC of $^{140}\text{BaCl}_2$ and 2–8 μC of $^{85}\text{SrCl}_2$ by injection, into a lateral tail vein, of 0.2–0.5 ml. of a solution of the two carrier-free radioactive compounds in 0.01N-HCl.

The animals in each of the two groups were killed, in pairs by exsanguination under ether anaesthesia, at intervals over a period of 80 days after injection.

The femora, molar and incisor teeth, liver, lungs, submaxillary glands and a sample of skeletal muscle were removed for assay of their radioactivity.

Preparation of samples and radioactive assay. All samples were weighed immediately after removal. Samples of soft tissues were ashed overnight at 550° in silica crucibles in a muffle furnace, and the resulting ash was dissolved in 5 ml. of 3N-HCl for assay of the radioactivity.

The femora were gently scraped to remove adherent muscle and marrow. The femora were then divided into proximal, distal and shaft regions by cutting the bone transversely about one-quarter of its length from each end. The parts of the femur and the bones and teeth were each dissolved in 5 ml. of 6N-HCl.

The activity due to ^{85}Sr and ^{140}Ba in each sample was determined by γ -scintillation counting by the method described by Taylor, Bligh & Duggan (1962).

To allow ready comparison of the results obtained from animals of widely differing age and weight all results are expressed as the 'percentage of the injected activity/g. wet wt. of tissue/100 g. body wt.'.

Determination of calcium. The total calcium content in the solutions of soft-tissue ash was determined by precipitation as calcium oxalate followed by titration with standard KMnO_4 (Cumming & Kay, 1945). The calcium contents of solutions of bones and teeth were determined by the addition of an excess of standard EDTA solution followed by back-titration with MgSO_4 solution (Schwarz-enzbach, 1957).

RESULTS AND DISCUSSION

Bone. The data on the uptake and retention of ^{140}Ba in the three parts of the femur (Fig. 1) indicate that the highest concentrations of ^{140}Ba are found in the distal region and the lowest in the shaft. This order of uptake would be expected since, particularly in the young animal, the distal region contains the most active areas of bone growth and remodelling.

In the older animals 60–80% of the ^{140}Ba initially deposited is removed from all three regions of the femur during the first 14 days after injection. In the young animals, however, this rapid removal of ^{140}Ba is seen only in the distal region, the loss of activity from the proximal region being much less, and little if any from the femur shaft.

Comparison of the ^{85}Sr : ^{140}Ba ratios (Table 1) shows that, except at very short times after injection and in the femur shaft of the young animal, the percentage uptake of ^{140}Ba is generally greater than that of ^{85}Sr . A similar comparison of these ratios with the ^{85}Sr : ^{45}Ca ratios measured under similar conditions (Table 1) shows that the uptake of ^{140}Ba is always less than that of ^{45}Ca , except for the shortest time-intervals. In the old rats the maximum concentration of ^{140}Ba in all three parts of the femur is only about one-half of that found in the young animals, and the uptake of ^{85}Sr appears to be reduced even further.

The ^{85}Sr is removed more rapidly than ^{140}Ba from the proximal and distal ends of the femur during the first few days after injection, but thereafter the ^{85}Sr : ^{140}Ba ratios do not change significantly.

The mechanisms by which barium is deposited in bone are little understood, but its general pattern of uptake shows some similarities to that of calcium and strontium. Calcium is deposited in bone by an initial rapid exchange with Ca^{2+} ions in the exchangeable fraction of the bone salt, followed by a slower transfer of part of the material into the non-exchangeable fraction. The greater retention of ^{45}Ca in bone as compared with the radioactive isotopes of strontium has been explained largely by the fact that the urinary excretion of strontium is greater than that of calcium (McDonald, Lorick & Petriello, 1957). However, Likins, Posner, Kunde & Craven (1959) have suggested that some strontium may also be released preferentially from bone as a result of the partial elimination of the larger Sr^{2+} ion during recrystallization of calcium hydroxyapatite in the bone.

