

for a specific species - virus combination. With the variety of highly differentiated and specialized cells of the animal organism, one must anticipate rather a multiplicity of cell - virus reactions, much wider than that established for monocellular organisms and their viruses.

Summary. 1) Adult human and rabbit Fallopian tube fragments, which maintained in *in vitro* cultures their specific histological structure and coordinated vibratory activity, were submitted to infection with polio, adeno, bovine rhinotracheitis, herpes and other viruses. 2) The organized ciliated epithelium when compared with dedifferentiated epithelium in the same cultures showed in all cases a relative resistance to the cytopathic action of viruses, manifested by a marked delay in cell destruction, more pronounced in the case of bovine rhinotracheitis or polio and less marked in the case of herpes or vaccinia viruses. 3) This resistance could not be abolished either by immobilization of cilia with

anesthetics or by treatment of cell surface with hyaluronidase or trypsin. 4) The meaning and implication of these data are discussed.

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Effect of Parathyroidectomy on Distribution of Radiocalcium. (24645)

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Tracer experiments with injected Ca^{45} have demonstrated rapid exchange between blood and bone calcium which can vary with age and with the metabolic state of bone(1,2). It has been suggested that parathyroid hormone might directly affect the amount of "exchangeable bone calcium"(3), but recent evidence indicates that the hormone can act on that portion of bone unavailable for rapid exchange(4,5). While it appears established that parathyroid hormone directly increases effective solubility of bone mineral(6), it is not certain how this effect might influence the amount of bone calcium available for rapid exchange. In the present study the effect of parathyroidectomy on the early exchange of a tracer dose of Ca^{45} in rats was examined to shed some light on this question.

Methods. Distribution of a tracer dose of Ca^{45} was studied in groups of young (70 to 82 days) and old (289 to 302 days) male Holtzman rats. In 3 groups of young rats, Ca^{45} was given at intervals of 1 day, 6 to 8 days, and 28 to 30 days after parathyroidectomy or after sham operation. In one group of old rats, Ca^{45} was given 7 days after parathyroidectomy or sham operation. Parathyroidectomy was performed by electro-cautery under nembutal anesthesia. In sham operations the parathyroids were identified but not cauterized. In each animal distribution of radioactivity was measured 6 hours after intraperitoneal injection of a tracer dose of 3 to 6 μC of Ca^{45} with less than .005 mg of carrier calcium dissolved in 0.5 ml of normal saline. Plasma radioactivity was measured in samples of tail vein blood obtained 2 and 4 hours

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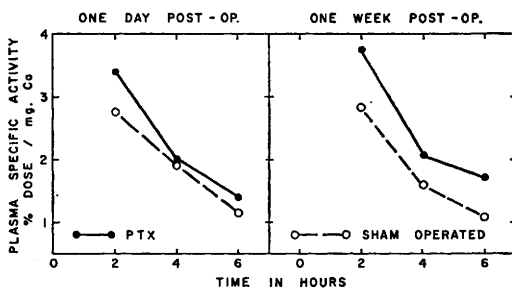


FIG. 1. Plasma specific activity after Ca^{45} inj. in parathyroidectomized and sham-operated rats. Animals studied one day after operation on left and one week after operation on right hand graph.

after injection. At 6 hours the animals were anesthetized with ether and sacrificed by heart puncture. Stomach and intestine were removed and their contents pooled with the feces (G-I sample), urine was collected during 6-hour period, and in those experiments done on young rats one month after operation, femur, heart, liver and kidney were removed for measurement of radioactivity. Serum and urine were planchettted directly, G-I and tissue samples were ashed, dissolved in HCl and then planchettted. Radioactivity was assayed in a windowless flow counter and was corrected for absorption, using a previously prepared curve. Total calcium content in serum, urine, G-I sample and tissue was determined by precipitation as oxalate and permanganate titration(7). Data are presented in terms of specific activity calculated as per cent of injected dose/mg of Ca. Following initial equilibration in the extracellular fluid space, which is probably complete in a few minutes, further changes in plasma specific activity are chiefly due to exchange with bone and tissue calcium. The amount of bone and tissue calcium which has exchanged at 6 hours can be calculated from the injected radioactivity minus the amount in G-I sample, urine, and extracellular fluid, *i.e.*, per cent of injected radioactivity in bone and tissue, divided by plasma specific activity, which is taken as equal to the specific activity of exchanging calcium. The resulting value is termed the 6-hour exchangeable calcium. It is not identical with exchangeable bone calcium but consists of several components(6) including 1) rapidly exchangeable bone calcium, 2) exchangeable calcium in muscle and skin (the

amount in other organs is $<1\%$ of injected radioactivity), 3) calcium added to the skeleton as new bone. From data in the literature (2,8,9) it appears likely that the bulk of "6-hour exchangeable calcium" represents exchangeable bone calcium.

