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Comparative Metabolism of Phosphorus in Normal and Lymphomatous Animals.*

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When radioactive phosphorus is fed to normal rats, mice or chickens[1-4] in an ordinary diet, a large percentage of the phosphorus is deposited in the bony skeleton. This more or less selective deposition of phosphorus in bone, suggested to us the possibility of using radioactive phosphorus as a source of therapeutic irradiation in leukemia. In preliminary experiments, mice with lymphatic and myelogenous leukemia were fed radiophosphorus in relatively small amounts and there was no definite influence on the course of the disease. However, at autopsy, some of the tissues were assayed for activity and it was unexpectedly found that in leukemia there is an abnormality in the handling of a single dose of tagged phosphorus. Before pursuing this question further, it seemed to us important to determine first the total phosphorus content of leukemic, lymphomatous and normal tissues as a basis for further study. The findings[5] show that per gram wet weight, lymphomatous tissue or tissues infiltrated with lymphoid cells have no greater total phosphorus content than their normal analogues, *i. e.,* lymph glands and various uninfiltrated viscera. We wish here to report observations on normal and lymphomatous mice which show that a single dose of phosphorus is handled differently in the latter group of animals.

The phosphorus used in these experiments was made radioactive in the cyclotron of Lawrence and Cooksey[6] by bombarding red phos-

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1 Chiewitz, O., and Hevesy, G., *Nature,* 1935, **136**, 754.

2 Cook, S. F., and Scott, K. G., *Proc. Nat. Acad. Sci.,* 1937, **23**, 528.

3 Chiewitz, O., and Hevesy, G., *Det. Kgl. Danske Videnskabernes Selskab. Biologiske Meddelelser,* 1937, **13**, 9.

4 (a) Lawrence, J. H., *Handbook of Physical Therapy,* Amer. Med. Assn., 1938; (b) Hamilton, J. G., and Alles, Gordon A., *Am. J. Physiol.,* in press.

5 Tuttle, L. W., Scott, K. G., and Lawrence, J. H., to be published.

6 Lawrence, E. O., and Cooksey, D., *Phys. Rev.,* 1936, **50**, 1131.

phorus with deuterons having an energy of approximately eight million volts. As stated above, P^{32}, the radioactive isotope, is chemically similar to P^{31}, the naturally occurring element. It has a half life of about 14.8 days. Because of the beta ray emission, radiophosphorus can be detected and quantitated by means of an electroscope or a Geiger counter. After being made radioactive, the phosphorus was converted into a neutral solution of sodium phosphate and given to the animals subcutaneously in small "tracer" doses.

Forty Strong A strain mice,[7] approximately 3 months of age, and of about the same weight, were used in this experiment. Twenty of them were inoculated subcutaneously in one axilla with a transmissible lymphoma.[8] When large palpable tumors had developed, 15 days after inoculation, 5 tumor animals and 5 control animals were each given subcutaneously 0.5 cc of a sodium phosphate solution containing 20 microcuries of P^{32} and 1.57 mg Na_2HPO_4 per cc. Isotonicity was attained by adding NaCl. Two days later a similar group of 10 animals were given the same dose and 2 other groups of 10 on the 2 succeeding days. Twenty-four hours after the phosphorus was administered to the last group, all of the animals were sacrificed, the wet tissues of each mouse were weighed and prepared individually for activity analyses. Thus there was a group of 5 normal and 5 lymphomatous animals sacrificed 1, 2, 3 and 5 days after phosphorus administration.

The results are summarized in the figures. The average activities per gram wet weight of whole animal and various tissues are plotted against days after injection. It is to be noted that on the average, the phosphorus exchange per gram tissue of the mouse as a whole is about the same for normal and lymphomatous animals. However, it is noted that when individual tissues are examined there are differences. The percentages for muscle and total animal were about the same in both groups of animals. This is not true of bone in the lymphomatous animals, where the values are lower than normal, nor of liver where the 24-hour peak is lacking. Apparently, the deposition of radiophosphorus in tumor tissue occurred partially at the expense of bone and liver. Also lymphomatous tissue has a greater exchange than lymph gland, which might be considered its analogue. It is clear that the total phosphorus content of a tissue does not necessarily determine the uptake or exchange of a given dose of phosphorus in that tissue. The latter is determined by the rate of metabolism of the element in question in a particular tissue, and this may

[7] Strong, L. C., *J. Heredity*, 1936, **27**, 21.

[8] Lawrence, J. H., and Gardner, W. U., *Am. J. Cancer*, 1938, **33**, 112.

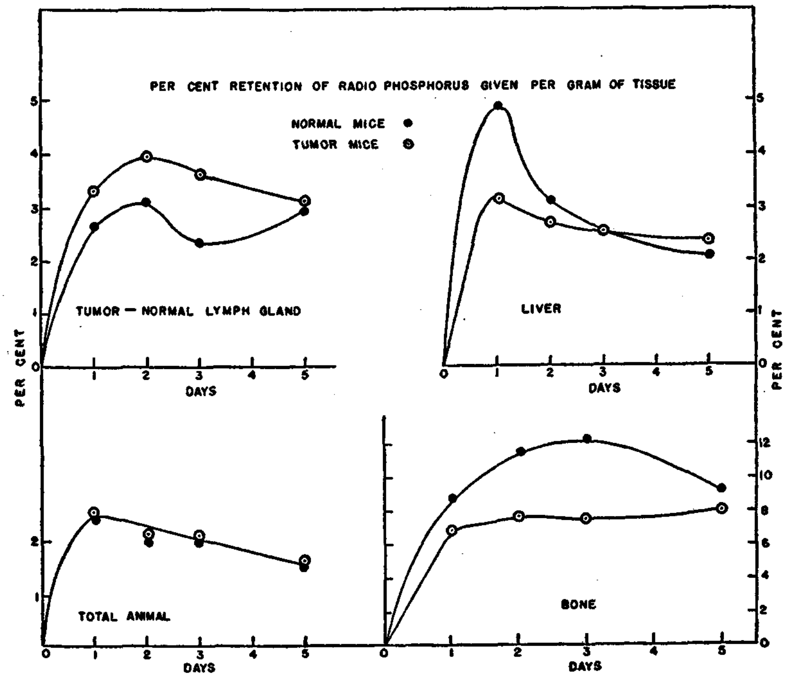

FIG. 1.

be complicated by the "laying down" of new tissue as is the case here.

The higher activities in bone and tumor tissue suggest the use of radiophosphorus as a source of therapeutic irradiation in conditions involving primarily the bone marrow. Recently by this method we have been able to produce remissions in cases of chronic leukemia (human), similar to those following the use of X-rays.

Further work is now in progress which includes the determination of the "tagged" phosphorus in the various organic and inorganic fractions and over longer periods of time, in an attempt to elucidate the variation in the handling of phosphorus by lymphomatous mice.