The comparison of the uptake of chloride, lactate and gluconate of strontium shows that the difference, if any, is much smaller than the individual variations. If there is any difference in the uptake of calcium chloride, lactate and gluconate, this difference will probably be of minor importance. This fact can be related to the observation of Greenberg and Gunther[8] that the blood calcium in dogs increases to the same extent whether the same dose of calcium is ingested in chloride, lactate or gluconate. The observation that the uptake in the skeleton is about 3 times higher after intravenous than after peroral administration suggests that approximately one-third of the ingested dose of a calcium or strontium salt is absorbed by the intestine. Strontium and calcium are excreted both in the feces and in the urine.

The selective fixation of radio-strontium in the skeleton, its fairly good yield, the suitable energy of its beta-rays, its convenient half-life and the innocuousness of small doses[9] have given a specific method of irradiation of the skeleton.

Summary. The metabolism of calcium and strontium has been studied on normal animals with the radioactive isotopes of those elements. Uptake in the skeleton of different salts of strontium has been compared. These experiments have furnished two practical findings: (1) a method to irradiate the skeleton selectively for therapeutic purposes, (2) the secondary production of appreciable amounts of a long-lived radioactive yttrium, the most likely among the artificial radioactive elements now known, which may be substituted for radium as a penetrating gamma-ray source.

11900

Radio-Calcium and Radio-Strontium Metabolism in Pregnant Mice.*

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Studies of calcium and strontium metabolism in mice with

8 Greenberg, D. M., and Gunther, L., *Arch. Int. Med.*, 1932, **50**, 855.

9 MacCance, A., and Widdowson. E. M., *Biochem. J.*, 1939, **33** II, 1822.

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radioactive isotopes have shown a selective concentration of these elements in the skeleton.[1] It was of interest to determine how pregnancy affects this metabolism and to what extent calcium and strontium, previously fixed in the skeleton of the mother, would migrate to the foetus and later to the milk.

Methods. Adult virgin and pregnant mice were injected with doses of 0.1 cc radioactive calcium lactate solution (containing 0.8 mg Ca and emitting radiation which produced about 200 counts/sec. with the Libby screen wall counter[2]) and radioactive strontium lactate solution (containing 1.6 mg Sr and emitting radiation equivalent to about one microcurie).‡ Throughout, the animals received a normal diet containing about 1% of $CaCO_3$. At different periods after the injection the mice were sacrificed and the radioactivity of bones, soft tissues and uterus of each mouse was measured separately. Assays of radio-strontium were determined with a DuBridge electrometer and those of radio-calcium with a Libby screen wall counter.[2] Aliquots of the injected dose were used as reference standards. The probable error for these measurements is ±3% for radio-strontium and ±10% for radio-calcium. Newborn mice were killed within 12 hours after birth and the radioactivity of their whole bodies assayed. On some samples, total calcium was determined and the specific activities calculated. In a few cases, newborn mice containing no radioactivity were given to "radioactive mothers," so that the amount of radioactivity transferred from the mothers to the adopted offspring through the milk could be determined.

Results and Discussion. The uptake in mothers, foetuses and offspring of radio-strontium and radio-calcium injected previous to or during pregnancy is given in Table I. It appears, as has been previously observed, that a few days after injection, most of the radioactive calcium or strontium is fixed in the bones, while the activity of the soft tissues and that of the uterus is low. Nevertheless, at birth there is an appreciable amount of radio-calcium or radio-strontium in the offspring. In the radio-calcium experiments, the specific activity of the whole body of the offspring was frequently higher than the specific activity of the mother's bone, although the radioactive calcium of the newborn mice originates mostly from the mothers' bones. Specific activities were 0.49, 0.36, 0.52 and 0.19% of the

[1] Pecher, Charles, PROC. SOC. EXP. BIOL. AND MED., 1941, **46**, 86.

[2] Libby, W. F., and Lee, D. D., *Phys. Rev.*, 1939, **55**, 245.

‡ These "tracer" activities of strontium and calcium were kept small enough to avoid an effect of the radiation on metabolism.

TABLE I.*
Distribution of Radioactive Ca and Sr in Mothers, Foetuses, and Offsprings at Different Periods After the Administration of the Labelled Isotopes.
(Percent of dose.)