Results. The results are summarized in Fig. 1 and Table I. In young animals plasma calcium concentration decreased to about 6 mg % one day after parathyroidectomy and did not change further one week or one month after operation. While plasma specific activity was somewhat higher in parathyroidectomized animals studied one day after operation than in sham-operated controls, the difference was significant only at 6 hours ($p < .05$) but not at 2 and 4 hours. In rats studied one week after operation there was a greater difference in plasma specific activity between parathyroidectomized and control rats, significant at 2 and 4 hours ($p < .05$) and highly significant at 6 hours ($p < .001$). Moreover plasma specific activity was significantly higher in parathyroidectomized animals one week after operation than one day after operation ($p < .01$). The third group studied one month after operation showed no further increase in specific activity after parathyroidectomy.

Radioactivity in the G-I sample was not altered by parathyroidectomy. There was more radioactivity in urine of parathyroidectomized rats presumably because specific activity was increased while total calcium excretion was little altered. Because of the large decrease in plasma calcium concentration, the calculated extracellular fluid radioactivity at 6 hours was decreased after parathyroidectomy. The sum of extracellular, urinary, and gastro-intestinal radioactivity was similar in parathyroidectomized and sham-operated rats, so that changes in "6-hour exchangeable calcium" per rat (Table I) reflect changes in plasma specific activity. In young animals the "6-hour exchangeable calcium" was 200 to 350 mg/kg body weight, assuming the body is 2% calcium these figures represent 1 to 1.75% of total bone calcium. A value for exchangeable calcium plus any accretion that has occurred at six hours can also be obtained directly from radio-

TABLE I. Effect of Parathyroidectomy on 6-Hour Distribution of Ca⁴⁵.

Group	No. of rats	Age (days)	Wt (g)	Plasma Ca (mg %)	Radioactivity in			Plasma specific activity (% dose/mg Ca)	Exchangeable Ca ⁴⁵	
					ECF*	Urine (b)	GI tract (c)		Per rat (mg)	Per body wt (mg/kg)
Young rats	9	76	264 ± 10	10.0 ± .2	4.7 ± .2	1.1 ± .2	3.7 ± .2	1.14 ± .06 (d)	79	301
		10	252 ± 20	6.1 ± .3	3.3 ± .2	2.3 ± .1	3.9 ± .3	1.40 ± .05	65	256
	8	75	240 ± 4	10.3 ± .3	4.2 ± .3	1.5 ± .5	3.7 ± .3	1.09 ± .09	83	347
		9	224 ± 5	5.9 ± .3	3.5 ± .2	2.2 ± .3	3.9 ± .2	1.70 ± .06	53	238
	6	76	268 ± 5	10.3 ± .2	5.8 ± .1	1.1 ± .2	4.6 ± .3	1.34 ± .05	66	263
		7	251 ± 8	6.5 ± .3	4.4 ± .3	1.5 ± .1	4.1 ± .3	1.73 ± .15	52	194
Old rats	4	292	422 ± 8	10.5 ± .1	12.9 ± .2	.2 ± .1	3.8 ± .4	1.87 ± .10	44	105
	4	299	409 ± 20	7.8 ± .2	9.7 ± .2	.4 ± .1	3.9 ± .2	1.94 ± .05	44	108

Figures are mean values with stand. error.

* Calculated as: $\frac{\% \text{ dose/ml plasma} \times (\text{plasma vol} + .65 \text{ interstitial fluid vol})}{\text{body wt. Interstitial fluid [Ca]}}$ is estimated as 65% of plasma Ca and assumed to have equal specific activity.

