non-hypophysectomized animals. Hypophysectomy also caused a shift in position of a considerable portion of the globule leucocytes from the tunica propria (where the largest percentage occurs in non-hypophysectomized rat) to the crypt epithelium.

Summary. Within 4 days after whole body x-irradiation (650 r), globule leucocytes were reduced to 1-2% of their normal number in the intestine of the rat. Reestablishment of normal numbers of cells began toward end of the first week after irradiation and was completed by the 5th week. The effect of irradiation on globule leucocytes was chiefly a local one, being prevented by shielding the intestine with lead during irradiation. Only with the LD_{100} 30 days dosage (800 r) was there a significant reduction in number of globule leucocytes in lead-shielded intestinal segments. This appeared to be the indirect result of stress induced by irradiation, since the effect was prevented by hypophysectomy. Hypophysectomy alone reduced markedly the number of intestinal globule leucocytes.

1. Kirkman, H., *Am. J. Anat.*, 1950, v86, 91.
2. Kent, J. F., Baker, B. L., Ingle, D. J., and Li, C. H., PROC. SOC. EXP. BIOL. AND MED., 1954, v86, 635.
3. Kent, J. F., *Anat. Rec.*, 1952, v112, 91.
4. Baker, B. L., Pliske, E. C., Kent, J. F., McGinty, J., Van Dyke, J. G., and Bethell, F. H., *Endoc.*, 1955, v57, 472.
5. Kent, J. F., Baker, B. L., Pliske, E. C., Van Dyke, J. G., and Bethell, F. H., PROC. SOC. EXP. BIOL. AND MED., 1955, v89, 142.
6. Dougherty, T. F., *Physiol. Rev.*, 1952, v32, 379.

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Strontium^{85} Metabolism in Man and Effect of Calcium on Strontium Excretion.* (22197)

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Sr^{90}, a β emitting isotope with a 25 year half life is one of the major hazards of nuclear fission because of its selective localization in the skeleton. Its entry into the human body and its pathways of elimination are, therefore, of great concern. Availability of a carrier-free γ emitting isotope of strontium, Sr^{85}, with a half life of 65 days, facilitated this investigation of the metabolism of radiostrontium in man(1). Data on metabolism of intravenously administered Sr^{85} are reported in this communication.‡

Methods. Carrier free Sr^{85}, 0.1-0.4 μc/kg body weight was injected intravenously in 4 human subjects. Blood samples and urine were obtained at 1, 4, 8 and 24 hour intervals initially. Subsequently, urine, stool and plasma were analyzed daily. Radioactivity was determined in 1-5 ml plasma and urine and on stool samples weighing up to 5 g. Significant counts on these samples were obtained up to 24 days. A Nuclear scintillation well counter, Model DS3 was used: through special lead shielding the background was reduced to 140-180 CPM.

Results. Fig. 1 shows plasma levels, urinary and fecal excretions of Sr^{85} of a 72 year

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1. Laszlo, D., Spencer, H., Brothers, M., Berger, E., and Hart, H. E., Int. Conf. Peaceful Uses Atomic Energy, Geneva, June 1955.

‡ Produced in Oak Ridge National Laboratory Cyclotron by the nuclear reaction of Rb^{85} (p,n) Sr^{85}. Radionucleides of Sr^{85} were isolated from the target material, Rb_2CO_3, and other impurities with no strontium carrier added. This separation was performed by H. T. Russell, Radioisotope Operations Division of Oak Ridge National Laboratory. We thank these laboratories for their cooperation.

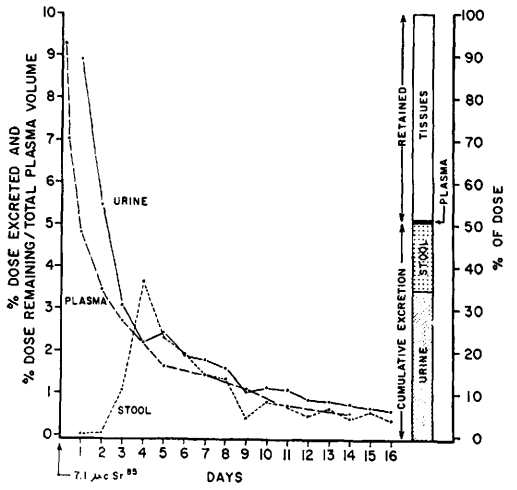

FIG. 1. Intravenous tracer dose of Sr^{85}; plasma levels, urinary and fecal excretions.

old ambulatory female with osteoporosis. (Case 3, Table I). Initially, plasma levels and urinary excretions declined rapidly, fecal Sr^{85} content was highest on 4th day and from there on plasma levels, fecal and urinary Sr^{85} excretions declined gradually with the lines falling closely together. In 16 days a total of 34.5% was excreted in the urine, 16.3% in the stool: 0.5% was present in the total plasma volume and 48.7% of the dose was retained in the tissues.

Similar experiments were performed on 3 other subjects. Plasma levels and urinary excretions of the first 48 hours of the studies are listed in Table I. Patients 1 and 4 had no skeletal disease. Patient 2 had Paget's disease of the bone. Significant differences in plasma levels and urinary excretions were noted in the 4 subjects. The 48 hour urinary strontium excretion ranged from 6.5-28.3%. The latter was excreted by pt. 4 who eliminated 57.2% in 15 days in the urine and 11.0% in stool.