Days between inj. and killing†	State of‡ pregnancy when killed	Mother's bones	Mother's soft tissues	Foetuses and uterus	Offspring	Accumulated in young mice during lactation period
		Experiment with Radio-strontium.				
2	n.p.	20.0	1.0	0.0		
2	p.III	17.5	1.5	0.11		
1	p.III	19.0		0.35		
4	n.p.	34.0		0.0		
4	p.I	24.1	0.9	0.0		
9	p.II	20.1		0.0		
9	12 off	18.5			2.65	
9	7 off	25.9			1.75	
9	10 off	15.0			3.0	
11	9 off	31.7			2.45	
11	9 off	12.9			1.54	
12	10 off	13.6			2.04	
12	10 off	15.1	1.0		3.2	
14	7 off	24.0			1.55	
15	8 off	20.7			1.49	
21	p.IV	13.0	0.13	0.024		
21	n.p.	13.9	0.10	0.0		
21	5 off	10.0	0.10		1.4	
21	6 off	12.2	0.15		1.9	
21	5	11.6	0.14		0.44	
45	6 off				0.28	
	Lact 20d	11.8				1.0
45	9 off				0.80	
	Lact 20d	13.0				0.80
45	6 off				0.18	
	Lact 7d	7.5				0.34
20	Lact 8d	7.9				2.15
		Experiment with Radio-calcium.				
1	n.p.	64.0	3.3	0.0		
1	n.p.	58.0		0.0		
1	p.IV	48.0	3.0	2.8		
10	p.IV	70.0	<1.2	1.8		
10	8 off	65.0	<1.2		16.3	
11	9 off	57.0	<2.0		3.8	
12	9 off	53.0			7.0	
20	8 off	28.0	<1.2		5.8	

*Each line of figure represents values from individual mice.
†The duration of pregnancy in mice is 21 days.
‡p.—pregnant; n.p.—not pregnant; I, II, III, etc.—1st, 2nd, 3rd, etc., quarter of the pregnancy; off.—offspring; lact.—lactation with duration in days of the lactation period.

administered dose per milligram of calcium for the newborn mice and 0.26, 0.26, 0.25 and 0.20% respectively for the mothers' skeletons (Exp. 9, 17, 18). These observations suggest that the last calcium fixed in the mothers' bones is the first to be removed.

When offspring containing no radioactivity were given to "radioactive mothers," a very appreciable amount of activity was found

in the adopted offspring after a few days (Table I). This demonstrates migration of these elements from the mother's skeleton to the offspring through the milk.

The immediate secretion of strontium in the milk was studied by injecting 0.1 cc radioactive strontium lactate solution intravenously into lactating mice; after 2 days, 19, 20 and 11.8% of the dose was recovered in the offspring. The immediate secretion of radioactive strontium in milk of 2 cows has also been studied.[3] During the 4 days following injection, 11 and 7.8% of the administered dose of radioactive strontium lactate (0.85 g of metallic strontium) was recovered in the milk.

In order to determine if the migration of the radioactive mineral salts from the mother's bones to the foetus and to the milk would alter the rate of excretion of radioactive strontium, the excreta of 6 mice previously injected with radioactive strontium were assayed for a period of one month. Three out of the 6 mice became pregnant. A slight increase (from 0.1-0.2% to 0.2-0.4% of the dose) in the daily rate of excretion of radioactive strontium occurred during the last 3 or 4 days of pregnancy, and particularly during the first 10 days of the lactation period.

Conclusion and Summary. Radioactive strontium and calcium have been used to study the mineral metabolism in mice during pregnancy. It appears that part of the calcium and strontium previously fixed in the skeleton of mice migrates to the foetus during the last days of pregnancy and to the offspring through the milk. When radioactive strontium lactate is injected intravenously into lactating mice and cows, appreciable amounts are excreted in the milk.

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Creatine-Creatinine Excretion in Neuromuscular Diseases Treated With Alpha-tocopherol and With Testosterone.*†

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Deficiency of vitamin E in guinea pigs and rabbits results in

[3] Erf, L. A., and Pecher, Charles, PROC. SOC. EXP. BIOL. AND MED., 1940, **45**, 762.

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† The alpha-tocopherol was kindly supplied by Merck & Co., Inc., Rahway, N. J.