† Calculated as: $\frac{100 - (a + b + c)}{(d)}$.

activity in the femur divided by plasma specific activity. Mean values one month after operation were 1.1% of total femur calcium in parathyroidectomized rats and 1.7% of total femur calcium in sham-operated rats.

The effect of parathyroidectomy was considerably different in old rats. There was a smaller decrease in plasma calcium concentration one week after parathyroidectomy, and plasma specific activity was almost the same in sham-operated and parathyroidectomized rats. There was a much smaller urinary excretion of Ca⁴⁵ and stable calcium. The amount of radioactivity in extracellular fluid was higher in control than in parathyroidectomized rats. This difference could account for the observed difference in specific activity since the values for exchangeable calcium were identical in parathyroidectomized and control animals. The "6-hour exchangeable calcium" was only 44 mg/rat or 100 mg/kg body weight. This represents about 0.5% of total bone calcium.

Discussion. The results suggest that parathyroid hormone does not affect the amount of bone calcium available for exchange directly. First, because there was no change in exchangeable calcium despite a decrease in serum calcium in old rats after parathyroidectomy, and second, because the change in exchangeable calcium in young rats after parathyroidectomy was not immediate but progressive, while the change in plasma calcium concentration was immediate. The progressive decrease in the "6-hour exchangeable calcium" is considered to be an indirect consequence of parathyroidectomy. If parathyroid hormone acts by direct resorption of bone then parathyroidectomy would lead to decreased bone resorption. Presumably this would result in less remodeling and less new bone formation. Since the proportion of calcium available for rapid exchange is greatest in newly formed bone(6), the exchangeable fraction would decrease as new bone formation decreased. In old rats, with less new bone formation in the controls, parathyroidectomy would be expected not to affect exchangeable calcium further.

Summary. The 6-hour distribution of a tracer dose of Ca⁴⁵ was studied in rats at

various intervals after parathyroidectomy and sham operation. In young rats studied one day after parathyroidectomy there was a marked decrease in plasma calcium and a small decrease in the "6-hour exchangeable calcium." One week after parathyroidectomy there was no further decrease in plasma calcium but a significant further decrease in 6-hour exchangeable calcium. In old rats studied one week after parathyroidectomy there was a somewhat smaller decrease in plasma calcium concentration and no change in 6-hour exchangeable calcium. It is concluded that removal of the parathyroids does not affect the amount of bone calcium available for exchange directly, but may act indirectly in the following sequence: decreased parathyroid hormone $\rightarrow$ decreased bone resorption $\rightarrow$ decreased new bone formation $\rightarrow$ decreased exchangeable calcium.

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Persistence of Heterologous Bone Marrow in Mice as Function of X-Ray Dose. (24646)

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Previous studies on recovery rate of mouse's immune mechanism after irradiation and treatment with AET[†] or bone marrow(1-4) led to formulation of the following hypothesis: There are many antibody-producing cells, or an antibody-producing cell, that can recognize degrees of antigenicity (homologous, closely related heterologous, and distantly related heterologous antigens); *i.e.*, degree of injury to the recognition mechanism by X-irradiation would increase in the order of mention. Makinodan and Gengozian(5,6) tested and confirmed this hypothesis on the basis of mouse's ability to produce titratable, circulat-

ing antibodies. A subsequent test would then be a biological one; *i.e.*, persistence and proliferation of foreign tissue in X-irradiated recipients as a function of genetic relation between donor and host. Our findings on such an investigation are reported here.

Materials and methods. Approximately 1100 (C3H x 101) F₁ male and female mice 12 weeks old were used as recipients. Bone marrow donors were normal male and female Sprague-Dawley rats (150-250 g), 12-week-old golden hamsters, weanling guinea pigs, and albino rabbits (1.5-2 kg). A constant-potential Phillips X-ray machine was used under following conditions: 250 kv; 15 ma; 160-170 r/min at 60 cm; inherent filtration, 1 mm of Al; added filtration, 1 mm of Al; and hvl, 0.5 mm of Cu. Mice were irradiated in circular perforated lucite container attached to re-

* Operated by Union Carbide Corp. for U. S. Atomic Energy Comm.

[†] AET = S, 2-aminoethylisothiuronium bromide hydrobromide (formerly called S, β -aminoethylisothiuronium bromide hydrobromide).