oxygen concentration below the level which would support cellular respiration. Following the initial influx no increase in cellular uptake is observed in the absence of oxygen, indicating that a passive diffusion of selenite into the cell does not occur. The ability of cyanide(8) to inhibit the uptake of selenium both in the presence of oxygen and of nitrogen supports this hypothesis.

When blood from these same sheep was incubated with zinc or cesium, no differences in cellular uptake were found, indicating that the increased uptake of selenium by cells of the selenium-deficient ewes was specific and not due to a simple increase in cellular permeability.

Similarly the *in vitro* uptake of sulfur was not influenced by dietary selenium intake. This would agree with the hypothesis(9) that at physiological levels selenium and sulfur do not follow identical metabolic pathways.

The convenience with which this technique can be conducted and the sensitivity and reproducibility it offers suggest its value as an assay of the dietary level of selenium of animals in the field and as an indication of areas(10) where selenium supplementation would prove beneficial.

Summary. Whole blood from ewes being fed a purified diet containing urea as the sole nitrogen source was used to determine the *in vitro* uptake of selenium by ovine blood cells. Selenium-^{75} as selenite moved into the ovine blood cell *in vitro* via an oxygen-dependent transport mechanism. The magnitude of this influx was inversely proportional to the dietary intake of selenium, but was not affected by dietary Vit. E. The uptake of sulfur, zinc, or cesium was not influenced by dietary selenium level.

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Calcium Metabolism in the Rat Studied with Calcium^{45}: Effect of Age. (28684)

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We have undertaken a series of investigations directed toward establishing the main parameters of calcium metabolism in rats in a variety of experimental states; the present paper deals with the effect of age, which is considered to have a profound effect on calcium metabolism(1,2,3).

Previous investigations have indicated that with advance in age there is an initial increase in bone density(4) which, in old age, remains constant in rats or decreases in man (5), an increase in the calcium-pyrophosphate ratio(6), alteration in intestinal absorption of calcium (decreased — 1, 7, 8; increased — 9), reduced calcium retention(7), changes in the kinetics of Ca^{45} specific activity of tissues(10) and a decline in endochondral osteogenesis(11). The majority of these studies were mainly concerned with senescence. The present report concerns the differences in calcium metabolism between young actively growing rats and adult animals at the growth plateau.

Material and methods. Two groups of

TABLE I. Calcium Kinetics in Young and Adult Rats.

	Young rats	Adult rats	T-test
No. of rats	26	26	
Weight, g	132.4 ± 2.04	432.5 ±10.51	
Mean calcium intake, mg /day	40.67 ± 3.56	43.14 ± 4.88	‡
Pool, mg	99.95 ± 5.36	62.09 ± 3.35	5.99*
Vo+, mg/day	69.46 ± 1.80	32.81 ± 1.58	15.29*
Vo−, "	40.34 ± 3.70	16.46 ± 2.78	5.16*
△, "	29.11 ± 2.95	16.35 ± 2.64	3.08†
Vu, "	.64 ± .09	.63 ± .07	‡
α, %	86.6	52.6	4.35*

* Value of 't' > P .001.
† Value of 't' > P .01.
‡ No difference.

male Wistar rats of the same colony, aged 2 months and one year respectively, were used. The technique, which combines classical balance data and Ca^{45} measurements, has been described(12,13). After an intravenous injection of a tracer dose of Ca^{45} (45 μc) the various parameters of calcium metabolism were calculated from a detailed analysis of the integrated plasma specific activity curve, and from the amounts of calcium ingested and excreted by way of urine and faeces. The animals were fed a balanced diet containing 4 mg of calcium and 4 mg of phosphorus per gram, and food intake in the 2 groups was held to be of the same order during the test period in order to eliminate the influence of a variable calcium supply on calcium metabolism(14).

