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THE GLUCOSE NECESSARY TO MAINTAIN THE GLUCEMIA IN EVISCERATED DOGS

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The study of carbohydrate changes in eviscerated animals as a method for investigating the glucose utilization in the peripheral tissues has been carried out by Soskin (1, 2) on the dog, by Mirsky and Broh-Kahn (3) on the rabbit, and by Russell (4) on the rat. We have carried out a large number of experiments in dogs in order to evaluate this method and to compare the results obtained in normal dogs with those obtained in hypophysectomized, diabetic and thyroid-treated dogs.

Experimental procedure. We have used dogs weighing between 13 and 23 kgm., most of which were males. The animals were allowed no food during the 18 hours preceding the experiment. They were anesthetized with chloralose at a concentration of 0.8 per cent in an 0.8 per cent NaCl solution. Normal controls were given 10 ml. per kilo of this solution intravenously, while hypophysectomized animals generally required 20 per cent less solution and thyroid-treated animals 20 per cent more. In this way a fairly uniform degree of anesthesia was obtained without interference with the glucose concentration of the blood.

The animals were eviscerated by the method described by Soskin and Mirsky (5), isolating the liver from the general circulation by the insertion of a glass cannula in the vena cava. Blood transfusions were given until the arterial blood pressure rose above 140 mm. Hg. Normal dogs were used as donors except for the diabetic animals where similarly diabetic donors were preferred. The animals were maintained under artificial respiration for the duration of the experiment. A standardized solution of glucose was delivered into the jugular vein at the rate of 1 ml. every 2 minutes, thus maintaining an almost continuous flow of glucose through the body.

In order to follow the changes in carbohydrate metabolism, blood glucose, blood lactic acid and muscle glycogen values were obtained. Blood obtained from the carotid artery was deproteinized after the method of Somogyi and glucemia determinations were made according to the method of Hagedorn and

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Jensen. The glucemia was determined initially and every thirty minutes during the three-hour experimental period. The blood lactic acid was determined initially and at the end of the experiment by the method of Friedemann and Kendall (6) in the West aeration apparatus. Glycogen determinations were performed on the tibialis anticus, extensor digitorum longus and triceps surae muscles by the method of Pflüger; final titrations followed the method of Bertrand. One leg was used for the initial and the other for the final values.

We observed that the arterial blood pressure of eviscerated animals dropped to low levels. Glucose curves obtained at pressure levels below 50 mm. Hg gave erroneous values and were not taken into account. However, when the evisceration was performed in less than 20 minutes, and clotting in the vena cava was prevented by the use of a very clean dry glass cannula, and the animals were maintained on heated tables under artificial respiration, and adequate blood transfusions were given before beginning the glucose injection, then the blood pressure was maintained well above 50 mm. Hg. In this way blood sugar curves of 3 hours' duration, with a few of 2 hours' duration when the blood pressure was falling rapidly, were obtained. All experiments ending with pressure levels below 50 mm. Hg were discarded. By this criterion 78 out of 87 dogs were considered. The final pressure level was 110 to 80 mm. Hg in 13 cases, 60 to 80 mm. Hg in 52 cases and 50 mm. Hg in 13 cases. All animals were in relatively good shape with active reflexes at the end of the experiment.

The amount of glucose necessary to maintain the initial blood level was between 50 and 250 mgm. per kilo per hour. As shown in tables 1 and 2, various doses were tried on the following: 17 normal dogs, 14 hypophysectomized dogs, 15 dogs made diabetic through the injection of anterior pituitary extracts (7 ml. per kilo of a 20 per cent anterior pituitary extract given intraperitoneally, daily, during the 5 preceding days), 4 of which were previously thyroidectomized, 11 dogs pancreatectomized 24 hours before the experiment, and 11 dogs treated with desiccated bovine thyroid (0.5 gram per kilo per day administered by gastric tube during the 5 preceding days). The blood sugar values are expressed as the difference between the first and the last value of the curve. Positive or negative signs with ± 8 are considered as equal. Individual variations within the same dose level are great.

However, summarizing from the data in table 3, it is apparent that the amount of glucose needed to maintain the initial blood sugar in eviscerated dogs is as follows: In normal dogs, 100–200 mgm. per kilo per hour; in hypophysectomized dogs, 100–150 mgm. per kilo per hour; in hypophyseal diabetic dogs (thyroidectomy having no effect), 150–200 mgm. per kilo per hour; and in both pancreatic diabetic and thyroid-treated dogs, 150–200 mgm. per kilo per hour.

