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Deposition of Liver Glycogen in Normal Mice and in Mice Bearing Sarcoma 180.*

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(Introduced by C. P. Rhoads.)

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Previous investigation in this laboratory has demonstrated an impairment in the ability of patients bearing gastric cancer to lay down liver glycogen after the oral administration of glucose.[1] If small laboratory animals can be shown to be similarly affected by the presence of a tumor, more extensive and detailed studies of the abnormality would be possible. In animals the factors which normally influence glycogen storage can be better controlled. Moreover, the influence of tumor type and size as well as other variables pertinent to the study can be investigated more easily than is possible in human subjects.

This paper describes the results of measurements of liver glycogen in normal mice and in mice bearing sarcoma 180 implants before and after glucose administration.

Methods. Young, adult male mice, CFW strain, which were obtained from Carworth Farms, and which weighed from 16 to 26 g were used in all experiments. All animals were allowed drinking water *ad libitum* and were placed on a diet of Purina Laboratory Pellets for at least 2 days, to eliminate gross differences in nutritional state before use.

These animals were divided into 4 experimental groups. Two groups had had sarcoma 180 implanted into the axillary region 7 to 14 days previous to the experiment. Of these animals, one group provided fasting liver glycogen levels while the other group was treated with glucose before liver glycogen assay was made. The other 2 groups consisted of normal mice. One group was fasted and one was given glucose. All animals were weighed frequently and on some occasions the food intake was followed. Except for those animals which had borne tumors for 12 to 14 days, all appeared healthy.

At 4 p. m. on the day preceding each experiment, the mice were deprived of food and placed in clean cages in groups of 2 to 4 in a dark, quiet, air-conditioned room.[2] After 16 hours, they were either sacrificed for the determination of fasting glycogen levels or were given an intraperitoneal injection of 100 mg of glucose (0.25 ml of 40% glucose in water) and sacrificed 2 hours later to allow measurement of the increase in liver glycogen over the control value. The mice were killed by severing the spinal cord at the base of the brain to minimize struggle. The whole liver was removed, weighed, and dropped into 30% KOH within 60 seconds of the time of death. Liver glycogen was determined by the Good, Kramer and Somogyi[3] modification of Pfluger's method.

Results. As can be seen in Table I, the 16-hour fast sufficed to reduce the liver glycogen levels to a uniformly low level in both normal and sarcoma-bearing animals. The difference between the fasting levels in the groups of animals tested after bearing tumors for 7-10 days and 10-14 days is probably due to the small numbers of animals used and in any case is not significant in so far as this study is concerned, since these experiments were not designed to demonstrate differences in rates of glycogen depletion.

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1 Abels, J. C., Young, N. F., and Homburger, F., in preparation.

2 Swensson, Ake, *Acta Phys. Scand. Supp.*, 1945, **2**, 33.

3 Good, C. A., Kramer, H., and Somogyi, M., *J. B. C.*, 1933, **100**, 485.

TABLE I.
Deposition of liver glycogen

Group	Days after tumor implant	No. animals	Glucose, mg	Avg. body wt, gm	Liver glycogen, %	Total mg liver glycogen
Normal	—	27	0	19.6	0.29±0.02*	3.1
"	—	33	100	20.9	2.25±0.03	26.9
Sarcoma 180	7-10	5	0	18.0	0.19±0.02	2.3
" "	11-14	5	0	18.1	0.46±0.14	3.3
" "	7-10	17	100	20.4	1.15±0.08	14.4
" "	11-14	16	100	18.7	1.25±0.05	15.1

* Probable error of mean value.

All glycogen values are expressed in terms of glucose. Under the conditions of these experiments, the normal mice stored liver glycogen to the extent of 23.8% of the injected glucose as contrasted with only 12.0% by those animals with tumors. The probable errors of the means indicate that this is a highly significant difference whereas the difference between the mean values of the two tumor-bearing groups is not statistically significant.

Discussion. In view of the fact that, (a) the tumor-bearing mice did not lose weight; (b) their fasting liver glycogen concentrations were as high as those of normal mice; and (c) their food intake was as high as the normal, this difference can not be explained on a nutritional basis in the usual sense. Neither was the bodily activity of the tumor-bearing mice observed to be greater than that of the controls during the period between glucose injection and sacrifice. It is clear from the data that the length of time which the mice have borne the tumors, at least between 7 and 14 days, has no influence on the glycogen content. Neither was the mass of the tumor found to influence the extent of glycogen storage. A group of animals bearing tumors having an average weight of 325 mg averaged 1.32% liver glycogen whereas a group with 1,200 mg tumors were found to average 1.24%. Greenstein[4] found that the decrease in liver arginase and catalase activities of animals bearing tumors were likewise independent of the age of the tumor. It is possible that the impaired glycogenesis may result from a similar effect on the enzyme systems in the livers.

Conclusion. Male mice bearing sarcoma 180 implants exhibit an impairment in their ability to store liver glycogen after glucose administration. This is similar to the defect in patient with gastric cancer.

[4] Greenstein, J. P., *J. Nat. Cancer Inst.*, 1942-1943, **3**, 419.

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Arginase and Catalase Activity in Livers of Patients Having Benign and Malignant Gastric Lesions.*

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The comparison of activities of certain enzymes of normal adult tissues with those of tissues undergoing rapid proliferation has revealed differences. These have given rise to much speculation regarding the possible relationship of enzyme activity to neoplastic growth. One important phase of this work

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