

THE BLOOD SUGAR IN MICE DURING GROWTH OF EHRLICH'S CARCINOMA

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The development of the ascites form of Ehrlich's carcinoma in mice is accompanied by a decrease in the blood glucose level, which is inversely proportional to the number of cancer cells in the ascites fluid. The hypoglycemic effect of the cancer cells in mice with Ehrlich's carcinoma can be abolished by large doses of glucose, hydrocortisone acetate, or by swimming in cold water (stress).

Cancer cells in the body are in a state of relative glucose and oxygen lack [3]; nevertheless; their viability is provided for by their ability to obtain, ferment, and assimilate glucose even if present in a very low concentration in the surrounding medium [2, 5-7, 9]. In the presence of large tumors or widespread metastasization, severe hypoglycemia may develop [4, 8, 10, 11, 14] and may sometimes lead to death. After operative removal of the tumor the normal blood sugar level is restored [12, 13]. The hypoglycemia syndrome does not necessarily appear during development of malignant neoplasms if the compensatory powers of the body are sufficient to counteract the hypoglycemia.

This paper gives the results of a study of the blood glucose level of mice with an inoculated Ehrlich's carcinoma and the effect of exogenous glucose, hydrocortisone, and physical exertion (swimming in cold water) as a means of evoking stress, on this parameter.

EXPERIMENTAL METHOD

Experiments were carried out on 139 mice weighing 23.2 ± 2.3 g, most of which were inoculated intraperitoneally with Ehrlich's carcinoma. Starting from the 4th day, groups of 5-11 animals were decapitated daily (70 mice altogether). The remaining animals received daily intraperitoneal injections of 2 mg/g or 10 mg/g of 40% glucose solution, and 0.5 mg or 5 mg hydrocortisone acetate (Gedeon Richter, Hungary) subcutaneously; cold mice were made to swim for 15 min in water at 17-19°C immediately after the inoculation. The longest duration of the experiment was eight days. Controls were set up for each experimental group. The glucose concentration [1] in the blood and ascites fluid was determined in all animals after decapitation.

EXPERIMENTAL RESULTS

On the first four days after inoculation of the tumor, the blood glucose level of the control and experimental mice was the same (90.8 ± 5.4 mg %). Later it fell in the latter group to reach 54.9 ± 5.0 mg %, i.e., 60% of the initial level, by the 8th day (Fig. 1). In the four mice which survived until the 11th day the mean blood glucose level was only 45.2 mg %.

Progressive hypoglycemia in the mice with Ehrlich's carcinoma was accompanied by an increase in the volume of ascites fluid (on the average from 1.5 to 10.6 ml from the 5th to the 8th day) and a simulta-

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TABLE 1. Blood Glucose Concentration (in mg %) in Control Mice with Cancer

| Group of animals | Treatment | | | | |
|----------------------------|-------------------------------|-----------------|--------------------------------------|-----------------|-----------------|
| | glucose in total dose (in mg) | | hydrocortisone in total dose (in mg) | | swimming |
| | 1840 | 360 | 40 | 4 | |
| Control | 50,9 ± 3,2 (4) | 98,9 ± 2,1 (4) | 59,7 ± 15,2 (4) | 70,8 ± 14,9 (4) | 66,1 ± 2,1 (5) |
| P ¹ With tumors | <0,01 | >0,5 | >0,5 | >0,5 | <0,01 |
| P ² | 79,8 ± 10,6 (10) | 43,9 ± 3,2 (11) | 70,8 ± 8,7 (9) | 27,9 ± 2,2 (6) | 81,2 ± 8,3 (12) |
| | <0,05 | >0,05 | >0,05 | <0,01 | <0,05 |

Note. Number of animals shown in parentheses, P¹) compared with intact mice; P²) compared with the 8th day for mice with tumors receiving no treatment.

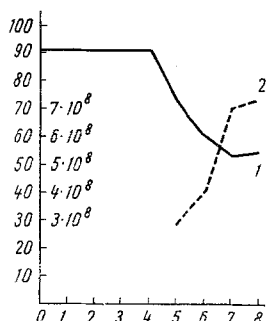


Fig. 1. Change in blood sugar (1) and number of tumor cells (2) during development on Ehrlich's ascites carcinoma. Ordinate, left, blood glucose concentration (in mg %); right, number of tumor cells. Abscissa, time (in days).

neous increase in the number of cancer cells: in the ascites fluid as a whole it increased during these days from 2.8×10^8 to 7.3×10^8 (Fig. 1).

The number of cancer cells in the ascites fluid was thus inversely proportional to the glucose concentration with effect from the 5th day after inoculation of the tumor, i.e., from the time when the number of cancer cells could easily be measured. In no case could glucose be detected in the ascites fluid of the mice with a tumor even in traces; i.e., its concentration was below the limit of sensitivity of the method. These results confirm those obtained previously [2].

It is clear from Table 1 that 5-6 h after the last injection of glucose (360 mg) and hydrocortisone (40 and 4 mg) into the control animals the blood glucose level was unchanged. After administration of large doses of glucose (1840 mg) and systematic physical exertion (swimming in cold water) these animals developed hypoglycemia.

After administration of large doses of glucose and after stress (swimming) a statistically significant increase in the blood sugar level was observed, by contrast, on the 8th day in the mice with tumors compared with the animals exposed to none of these factors. The same tendency was observed in the experimental mice treated with 40 mg hydrocortisone. After injection of the smaller dose of hydrocortisone (4 mg), however, the blood sugar concentration in the animals of the experimental group showed a statistically significant decrease, and a tendency toward the same effect was observed after administration of 360 mg glucose to the mice with tumors.

Consequently, healthy mice and mice inoculated with Ehrlich's carcinoma responded differently to the same agents; in addition, the regulatory mechanisms maintaining the constancy of the blood sugar level of the mice with malignant tumors are in a state of much greater stress and are more easily changed. Despite the injection of very large doses of glucose and hydrocortisone, as well as the increased production of endogenous glucocorticoids (stress), in no case could even traces of glucose be found in the ascites fluid of the experimental animals.

The development of the ascites form of Ehrlich's carcinoma is thus accompanied by increasing hypoglycemia. Certain extremal factors (large doses of glucose and hydrocortisone, swimming in cold water) can abolish the hypoglycemic effect of cancer cells and maintain an almost normal blood glucose level. However, even in these cases, glucose concentration in the medium surrounding the cancer cells is extremely low.

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