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Relation of Glycemia Level to Anoxic Survival of Primitive Respiratory Center in the Young Rat.

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Recently Selle[1] has shown that glucose and insulin have practically the reverse effects on the survival of the isolated respiratory center in the decapitated young rat head. It was likewise demonstrated[2] that glycotropic substances such as adrenaline and pituitary extract prolong, while others such as ephedrine, insulin, and iodoacetic acid, shorten the survival time of the respiratory center of the isolated young rat head. Starvation shortens survival time, presumably as less glucose remains available. It has recently been reported[3] that the aromatic sympathomimetic amines causing hyperglycemia without central excitation markedly prolong survival of the respiratory center while those causing central excitation concurrent with hyperglycemia shorten total survival time even though more gasps occur. This latter can be explained by the fact that the excited center discharges impulses more rapidly (lowered CO_2 threshold) resulting in quicker depletion of the available energy substratum.

In order to correlate survival time with glycemic level in the absence of neurogenic effects 113 young rats were decapitated by methods previously described[2] and the length of survival time determined by the measured duration of gasping. Blood sugar of each rat at the time of decapitation was determined by the Folin-Wu micro method[4] using a 0.1 ml sample of blood. Different blood sugar levels were achieved by (a) starvation, (b) glucose feeding (intragastrically), and (c) in 9 instances by injection of insulin intraperitoneally in order to reach extremely low blood sugar levels. It should be mentioned that with starvation plus insulin we were able to lower blood sugars to 19 mg % without convulsions in the young rats (approximately 24 days of age). All blood glucose readings were made objectively with a photelometer which had been calibrated with carefully prepared fresh dextrose standards. Intragastric feeding was done by a spinal puncture needle the end of which had been rounded and buffed to smoothness, with very few cases of failure in passing it down the oesophagus. All failures were discarded. By using relatively large doses of glucose (2 ml of 25%) we were able to reach blood sugar levels as high as 485 mg % but the results showed that prolongation of survival by glucose feeding was insignificant above the 180 mg level; in other words even though the glucose level may be high the rat apparently is unable to utilize a surplus above 180 mg %. This undoubtedly is due to the fact that the ischemic respiratory center is a dying center which is unable to utilize the extra fuel substance. Perhaps the very young (newborn) animal could utilize this extra energy to better advantage than the older one.[5,6]

Considerable individual differences in survival time appear and at first led us to believe that no correlation existed between glycemic level and survival time. However, if all the cases are plotted graphically, the "scatter graph" so produced shows a definite trend in one direction. Fig. 1 illustrates this relationship in 113 animals of a limited weight range. As far as possible we used rats weighing from

[1] Selle, W. A., *Am. J. Physiol.*, 1944, **141**, 297.

[2] Hiestand, W. A., Tschirgi, R. D., and Miller, H. R., *Am. J. Physiol.*, 1944, **142**, 153.

[3] Tschirgi, R. D., and Hiestand, W. A., *Anat. Rec.*, 1945, **89**, 15.

[4] Folin, O., and Wu, H., *J. Biol. Chem.*, 1928, **77**, 2.

[5] Himwich, H. E., Bernstein, A. O., Herrlich, H., Chesler, A., and Fazekas, J. F., *Am. J. Physiol.*, 1942, **135**, 387.

[6] Himwich, H. E., Fazekas, J. F., and Homburger, E., *Endocrinol.*, 1943, **33**, 96.

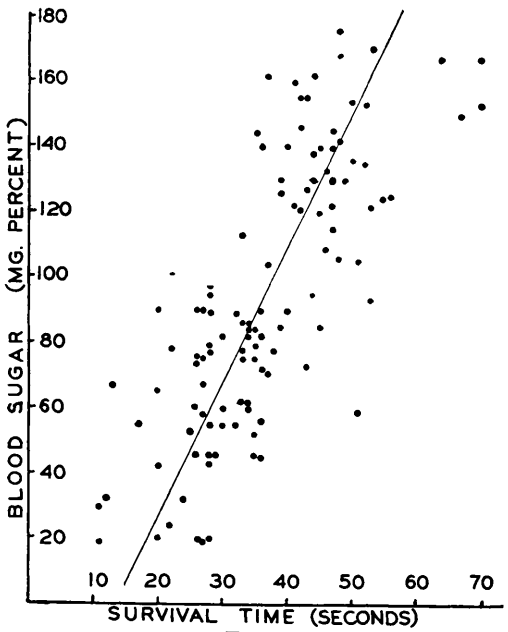

FIG. 1.

Showing trend in relationship between blood sugar levels below 180 mg% and respiratory center survival in 113 isolated young rat heads. The correlation for these data (Pearson r) is .737 ± .03.

TABLE I.

Weights, Survival Time, and Blood Sugar Levels of 10 Young Rats Fed Glucose Intragastrically. These are not included in Fig. 1.

Wt of rat, g	Survival time (sec)	Blood sugar (mg%)
48	55	485
45	50	458
47	67	438
48	61	403
45	59	395
55	36	322
42	55	290
43	59	282
55	44	215
55	52	205

50 to 60 g and of nearly the same age, the animals thus being young enough to have the second (anaerobic) series of gasps. As some were starved to reduce their blood sugar their weight fell, in some cases as much as 30%. Some given food *ad libitum* temporarily increased in weight. All weights listed are those taken immediately before decapitation.

As has been previously shown [2,5,6,7] the second series of gasps of the isolated head is anaerobic whereas the first series is oxidative. Therefore the duration of survival of the respiratory center is limited by its ability to continue using the anaerobic (glycolytic) energy. It is therefore reasonable that glycemic level should be a major factor in survival. It has been shown[6] that the survival period of the anoxic infant (rat or cat) but not that of the adult is prolonged by hyperglycemia. This is due to the inability of the adult to sustain a higher rate of cerebral metabolism from glycolysis and no doubt accounts for the absence of the second or anaerobic series of gasps in (most) adult rats. It appears from this and work of others that survival of the center depends upon 3 factors: (a) amount or availability of glucose, (b) state of activity of the center, and (c) the age of the animal. The last factor no doubt involves the animal's ability to utilize glucose as an anaerobic substratum which has been well explained by Himwich *et al.*[6]

Summary. The survival time (period of gasping) of the respiratory center and blood sugar level of 123 young rats were determined. A rough correlation exists between the two and it is concluded that glycemia is a significant factor in survival of the primitive respiratory center. Hyperglycemia above 200 mg % does not significantly prolong survival time beyond that of the 180 mg level.

[7] Selle, W. A., PROC. SOC. EXP. BIOL. AND MED., 1943, **54**, 291.