5958

Glucose Utilization by Brain.

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Medium-sized dogs were lightly anesthetized by intraperitoneal injection of 60 mg. per kilo of sodium amytal. Occasionally small amounts of ether were used during the operation. The femoral artery and vein and sagittal sinus were exposed and blood samples drawn practically simultaneously from the 3 vessels at half-hour intervals. For 2 to 2½ hours the dog was allowed to lie quietly and was kept warm, with no further treatment. After this time, 10 or 20 units of insulin were given intravenously, and blood samples taken as before for another 3-5 hours. Sugar (reducing substance) was determined by a slightly modified Shaffer-Hartman method after deproteinizing with the usual tungstic acid reagent, duplicate analyses agreeing nearly always. As run, with precautions against oxidation of the reagent by dissolved oxygen, the titration with 0.005 N sodium thiosulphate was entirely linear for known glucose solutions from quantities of 0.05 mg. or less to over 0.6 mg. Glucose added to blood was regularly recovered. In actual determinations, a blank and 2 or more known glucose solutions were included in the series and the blood values determined by interpolation.

Average results of 14 complete experiments are given in Table I, and a single experiment illustrated in Figure I. The animals were not in the post-absorptive state, so that the venous values, over

TABLE I.

Time in hours	Blood Sugar, mg. % Artery (Femoral)	Artery—femoral vein	Artery—sagittal sinus
0.5	144	27	49
1.0	140	25	50
1.5	135	18	38
2.0	130	18	34
2.5 (Insulin injected)	128	17	35
3.0	130	21	48
3.5	121	15	38
4.0	101	17	32
4.5	56	6	12
5.0	44	5	13
5.5	75	5	13
6.0	75	15	25
6.5	90	25	30
7.0	95	20	30

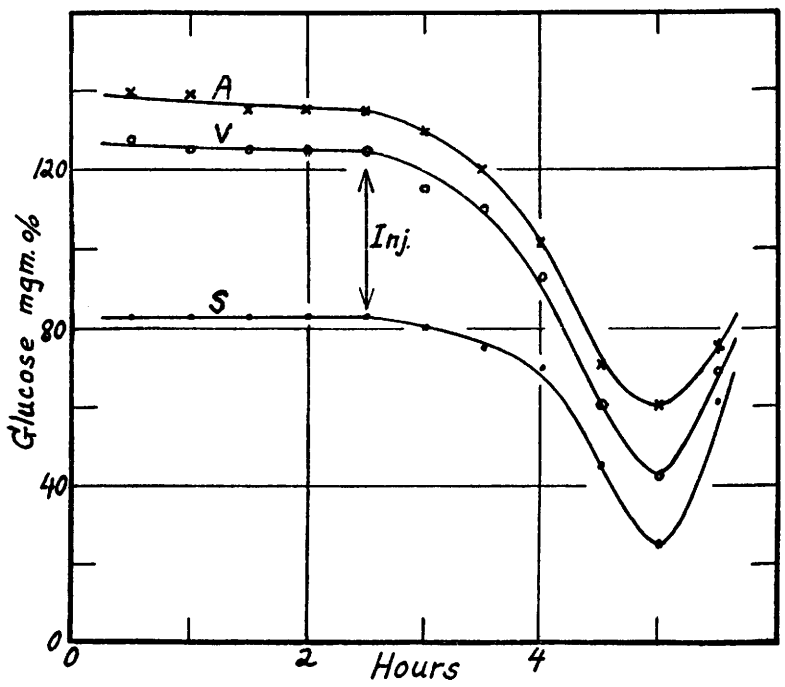

FIG. 1.

March 1, 1930. Dog, 11.2 K. Sodium amytal, 40 mg. per kilo intraperitoneally. First sample 10:05 a. m. Insulin, 10 units, intravenously at ↕

x——x Arterial blood sugar (femoral).
o——o Venous blood sugar (femoral).
•——• Sinus blood sugar (sagittal).

110 mg. %, are not high. The arterio-venous difference of 17 mg. % just before insulin injection is greater than usually obtained in the post-absorptive state,[3] but is well within the range for animals after administration of glucose. The sinus blood sugar was consistently, in every experiment, lower than the systemic venous blood and averaged, just before insulin, 35 mg. % below the arterial.

Following insulin, all sugar values fell to a low point in 2½ hours and then slowly returned towards normal. At the low point of the curve, venous blood sugar averaged 39 mg. % and the arterio-venous and arterio-sinus differences were much diminished, respectively to 5 and 13 mg. %. Although the arterio-venous difference has been shown in starved animals to be greater under insulin than in controls,[1, 11] the present contrary findings on fed animals are not necessarily in conflict. Schmidt's[11] findings on dogs under ether do

[1] Cori, C. F., *Physiol. Rev.*, 1931, **11**, 143.

show, in fact, lesser arterio-venous sugar differences as the blood sugar falls under insulin than before. The early rise in arterial values was not present in the best experiments.

