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Parathormone Bio-Assay of Plasma in Hypercalcemic Tumor Rabbits.* (29194)

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There is increase in plasma calcium and decrease in plasma phosphorus in rabbits with VX-2 carcinoma(1). Bone reabsorption has also been noted in tumor animals. Possibility that the tumor produces a parathormone-like substance seems likely. Lemon(2) has shown an increase of such substances in hypercalcemic patients with neoplastic disease. Assay of plasma from hypercalcemic tumor bearing rabbits for parathormone-like activity is reported here.

Procedure. Fifteen white New Zealand rabbits weighing 2.5 kg each were used. Two ml of VX-2 carcinoma tumor suspension were injected into right thigh of ten rabbits. Five rabbits served as controls. Heparinized blood samples were obtained weekly by ear vein drip method, immediately chilled with ice, and centrifuged in cold at 3000 rpm for fifteen minutes. Plasma was removed and stored at −10°C. Plasma calcium was determined by Skeggs modification(3) of Moser and Williams method(4).

Plasma was assayed for parathormone-like activity using a modification of method described by Lemon(2). White Swiss mice weighing 25 g were divided into 77 groups of 5 each. After a 4-hour fast each mouse was hydrated by intraperitoneal isotonic saline injection, 5% of body weight. Groups of mice were then treated as follows:

Three units parathormone, 8 groups.

One unit parathormone, 7 groups.

Plasma from hypercalcemic tumor rabbits, 22 groups.

Plasma from normal rabbits, 18 groups.

Five % dextrose solution, 19 groups.

Each mouse was injected with 0.25 ml of test substance subcutaneously. Fifteen minutes after injection each group was placed in a metabolic cage and urine collected separately from feces for 4 hours. Total 4-hour urinary phosphorus excretion was determined by method of Fiske and Subbarow(5).

Results. Total urinary phosphorus per group is shown in Fig. 1. There is an increase in phosphorus excreted by parathormone treated mice as compared to controls, with no significant difference between 3 unit and 1 unit dosage. Similarly, no significant difference exists in phosphorus excretion between control groups and mice receiving normal rabbit plasma. However, 8 of 22 groups treated with hypercalcemic (18.5 to 27.0 mg%) rabbit plasma excreted more urinary phosphorus than any groups receiving normal rabbit plasma. Analysis of difference of means in parathormone treated groups compared to control groups demonstrates statistically significant difference ($P<0.001$). An analysis of variance between groups treated with normal rabbit plasma and those receiving hypercalcemic rabbit plasma indicates a significant difference in variability between the two groups (null hypothesis $P \cong 0.02$).

Discussion. Parathormone bio-assay is based on increase in urinary excretion of phosphorus(6) after administration of exoge-

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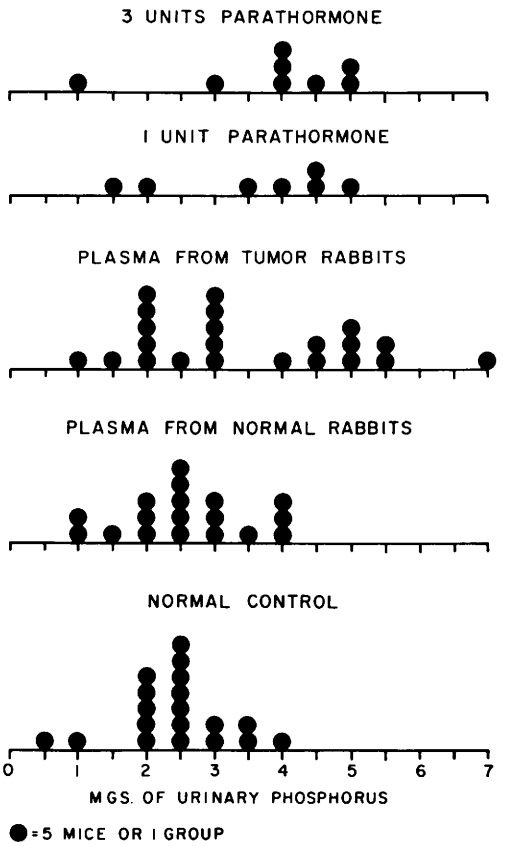

FIG. 1

nous parathormone. Lemon(2) used a change in the urinary phosphorus-to-calcium ratio as method for bio-assay of parathormone-like activity. In the present experiment the phosphaturic effect is used as index of this activity. It is demonstrated (Fig. 1) that commercial parathyroid extract, under the conditions of this experiment, does cause increase in urinary phosphorus. A similar effect was observed in 8 of 22 groups of mice receiving hypercalcemic rabbit plasma, and statistical analysis indicated this to be highly significant difference from groups receiving normal rabbit plasma.

Histopathologic study of hypercalcemic VX-2 carcinoma rabbits shows absence of parathyroid hyperplasia. Also excision of tumor reverses hypercalcemia, indicating likelihood that circulating parathormone-like substance is produced by tumor.

Summary and conclusions. Serum from hypercalcemic VX-2 carcinoma rabbits has a phosphaturic effect similar to exogenous parathormone when injected into mice. The most likely explanation is production of parathormone-like substance by tumor tissue.

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Food Restriction and Lipogenesis in the Rat. * (29195)

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Restriction of feeding time of rats to a period of 1-2 hours per day has been reported to increase activity of lipogenic mechanisms over that observed in animals permitted to eat spontaneously throughout the day(1-4). Hollifield and Parson(5) have recently confirmed that the lipogenic mechanisms are markedly increased in rats allowed access to food for only 2 hours per day and added the interesting and practical observation that, within a few days after this time-restricted feeding program was initiated, the rats trained to eat in a 2-hour period con-

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