The blood lactic acid values, which initially varied between 8 and 14 mgm. per 100 ml. of blood, showed in almost all cases a progressive rise during the experiment, giving a positive difference of 10 to 50 mgm. per cent between initial and final values (tables 1 and 2). The difference between initial and final muscle glycogen values is very variable. Most of the initial values were between 400 and 600 mgm. per cent.

DISCUSSION. We have observed that when the arterial blood pressure is maintained below 50 mm. Hg, there is a marked reduction in the sugar consumption, probably due to the consequent state of anoxia. However, eliminating all animals in which the blood pressure fell to such low levels, we were able to obtain regularly rising or falling blood sugar curves which permitted us to establish the approximate amount of glucose necessary to maintain the glucemia at its initial

TABLE 1

Carbohydrate balance of eviscerated dogs receiving continuous glucose injection

GLUCOSE INJECTED	NORMAL				HYPOPHYSECTOMIZED			
	Glucemia (mgm. %)		Lactic acid (mgm. %) difference	Glycogen (mgm. %) Difference	Glucemia (mgm. %)		Lactic acid (mgm. %) difference	Glycogen (mgm. %) difference
	Difference	Initial Final			Difference	Initial Final		
mgm./kgm./hr.								
50	−63	(94- 31)	+26	+108	−45	(90- 45)	+26	−115
50	−52	(92- 40)	+26	+109	−27	(95- 68)	−1	−172
50	−15	(87- 72)	+28	+10				
100	+9	(41- 50)	+30	+133	+93	(71-164)	+7	+197
100	=4	(85- 81)	+51	+162	−25	(97- 72)	+7	−103
100	=4	(94- 98)	+6	+119	=6	(103- 97)	+23	−127
100					+9	(78- 87)	+5	−116
100					+11	(83- 94)	+12	−460
150	−20	(77- 57)	+16	−285	+61	(76-137)	+52	−80
150	=4	(46- 50)	+8	−59	=2	(68- 66)	+39	−3
150	=0	(102-102)	+23	−57	+16	(78- 94)	+46	−200
150					+22	(90-112)	+83	−105
150					=4	(109-105)	+14	−67
200	+46	(74-119)	+64	+63	+11	(66- 77)	+25	−150
200	=0	(96- 96)	+3	+43				
200	−9	(103- 94)	+24	−136				
200	=2	(80- 82)	+19	+64				
200	+16	(78- 94)	+15	+25				
250	+54	(60-114)	+73	+98				
250	+118	(94-212)	+28	−70				
250	+62	(75-148)	−5	−124				

level, in eviscerated animals. Our results, however, when calculated as sugar utilization on the basis of Soskin's calculations, (1) did not give consistent values; in fact, we found these calculations of no possible use in our experiments.

Therefore, we have based our conclusions mainly on the blood sugar curve, referring to the amount of glucose in milligrams per kilo per hour necessary to maintain the initial blood sugar level.

Individual variations were very great making it impossible to arrive at exact

doses. However, disregarding certain isolated cases, the results on a large series of animals indicate that eviscerated normal dogs require from 100–200 mgm. of

TABLE 2

Carbohydrate balance of eviscerated dogs receiving continuous glucose injections

GLUCOSE INJECTED	DIABETIC (A.L.H.)				DIABETIC (PANCREATIC)				THYROID-TREATED			
	Glucemia (mgm. %)			Lactic acid (mgm. %) difference	Glycogen (mgm. %) difference	Glucemia (mgm. %)			Lactic acid (mgm. %) difference	Glycogen (mgm. %) difference	Glucemia (mgm. %)			Lactic acid (mgm. %) difference	Glycogen (mgm. %) difference
	Difference	Initial	Final			Difference	Initial	Final			Difference	Initial	Final		
mgm./kgm./hr.															
100	−12	(134-122)		+45	−200						−35	(100- 65)		+23	−26
100	+9	(134-143)		+20	−105						+31	(91-122)		+24	−20
100	−40	(259-219)		+5	−8						−9	(76- 67)		+22	−190
150	−271	(203-131)		+40		−80	(274-194)		+47	−110	−0	(112-112)		+57	−220
150	=2	(129-127)		+50	−94	−42	(272-230)		+15	−50	−34	(121- 97)		+44	−127
150	−68	(205-151)		+4	−365	−22	(216-184)		+10	−10	−12	(91- 79)		+34	+154
150	+25	(133-158)		+10	−33										
150	+83	(182-268)		+2	−80										
200	=5*	(144-149)		+20		+40	(244-284)		+7	−150	+81	(83-164)		+40	−24
200	+19*	(170-189)		+19	+120	+124	(199-323)		−13	−114	+51	(103 -154)		+68	−82
200	=4*	(157-161)		+30	+160	−53	(283-230)		+17	+10	=3	(68- 65)		+18	+17
200	−22	(190-178)		+6	+68	+46	(222-268)		+8	+64	+18	(96-114)		+27	+172
200	+67	(145-212)		−19	−28	+87	(144-231)		+6	+37	+42	(91-133)		+25	+14
200	=6	(265-259)		+20	−35										
200	=4	(183-187)		+72	+130										
200	−34	(158-124)		+42	−17										
250	+60	(189-249)		+34	−324	+61	(242-303)		+57	−9					
250	+28	(162-190)		+40	+102	+105	(231-336)		+14	−90					
250	+40	(136-176)		+16	−110	+78	(170-248)		+11	−10					