The excretion of ^{85}Sr and ^{140}Ba by this strain of rat has been studied by Bligh (1960), who showed that over a period of 21 days after intravenous injection the urinary excretion of ^{85}Sr was greater than that of ^{140}Ba by a factor of about 1.9 in the young animal and about 1.4 in the older rat. The total excretion of ^{85}Sr and ^{140}Ba over this period was closely similar. The old rats, however, excreted about twice as much as the young ones. These differences between the urinary excretion of ^{85}Sr and ^{140}Ba are much less than the corresponding differences that have been observed with ^{45}Ca and ^{85}Sr or ^{89}Sr (McDonald *et al.* 1957; Bligh, 1960),

and they do not appear to be large enough to explain completely the observed differences between the retention of ^{85}Sr and ^{140}Ba in bone, particularly in the older animals. Since the Ba^{2+} ion is larger than the Sr^{2+} ion (ionic radii: Ca^{2+} , 0.99 Å; Sr^{2+} , 1.13 Å; Ba^{2+} , 1.35 Å), it seems likely that, if the suggestion of Likins *et al.* (1959) is correct, barium would be released more readily than strontium during recrystallization of the hydroxyapatite. To explain the greater retention of ^{140}Ba in bone, therefore, it seems necessary to suggest that some additional mechanism may also be involved in the deposition of barium in bone. It has been shown by Schubert & Conn (1949) that tracer amounts of $^{140}\text{Ba}^{2+}$ ions in solution may react with SO_4^{2-} ions to form a radiocolloid even though the total concentration of the ions may be insufficient to exceed the normal solubility product of barium sulphate. If this phenomenon also occurs *in vivo*, perhaps by reaction of Ba^{2+} with PO_4^{3-} ions, it seems likely that some of the ^{140}Ba

might be deposited in bone by adsorption of colloidal particles on to the bone surfaces and this process might not be solely confined to surfaces that are actively calcifying. A similar type of mechanism has been suggested for the deposition of rare-earth elements in bone by Jowsey, Rowland & Marshall (1958).

Some support for this suggested mechanism is found in the observations of Bauer *et al.* (1956) that, in the rat, the accretion rate of ^{140}Ba is about twice that of ^{45}Ca , and that ^{140}Ba is more rapidly transferred from the exchangeable to the non-exchangeable fraction of the bone salt. These observations appear to be consistent with the hypothesis that the barium is deposited in bone partly by ionic exchange with calcium at actively calcifying surfaces and partly by the rapid and more irreversible process of surface adsorption.

This hypothesis offers an explanation of the observation that in old animals the uptake of ^{85}Sr is reduced to a greater extent than that of ^{140}Ba .

Fig. 1. Variation, with time after injection, of the concentration of ^{140}Ba in the proximal (Δ , $\blacktriangle$), distal ($\circ$, $\bullet$) and shaft ($\square$, $\blacksquare$) regions of the rat femur. Δ , $\circ$, $\square$, Young rats (aged 6–8 weeks); $\blacktriangle$, $\bullet$, $\blacksquare$, old rats (aged 13 months). Experimental details are given in the text.

Table 1. *Relative concentrations of ^{45}Ca , ^{85}Sr and ^{140}Ba in three parts of the femur of young and old rats at various times after intravenous injection*
 Experimental details are given in the text. Young rats were aged 6-8 weeks and old rats 13 months. The ^{85}Sr : ^{45}Ca ratios were obtained by Van Cleave & Kaylor (1958) for young rats and by D. M. Taylor (unpublished work) for old rats.

