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On the carbohydrate metabolism of malignant tumors.

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The free sugar, lactic acid and glycogen content of spontaneous and transplanted mouse carcinoma and of Jensen rat sarcoma has been investigated under various conditions. It was found that the free sugar content of these tumors was lower than that of any other tissue of the mouse or the rat so far investigated. Thus 16 tumors showed as an average 0.047 per cent free sugar, the maximum being 0.069 and the minimum 0.036. Comparative values for mouse organs have been obtained on a former occasion and showed as an average: liver, 0.300 per cent; muscle, 0.079 per cent; kidney, 0.126 per cent; brain, 0.059 per cent. Glucose administration had a marked effect on the free sugar concentration of the tumors. The tumors were analyzed 15, 30 and 60 minutes after giving glucose intraperitoneally. After 15 minutes the free sugar values were from 0.287 to 0.176 per cent at a blood sugar level from 0.634 to 0.396 per cent. After 30 minutes the free sugar values were from 0.311 to 0.184 per cent at a bloodsugar level from 0.464 to 0.230 per cent. After 60 minutes the free sugar values were from 0.078 to 0.057 per cent at a bloodsugar level from 0.194 to 0.166 per cent. A hyperglycemia produced by epinephrin also raised the free sugar concentration of the tumors.

The lactic acid values of 8 individual tumors ranged from 0.013 to 0.089 per cent, average 0.038 per cent. Comparative lactic acid values for other mouse tissues were: liver, 0.051 per cent for mice starved from 0 to 2 hours, and 0.011 for mice starved from 17 to 22 hours; muscle, 0.112 per cent. The lactic acid content of the tumors was considerably increased after glucose administration. Thus in 4 cases, where the tumors constituted from 2.7 to 22 per cent of the body weight of the animals, values of 0.117, 0.166, 0.160 and 0.141 per cent lactic acid were obtained; average 0.146.

The glycogen in 6 tumors varied from 0.122 to 0.303 per cent, average 0.196 per cent.

Warburg and co-workers^{1, 2, 3, 4} have shown that tumor tissue *in vitro*, in the absence as well as in the presence of oxygen, had an unusually large glycolytic power. They also found that the glycolysis was bound to the structure and did not take place in the liquid medium of the cells, which made it very probable that the energy derived from the splitting of glucose into lactic acid was utilized by the tumor cells, in other words, that the phenomena observed *in vitro* were also taking place *in vivo*. Our experiments support the idea that tumor tissue splits very large amounts of glucose into lactic acid under *vivo* conditions. Warburg found that the rate of glycolysis of tumor tissue *in vitro* was increased with increasing glucose concentration. Thus raising the sugar concentration from 0.04 to 0.2 per cent nearly doubled the rate of glycolysis, while just above 0.2 per cent glucose the rate was already at its maximum. A similar increase in the rate of glycolysis of the tumor tissue seems to occur in the living animal, when the sugar concentration of the tumors is raised from its resting level of 0.047 per cent to 0.2 per cent and more by the administration of glucose, since the lactic acid concentration in the tumors is raised 3 to 4 times after the glucose administration.

¹ Warburg, O., and Minami, S., *Klin. Wochenschr.*, 1923, ii, 776.

² Warburg, O., *Bioch. Z.*, 1923, cxlii, 317.

³ Minami, S., *Bioch. Z.*, 1923, cxlii, 334.

⁴ Warburg, O., Posener, K., and Negelin, E., *Bioch. Z.*, 1924, cvii, 309.