* Thyroidectomized.

TABLE 3

Difference between initial and final glucemia in eviscerated dogs with continuous glucose injection

GLUCOSE INJECTED	NORMAL			HYPOPHYSECTOMIZED			DIABETIC (A.L.H.)			DIABETIC (PANCREAT.)			THYROID-TREATED		
	−	=	+	−	=	+	−	=	+	−	=	+	−	=	+
mgm./kgm./hr.															
50	3			2											
100	1	2		1	1	3	2		1				2		1
150	1	2			2	3	2	1	2	3			2	1	
200	1	2	2			1	2	4	2	1		4		1	4
250			3						3			3			

−, fall of blood sugar; =, maintenance of blood sugar (± 8 mgm. %); +, rise of blood sugar.

glucose per kilo per hour to maintain their initial glucemia level. These results are in accordance with those of other investigators (10). In the hepatectomized

dog, Mann (11) observed that 250 mgm. of glucose per kilo per hour were required in animals which were not anesthetized, but were kept quiet and warm. He also calls attention to the wide individual variation.

Hypophysectomized eviscerated dogs required 100–150 mgm. of glucose per kilo per hour to maintain their glucemia level. This dose is within the range of that for normal dogs. It is worth mentioning that the blood pressure in hypophysectomized dogs tends to fall more rapidly than in other cases. Soskin et al. (7) observed that hypophysectomized dogs gave lower than normal sugar utilization values. In the five dogs studied they report a consumption subnormal even to the level for pancreatectomized animals. These same authors noted that glycogen is very stable, which fact we could not confirm.

In non-eviscerated hypophysectomized dogs Chambers et al. (8) did not observe an increased sugar consumption. The rabbit and rat, on the other hand, seem to need very high sugar levels, as observed by Greeley (9). He used 700 mgm. of glucose in the hypophysectomized rabbit to prevent hypoglycemic levels upon fasting. Russell (4) reported that 250 mgm. of glucose were needed to maintain the glucemia in hypophysectomized and eviscerated rats as compared to 135 mgm. of glucose needed in the eviscerated controls.

The results obtained in pancreatectomized dogs were more uniform and these animals required a maintenance dose of 150–200 mgm. of glucose per kilo per hour. Animals made diabetic through the injection of anterior pituitary extract required from 150–200 mgm. per kilo per hour. Previous thyroidectomy in 4 of these dogs in no way affected the results. The amount of glucose needed to maintain the high initial blood level of a diabetic dog is within the range of the normal, although within the higher values. Soskin (2) observed that anterior pituitary extract does not influence the rate of sugar utilization by the extrahepatic tissues of normal dogs. Soskin (1, 2) also maintains that pancreatectomized animals utilize less sugar at a given glycemia level than do normal dogs at the same level. Mirsky and Broh-Kahn (3) observed an increased peripheral utilization of glucose in the thyroid-treated rabbit.

In our experiments it was found that eviscerated thyroid-treated dogs, just as pancreatectomized animals, required 150–200 mgm. glucose per kilo per hour to maintain the initial glycemia level. This is within the normal range, although within the higher values.

CONCLUSIONS

1. Whether the eviscerated dog can be regarded as normal except for the deprivation of liver and viscera is a questionable hypothesis.

2. Calculation of the carbohydrate balance from the data obtained in our experiments on eviscerated dogs gave improbable results.

3. When the blood sugar curve alone is considered, in the absence of hypotension or asphyxia, it is possible to determine the amount of glucose that must be injected in order to maintain the initial glucemia level. Although individual variations are great, studies on a large number of animals reveal that the maintenance dose of glucose is 100–200 mgm. per kilo per hour for normal dogs, 100–150 mgm. per kilo per hour for hypophysectomized dogs, 150–200 mgm. per kilo

per hour for dogs made diabetic by the injection of anterior pituitary extract, and 150–200 mgm. per kilo per hour in both pancreatectomized and thyroid treated dogs.

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