Time after injection	Distal end						Shaft						Proximal end					
	Young rats			Old rats			Young rats			Old rats			Young rats			Old rats		
	^{85}Sr : ^{140}Ba ratio	^{85}Sr : ^{45}Ca ratio	^{85}Sr : ^{140}Ba ratio	^{85}Sr : ^{45}Ca ratio	^{85}Sr : ^{140}Ba ratio	^{85}Sr : ^{45}Ca ratio	^{85}Sr : ^{140}Ba ratio	^{85}Sr : ^{45}Ca ratio	^{85}Sr : ^{140}Ba ratio	^{85}Sr : ^{45}Ca ratio	^{85}Sr : ^{140}Ba ratio	^{85}Sr : ^{45}Ca ratio	^{85}Sr : ^{140}Ba ratio	^{85}Sr : ^{45}Ca ratio	^{85}Sr : ^{140}Ba ratio	^{85}Sr : ^{45}Ca ratio	^{85}Sr : ^{140}Ba ratio	^{85}Sr : ^{45}Ca ratio
8 min.	1.09	—	0.88	1.39	0.93	1.13	—	—	0.82	1.33	1.24	1.00	0.82	1.11	0.82	1.11	—	—
0.5 hr.	1.23	0.90	0.79	0.93	—	1.06	1.16	—	0.72	1.20	1.23	0.90	0.76	1.39	0.76	1.39	—	—
3 hr.	1.05	0.69	0.88	0.98	—	1.07	0.96	—	0.86	0.94	1.15	0.91	0.90	0.90	0.91	0.90	—	—
8 hr.	0.97	0.59	0.76	—	—	1.17	0.98	—	0.79	—	1.05	0.41	0.81	—	0.81	—	—	—
20 hr.	0.92	0.58	0.70	0.64	—	1.08	0.84	—	0.90	0.69	0.99	0.44	0.73	0.56	0.73	0.56	—	—
40 hr.	0.89	0.49	0.60	—	—	1.12	0.67	—	0.74	—	1.04	0.33	0.80	—	0.80	—	—	—
5 days	0.87	—	0.58	—	—	1.14	—	—	0.75	—	1.00	—	0.61	—	0.61	—	—	—
14 days	0.83	—	0.59	—	—	1.07	—	—	0.61	—	1.01	—	0.53	—	0.53	—	—	—
28 days	0.87	—	0.62	—	—	1.12	—	—	0.64	—	0.96	—	0.62	—	0.62	—	—	—
50 days	0.76	—	0.59	—	—	1.01	—	—	0.62	—	0.87	—	0.63	—	0.63	—	—	—
80 days	0.74	—	0.59	—	—	1.00	—	—	0.61	—	0.86	—	0.61	—	0.61	—	—	—

In older animals growth and remodelling of bone proceed at a much lower rate, and the larger and more compact crystals that are found in older bone leave a smaller surface area available for reactions. Thus, if ^{140}Ba is deposited partly by surface adsorption and partly by exchange with Ca^{2+} ions at calcifying surfaces, it might be expected that its uptake would be greater than that of ^{85}Sr which is taken up mainly by exchange processes.

Teeth. The concentrations of ^{85}Sr and ^{140}Ba found in the molar and incisor teeth (Table 2) also show marked differences with age. The incisor teeth, which are in a state of continuous eruption throughout the life of the rat, accumulate both ^{140}Ba and ^{85}Sr during the first 5 days after injection and thereafter the concentrations of both ^{85}Sr and ^{140}Ba decrease. The teeth of the older animal take up about twice as much activity as those of the young animal and in both age groups the uptake of ^{85}Sr is greater than that of ^{140}Ba . Unlike bone, teeth do not undergo resorption and remodelling and, except in the molars of the older animals, there is no initial rapid loss of activity from the teeth.

In both young and old animals the activity in the incisor teeth falls slowly between 5 and 28 days after injection and then falls much more rapidly. The later more rapid decrease probably represents loss due to attrition at the grinding surfaces of the teeth. The rate of eruption of the lower incisor teeth of the rat is about 2.8 mm./week (Schour & Massler, 1949) and the length of the calcified part of the teeth in our animals is about 15 mm. If the ^{85}Sr and ^{140}Ba are predominantly deposited in the actively calcifying region of the teeth it would, therefore, take about 5 weeks for the major part of the activity to begin to reach the grinding surfaces.

In the molar teeth the uptake of both ^{85}Sr and ^{140}Ba is more rapid than in the incisor and the maximum activity is attained about 8 hr. after injection. The amount of ^{85}Sr and ^{140}Ba taken up by the molars is similar in both young and old animals. However, in the young animals the concentration does not change appreciably between 20 hr. and 80 days after injection, whereas in the old rat the concentration falls between 8 hr. and 28 days after injection and then shows little further change.

The retention of ^{85}Sr and ^{140}Ba in the molars of the young animal presumably results from the fact that at this age the teeth are not fully calcified and most of the activity initially deposited is rapidly incorporated into the permanent teeth. In the older animal the situation is more complex and about 70% of the activity initially deposited is removed between 8 hr. and 28 days after injection. Thereafter the activity remains more or less constant, suggesting that the residual ^{85}Sr and ^{140}Ba is firmly fixed in the tooth. Some incorpora-

tion of activity into the permanent tooth structure would be expected as even in the adult rat the molar teeth are still slowly erupting (Schour & Massler, 1949).