Although we have not determined blood flow ourselves, many data[2, 7, 8, 12] indicate a normal flow of 140 cc. per minute per 100 gm. brain tissue, which is cut to about 50 in moderate narcosis. For the leg, the equivalent figure is 5 cc.[8] Calculating the actual amount of sugar taken up by the anesthetized brain and the leg respectively, the values are 10.5 and 0.5 mg. per gm. per hour. If all this were completely oxidized, it would correspond to 8 cc. of oxygen used per gram per hour for brain and 0.4 cc. for the leg. The actual oxygen consumption of dog brain *in situ,* as determined by Gayda,[2] is 6, by Schmidt,[10] 9, for the unanesthetized animal. Comparison of the 2 sets of data indicates that all the sugar reaching the brain from the blood might be oxidized. This is in conformity with the finding of an R.Q. of 1 for the brain,[2, 5, 10] and with the relative constancy in the quantity of brain glycogen.[6] Also, McGinty[9] has found less lactic acid in the sagittal sinus blood than in arterial when asphyxial conditions are avoided. On the other hand, the sugar values are somewhat high compared to the oxygen consumption, so that small amounts might have been deposited as glycogen, changed to lactic acid, etc.

The sugar uptake by the extremity is also somewhat higher than the measured oxygen consumption. Himwich and Castle[4] found 0.36 cc. of oxygen taken up by resting muscle, and the value for the leg as a whole must be lower. It seems certain in this case that a considerable portion of the glucose disappearing is deposited as glycogen or changed to lactic acid.

Summary. The metabolism of the brain, as estimated by the glucose taken from blood in passing through it, is in agreement with that determined by analogous studies of oxygen and carbon dioxide

[2] Gayda, T., *Arch. di Fisiol.*, 1914, **12**, 214.

[3] Henriques, V., and Ege, R., *Biochem. Z.*, 1921, **119**, 121.

[4] Himwich, H. E., and Castle, W. B., *Am. J. Physiol.*, 1927, **83**, 92.

[5] Himwich, H. E., and Nahum, L. H., PROC. SOC. EXP. BIOL. AND MED., 1929, **26**, 496.

[6] Holmes, E. G., and Holmes, G. E., *Biochem. J.*, 1926, **20**, 1196.

[7] Hou, C. L., *J. Orient. Med.*, 1926, **5**, 20.

[8] Jensen, P., *Pflüger's Arch.*, 1904, **103**, 171.

[9] McGinty, D. A., *Am. J. Physiol.*, 1928, **85**, 395.

[10] Schmidt, C. F., *Am. J. Physiol.*, 1928, **84**, 223.

[11] Schmidt, V. A. A., *Arch. exp. Path. u. Pharm.*, 1930, **153**, 79.

[12] Winterstein, H., *Handb. d. norm. u. path. Physiol.*, 1929, **9**, 515.

changes. Brain metabolism so estimated is at least 20 times as intense as that of resting muscle. This average does not differentiate the higher respiration of gray matter from white, the large amount of non-neural elements, and similar factors tending to dilute a much higher value for the nerve cells proper. Insulin does not uniquely influence brain sugar utilization.

5959

Effect of Calcium Administration to Rachitic Rabbits.

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The rabbits used in this work were made rachitic with the McCollum diet 3143, which is high in calcium and low in phosphorus. The calcium is present, chiefly, in the form of calcium carbonate. Previous work with this diet has shown that after about 20 days the animals have more or less marked rickets, as evidenced by X-ray of the bones and by determination of the phosphorus in the serum.

The control animals were given the same diet with the addition of cod liver oil, about 1 cc. per 100 gm. of diet.

Calcium was given in the form of calcium chloride or calcium gluconate, both in the strength of 10 mg. Ca per cc. of solution, administered in one dose by stomach tube. The dose, both in controls and rachitic animals, varied from 25 mg. to 200 mg.

Blood was taken by heart puncture before the administration of calcium and again a few minutes afterwards.

The normal animals did not seem affected by the administration of calcium. Of the 24 rachitic animals, however, 12 died within 15 minutes of the administration. In these animals the blood was very thick and coagulated rapidly.

The cause of death in the rachitic animals was, probably, hypercalcemia. Before the administration of calcium both controls and rachitic animals showed, rather constantly, a serum calcium of about 12 mg. per 100 cc. After the administration of calcium one control animal showed a rise of the serum calcium to 19 mg., in the remaining controls the maximum rise was to 15 mg. In the rachitic animals quite a number showed extremely high values for serum calcium after calcium had been given by mouth. The maximum was 61 mg.,