Results. Table I shows means and standard errors of the mean of the different parameters of calcium metabolism. The mass of exchangeable calcium (Pool), bone anabolism (Vo+), bone catabolism (Vo—), the coefficient of intestinal absorption (α) and net gain or balance (△) are decreased in the adult rats, although the amount of calcium intake was the same in the two groups. Urinary excretion of calcium remained unchanged.

Discussion. (A) Effects on bone metabolism. The decrease in the pool size in the adult animals must be due to a decrease in the exchangeable calcium in their bones, for calcemia was normal, and a normal intra- and extracellular calcium is presumed in the absence of tetany. It is even more striking if one considers the body mass and the total skeletal calcium (1.8 g of calcium for a rat of weight 200 g, and 3.6 g for a rat weighing 495 g); the mass of soft tissues is correspondingly increased. There is a decrease in the balance in the adult rats, as has already been shown(3). This likewise is noteworthy if it is related to the actual skeletal masses in the 2 groups.

We showed(15) that hypophysectomy in the young rat resulted in a decrease in bone anabolism, bone catabolism, pool size, balance, and absorption coefficient. It is thus apparent that hypophysectomy and aging act in a similar direction on calcium metabolism. This supports the conclusion reached from histologic studies that hypophysectomy results in an acute reduction in endochondral osteogenesis like that developed more gradually in adults(16). These facts suggest that the hypophyseal activity is linked to the normal skeletal aging.

In the preceding discussion the weight of the animals is not considered as the independent variable because, in rats of the same age and of varying weight, a positive relationship exists between rate of bone anabolism and weight. In the case of aging such a relationship cannot explain the results as the heaviest animals have the lowest bone anabolism.

(B) Effects on intestinal absorption. The absorption coefficient is lowered in the adult group, denoting a decrease in absorptive capacities of the rats with age; this is in accord with previous observations(7,8,1).

(C) Effects on urinary excretion. In absolute values there is no difference in urinary excretion of calcium in the 2 groups, though on a body weight basis this would imply a reduction of urinary excretion in the adult rat.

The differences in calcium metabolism of these 2 groups of rats show the need for more detailed knowledge of the age-dependent changes in the dynamics of this system. A longer range of time within the life-span is being studied, and additional groups of animals are being examined at intermediate ages.

Summary. 1. The calcium metabolism of

adult rats (1 year old) has been compared with that of young growing rats (2 months old) by balance studies and tracer calcium. 2. In the adult rats the mass of exchangeable calcium, bone anabolism, bone catabolism, intestinal absorption and balance are reduced; but urinary excretion of calcium remains unchanged. 3. Similarities were noted between the effects of aging and those previously reported for hypophysectomy.

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In vitro Test Systems for Cancer Chemotherapy. II. Correlation of *in vitro* Inhibition of Dehydrogenase and Growth with *in vivo* Inhibition of Ehrlich Ascites Tumor.* (28685)

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The desirability of simpler methods for finding cancer chemotherapeutic agents or for determining their effectiveness has led to the development of a variety of *in vitro* procedures. Mammalian cell culture techniques, although less expensive and less laborious, have a number of innate disadvantages which are only partially understood. The difficulties include extrapolation to the *in vivo* situation, where the drug may be so modified, altered, metabolized or excreted as to render it more or less toxic, or more or less effective than originally observed in the *in vitro* assay. Development of host resistance may also make correlation between *in vitro* and *in vivo* tests difficult and at times unimpressive. Recently DiPaolo(1) has shown that compounds of proven clinical value or wide effectiveness in animal tumor systems are inhibitory in tissue culture; the exact conditions of the *in vitro* test may determine, in many instances, the extent of inhibition caused by any one compound, ranging from inactivity to high inhibition.

The present investigation utilizes Ehrlich ascites tumor cells which have been in continuous culture for 33 months and which have been used in a variety of *in vitro* tests. The results of these tests are compared with the results obtained when cells from the same cell line are grown in Swiss mice.

Materials and methods. An established

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