Soft tissues. The results given in Tables 3 and 4 for the concentration of ^{140}Ba and the $^{85}\text{Sr}:^{140}\text{Ba}$ ratios in liver, lung, muscle, submaxillary gland and blood serum show that the greatest activity occurs in the samples taken 10 min. after injection and that thereafter the activity of all the tissues falls roughly in parallel with that of the blood serum.

In both young and old animals the highest concentrations of ^{85}Sr and ^{140}Ba are found in the submaxillary glands and lungs. Comparison of the data for the calcium concentration in the various tissues (Table 5) with the corresponding concentrations of ^{140}Ba shows that the uptake is highest in those tissues having the highest calcium concentration. Except in the submaxillary gland, the concentration of ^{85}Sr always exceeds that of ^{140}Ba .

The submaxillary gland is the only one of the tissues studied in which the 'specific activity',

defined as the percentage of the injected activity of ^{140}Ba (or of ^{85}Sr)/g. of Ca, rises to exceed that of the blood serum. Dreisbach (1957, 1959) has shown that rat submaxillary glands also accumulate ^{45}Ca and ^{85}Sr , and (Dreisbach, 1962) has also shown that *in vitro* rat submaxillary-gland slices bind three times as much calcium as do serum proteins at the same ionic strength. Schachter, Dowdle & Schenker (1960) have shown that the accumulation of calcium by the submaxillary gland is not an active process dependent on oxidative phosphorylation, such as that found in the small intestine. It therefore seems unlikely that the uptake of barium or strontium is an active process.

The higher uptake of ^{140}Ba than ^{85}Sr in the submaxillary gland may be due to barium's being bound more readily than strontium by the substances that bind calcium. However, since for many amino acids and other metal-ion-binding agents the stability constants decrease in the order Ca^{2+} , Sr^{2+} , Ba^{2+} , it seems likely that some other factor or factors are involved. As with bone it appears possible that the deposition in the sub-

Table 2. Concentration of ^{140}Ba and the $^{85}\text{Sr}:^{140}\text{Ba}$ ratio in the molar and incisor teeth of young and old rats at various times after intravenous injection

Experimental details are given in the text. Young rats were aged 6–8 weeks and old rats 13 months.

Time after injection	Concn. of ^{140}Ba (% of injected activity/g. wet wt./100 g. body wt.)				$^{85}\text{Sr}:^{140}\text{Ba}$ ratio			
	Incisors		Molars		Incisors		Molars	
	Young rats	Old rats	Young rats	Old rats	Young rats	Old rats	Young rats	Old rats
10 min.	3.24	3.00	3.13	2.30	1.12	1.10	0.96	0.87
30 min.	6.20	2.87	5.37	1.96	1.16	0.96	0.98	0.76
3 hr.	7.45	8.93	5.97	4.93	1.30	1.33	1.02	1.01
8 hr.	7.40	11.70	6.22	5.57	1.26	1.27	0.92	0.77
20 hr.	6.60	12.70	5.27	5.39	1.47	1.46	1.02	0.80
40 hr.	8.14	15.00	5.39	3.60	1.50	1.50	0.92	0.99
5 days	9.60	17.17	5.98	2.62	1.54	1.52	0.99	0.90
14 days	8.41	16.53	5.37	2.29	1.55	1.40	0.95	0.61
28 days	7.96	15.01	5.47	1.58	1.72	1.54	0.91	0.57
50 days	2.27	5.84	5.54	1.87	1.53	1.29	0.81	0.45
80 days	0.88	1.08	5.25	1.59	1.42	0.69	0.91	0.51

Table 3. Concentration of ^{140}Ba in tissues of young and old rats at various times after intravenous injection

Experimental details are given in the text. Young rats were aged 6–8 weeks and old rats 13 months.

Time after injection	Concn. of ^{140}Ba (% of injected activity/g. wet wt./100 g. body wt.)									
	Muscle		Liver		Lungs		Submaxillary gland		Blood serum	
	Young rats	Old rats	Young rats	Old rats	Young rats	Old rats	Young rats	Old rats	Young rats	Old rats
10 min.	0.40	0.36	0.44	0.68	1.09	2.08	1.44	3.35	2.00	—
0.5 hr.	0.20	0.28	0.23	0.48	0.53	1.09	1.62	2.23	0.67	—
3 hr.	0.08	0.16	0.025	0.13	0.085	0.55	0.44	2.04	0.073	—
8 hr.	0.031	0.058	0.014	0.058	0.054	0.23	0.51	0.89	0.036	0.13
20 hr.	—	0.012	0.005	0.027	0.038	0.10	0.14	0.59	0.012	—
40 hr.	—	0.0053	0.003	0.012	0.018	0.065	0.060	0.30	0.0066	—
5 days	—	0.0012	0.004	0.007	0.013	0.050	0.022	0.12	0.0043	0.0096
14 days	—	0.0005	—	0.002	—	0.011	—	0.017	0.0020	0.0024