After radioactivity of the samples declined to low levels, a second tracer dose of Sr^{85} was injected to each patient at the midpoint of a 2 hour infusion of calcium gluconate, containing approximately 1 g Ca^{++}. The marked enhancement of urinary strontium excretion is shown in column B, Table I. A 5-15 fold increment is noted at one hour. The enhancement continued for several hours after termination of the calcium infusion and was followed by a temporary depression on the next 2 to 3 days. In spite of the marked increase of urinary Sr^{85} excretion, the plasma levels were only slightly different and fecal Sr^{85} excretions were not enhanced. The magnitude of the calcium effect upon urinary strontium excretion becomes evident by comparing the cumulative 24 hour Sr^{85} excretions following administration of the isotope with and without calcium in the 4 subjects: 4.40 vs 21.5%, 4.2 vs 13.7%, 8.9 vs 18.2%, and 18.6 vs 29.5% respectively.

To study whether strontium excretion is similarly enhanced if both the tracer and calcium are injected slowly, the 2 experiments listed

TABLE I. Effect of Intravenous Calcium on the Urinary Excretions and Plasma Levels of Sr^{85}.

	1 hr		4 hr		8 hr		24 hr		48 hr	
Case No.	A	B	A	B	A	B	A	B	A	B
1	.40	6.14	.63	5.82	.76	4.45	2.61	5.13	2.56	1.69
	(10.49)	(12.02)	(7.40)	(7.91)	(6.54)	(6.61)	(4.69)	(4.69)	(3.48)	(3.54)
2	.41	4.52	.44	3.70	1.26	2.89	2.05	2.58	2.38	1.19
	(7.37)	(7.77)	(4.26)	(4.37)	(3.42)	(2.95)	(2.19)	(2.27)	(1.69)	(1.65)
3	1.17	6.03	.96	4.95	1.26	2.22	5.52	5.01	5.48	3.51
	(12.50)	(13.62)	(9.26)	(8.88)	(7.01)	(6.93)	(4.80)	(4.38)	(3.43)	(3.50)
4a	1.38	7.85	3.13	7.19	4.36	6.68	9.80	7.80	9.61	6.16
	(10.36)	(9.01)	(7.08)	(5.99)	(5.08)	(4.61)	(3.33)	(2.80)	(2.16)	(2.02)
4b	.09	.11	.87	2.78	5.34	11.00	7.53	9.52	8.95	4.78
	(1.65)	(1.14)	(5.07)	(4.85)	(5.50)	(5.63)	(3.60)	(2.86)	(2.04)	(1.65)

Figures represent Sr^{85} in % dose excreted from 0-1 hr, 1-4 hr, 4-8 hr, 8-24 hr, 24-48 hr; % dose of total plasma volume in parentheses.

A = experiments without calcium; B = with calcium, see text.

Exp. 4a and 4b were performed on the same patient; in 4b Sr^{85} was infused in 5 hr without calcium (A) and with calcium (B).

under 4b were carried out. The isotope was infused for 5 hours. The plasma level of Sr^{85} rose gradually and was 5.5% at 8 hours (column A): it declined thereafter at rates comparable to that of the rapid injection of Sr^{85}. Urinary strontium excretion increased gradually and was highest at 8 hours. The cumulative 24 hour urinary excretion was 13.8% (column A). The marked enhancement of strontium excretion by simultaneous but slow administration of the same dose of calcium, approximately 1 g Ca^{++}, infused for 1 hour preceding and for 5 hours simultaneously with Sr^{85} is shown in column B. The cumulative 24 hour urinary strontium excretion rose to 23.4%.

These experiments illustrate that the major route of excretion of intravenously administered strontium is via the kidney; in 15 days as much as 57% was excreted in one patient. Calcium significantly increases renal clearance of strontium and thereby decreases the body load.

Summary. Radiostrontium metabolism following intravenous administration of tracer doses of strontium^{85} was studied in 4 human subjects. Plasma levels, urinary and fecal strontium excretion were measured. The plasma levels declined rapidly. The main route of excretion is via the kidney. Rate of strontium excretion seems to depend upon the state of bone metabolism. It was low in Paget's disease and high in senile osteoporosis. Simultaneous administration of calcium gluconate significantly enhanced the strontium excretion.

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Mechanical Fragility of Erythrocytes from Patients with Paroxysmal Hemoglobinuria.* (22198)

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It has been established that pH is an important factor in *in vitro* hemolysis of erythrocytes from patients with paroxysmal nocturnal hemoglobinuria (PNH). *In vitro,* hemolysis of PNH erythrocytes in normal human serum is characterized by: 1) a hemolytic system which requires properdin, complement and Mg^{++}(4), all normal constituents of normal serum; 2) absence of abnormal hemolysins or agglutinins in patient's serum(2,3,4); 3) maximum hemolysis at pH 6.5-7.0; 4) minimal hemolysis in normal human serum outside pH range 6-8.

As pH of PNH blood is decreased from pH 7.8, and hemolysis becomes maximum, it is conceivable that the hemolytic system could weaken the erythrocyte cell wall in such manner that *in vivo* trauma would augment hemolysis. This question was submitted to test by determining mechanical fragility (MF) *in vitro,* of normal and PNH erythrocytes in active and inactive properdin systems at varied levels of pH.

Materials and methods. To determine the effect of decreased pH on MF, hydrochloric acid of N/1.2 to N/8 was used to obtain the desired pH of blood samples. To maintain this pH during rotation, imidazole in HCl (3.44 g imidazole/100 ml of 0.2 N HCl) was used as buffer because of its effectiveness when used in small quantities(7). Although this solution is hypertonic, it becomes approximately isotonic (isotonic equals 1.72 g/100 ml of 0.1 HCl), when it is diluted with equal volume of HCl used to alter pH. Defibrinated blood samples were obtained from 3 normal males, 3 normal females and 3 patients with PNH. Of the 3 PNH pa-

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