Table 4. ⁸⁵Sr:¹⁴⁰Ba and ⁸⁵Sr:⁴⁵Ca ratios in tissues of young and old rats at various times after intravenous injection

Experimental details are given in the text. Young rats were aged 6-8 weeks and old rats 13 months. The ⁸⁵Sr:⁴⁵Ca ratios for the liver of young rats were obtained by D. M. Taylor (unpublished work), and for the submaxillary gland of young rats by Dreisbach (1959).

Time after injection	Muscle				Liver				Lungs				Submaxillary gland				Blood serum	
	Young rats		Old rats		Young rats		Old rats		Young rats		Old rats		Young rats		Old rats		Young rats	Old rats
	⁸⁵ Sr: ¹⁴⁰ Ba ratio		⁸⁵ Sr: ¹⁴⁰ Ba ratio		⁸⁵ Sr: ¹⁴⁰ Ba ratio		⁸⁵ Sr: ¹⁴⁰ Ba ratio		⁸⁵ Sr: ¹⁴⁰ Ba ratio		⁸⁵ Sr: ¹⁴⁰ Ba ratio		⁸⁵ Sr: ¹⁴⁰ Ba ratio		⁸⁵ Sr: ¹⁴⁰ Ba ratio		⁸⁵ Sr: ¹⁴⁰ Ba ratio	⁸⁵ Sr: ¹⁴⁰ Ba ratio
	1-11	1-37	1-16	0-77	1-13	1-34	1-16	0-53	0-53	0-76	0-26	1-19	0-26	0-76	0-26	1-19	—	—
10 min.	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—
0-5 hr.	1-41	1-30	1-89	0-75	1-29	1-53	1-42	0-28	0-28	0-44	0-24	1-82	0-24	0-44	0-24	1-82	—	—
3 hr.	1-91	2-08	2-83	0-73	2-13	1-70	1-63	1-03	1-03	0-36	0-42	3-24	0-42	0-36	0-42	3-24	—	—
8 hr.	3-63	4-18	3-63	0-60	3-96	1-97	1-73	0-76	0-76	0-33	0-80	3-59	0-80	0-33	0-80	3-59	—	—
20 hr.	—	4-73	4-90	0-52	6-21	2-16	1-25	0-58	0-58	0-21	0-46	3-86	0-46	0-21	0-46	3-86	—	—
40 hr.	—	4-18	6-30	1-16	7-06	1-88	0-72	0-36	0-36	—	0-36	2-62	0-36	—	0-36	2-62	—	—
5 days	—	3-77	—	—	9-03	—	1-00	0-92	0-92	—	0-62	—	0-62	—	0-62	—	1-75	—
14 days	—	16-0	—	—	19-7	—	1-52	—	—	—	3-63	—	—	—	3-63	—	1-94	—

Table 5. Concentration of calcium in tissues of young and old rats

Experimental details are given in the text. Young rats were aged 6-8 weeks and old rats 13 months. The results for muscle were obtained by Hansard & Crowder (1957). Other results are given as means $\pm$ S.D. of six observations.

Tissue	Concn. of Ca (mg./g. wet wt.)	
	Young rats	Old rats
Submaxillary gland	0.49 $\pm$ 0.16	0.27 $\pm$ 0.05
Lung	0.09 $\pm$ 0.04	0.22 $\pm$ 0.06
Liver	0.04 $\pm$ 0.01	0.03 $\pm$ 0.02
Plasma	0.07 $\pm$ 0.02	0.06 $\pm$ 0.01
Muscle	0.08	0.08 $\pm$ 0.03
Teeth		
Molars	198 $\pm$ 5	216 $\pm$ 8
Incisors	218 $\pm$ 16	233 $\pm$ 14
Femur		
Proximal end	121 $\pm$ 9	173 $\pm$ 12
Shaft	163 $\pm$ 17	227 $\pm$ 16
Distal end	99 $\pm$ 8	152 $\pm$ 11

maxillary gland may be influenced by the physical state of the ¹⁴⁰Ba in the body fluids. Studies of the transfer of ⁸⁵Sr and ¹⁴⁰Ba from mother to offspring through the milk (Bligh, 1960) have shown that more ¹⁴⁰Ba than ⁸⁵Sr is secreted in the milk, thus suggesting that the mammary gland also takes up more ¹⁴⁰Ba than ⁸⁵Sr.

In all the soft tissues studied the major effect of the age of the animal is that in the older animals the concentration of both ⁸⁵Sr and ¹⁴⁰Ba is higher than in the young animal. This is presumably a reflexion of the decreased uptake of ⁸⁵Sr and ¹⁴⁰Ba in bone, and of the increased concentrations of calcium in the tissues of the aging animal.

SUMMARY

1. The comparative metabolism of ⁸⁵Sr and ¹⁴⁰Ba has been studied in the ends and shaft of the femur, in the molar and incisor teeth, and in the serum, liver, lungs, muscle and submaxillary gland of rats aged 6-8 weeks and 15 months by using double-tracer techniques.

2. In bone the uptake of both ⁸⁵Sr and ¹⁴⁰Ba decreases with age, and more ¹⁴⁰Ba than ⁸⁵Sr is retained. It is suggested that this may be due to deposition of ¹⁴⁰Ba by surface adsorption as well as by exchange.

3. Both ⁸⁵Sr and ¹⁴⁰Ba are taken up by the incisor teeth of young and old rats, the uptake in the old animal being about twice that of the young rat. In molar teeth the uptakes of both ⁸⁵Sr and ¹⁴⁰Ba are similar in old and young animals, but in the old animal both are rapidly removed from these teeth, in contrast with the young animal where retention is prolonged.

4. After intravenous injection the concentrations of ^{85}Sr and ^{140}Ba in the soft tissues closely follow those in the blood, and except in the submaxillary gland the $^{85}\text{Sr} : ^{140}\text{Ba}$ ratio is always greater than 1. The submaxillary gland concentrates both ^{85}Sr and ^{140}Ba from the serum, but the concentration of ^{140}Ba is always greater than that of ^{85}Sr . The uptake of both ^{85}Sr and ^{140}Ba in soft tissues is generally in proportion to the calcium content of the tissues.

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Biochem. J. (1963) **87**, 618

Turnover of Liver Glutathione in Trauma

BY SARAH C. KALSER AND L. V. BECK*

Department of Pharmacology, School of Medicine, University of Pittsburgh, Pittsburgh, 13, Pa., U.S.A.

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Previous studies (Beck & Linkenheimer, 1952; Beck, Kalser & Alexander, 1961) have shown that mice subjected to tourniquet trauma exhibit a marked depletion of liver glutathione and also exhibit a decreased incorporation of tracer amounts of L- ^{35}S cysteine into liver glutathione. The latter finding suggested, as a working hypothesis, that the decrease in liver glutathione induced by trauma was due to an inhibition of glutathione synthesis rather than to a facilitation of glutathione degradation. Additional evidence for this concept was obtained in glutathione repletion (net synthesis) experiments (Kalser & Beck, 1962). After administration of large amounts of L-cysteine, a rapid repletion of liver glutathione occurred when the depletion of glutathione had been obtained by the administration of bromobenzene, but not when the depletion had been secured by tourniquet trauma. In the present experiments, turnover-

time and turnover-rate studies (Zilversmit, Entenman & Fishler, 1943) have been applied to the problem of whether trauma affects the synthesis or degradation or both of liver glutathione *in vivo*. Both short-term and long-term labelling experiments with L- ^{35}S cysteine have been performed. In the short-term experiments turnover is calculated from the rate of appearance of ^{35}S in liver glutathione. In such experiments the incorporation rate presumably approaches the rate of synthesis, since little labelled glutathione is available at these periods for degradation processes to influence the results. In long-term experiments turnover is calculated from the rate of disappearance of ^{35}S from the liver glutathione that has already become labelled. Although the initial impetus to this problem was to study glutathione synthesis in trauma, a far more important and widespread application resulted from the finding that the two types of experimental approaches generally used in turnover studies can lead to widely divergent results in certain situa-

* Present address: Department of Pharmacology, Experimental Programme of Medical Education, Indiana University, Bloomington, Ind., U.S.A.