THE EFFECT OF GLUCOSE ON THE GASEOUS METABOLISM OF THE ISOLATED MAMMALIAN HEART. By C. LOVATT EVANS (*Sharpey Scholar*).

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The object of the present series of experiments was to obtain some data with regard to the influence which glucose exerts on the gaseous exchanges of the normal heart, in order that its gaseous metabolism might subsequently be studied in the hearts of diabetic animals. The question to be decided in the present instance is apparently a simple one—we require to know whether the total gaseous exchange is quantitatively altered when glucose is added to or removed from the circulating blood; we further require to know whether there is any, and if so what, qualitative change in the metabolism of the heart tissue under these circumstances, as judged by the behaviour of the respiratory quotient.

It is well known that the respiratory quotient of the entire organism is raised when carbohydrate food is taken in quantity. One may quote as sufficient proof of this the work of Zuntz and Mering(1) and of Magnus Levy(2), but many others have confirmed this observation.

With regard to carbohydrate introduced parenterally, less work has been done, although the results which have been obtained seem to agree fairly well among themselves. Thus Zuntz and v. Mering (*l.c.*), and Wolfers(3) find that glucose introduced into the blood stream is oxidised and that the oxygen absorption following such an introduction of carbohydrate is not increased although the carbon dioxide production, and therefore the respiratory quotient, is raised. According to Verzár(4) starch introduced into the blood stream is first converted into sugar which is then oxidised in the same manner as glucose.

Little is known of the gaseous metabolism of isolated organs and tissues, or of the extent to which the various food-stuffs are used by different organs as sources of energy. As examples of such investigations one may mention the works of v. Frey and Gruber on skeletal muscle(5), Vernon on the kidney(6), Cohnheim and Pletnew on the intestine(7), Masing on the liver(8), Rohde on the heart(9), Evans on the heart(10), and Starling and Evans on the lungs(11).

The fact observed by Rohde (*l.c.*) and confirmed by the present writer (*l.c.*), that the respiratory quotient of the isolated heart varies within the same limits as that of the entire animal (*e.g.* from ·65 to ·95 or more), indicates that the metabolism of such an isolated organ is qualitatively closely allied to that of the body taken as a whole, or is even identical with it. In other words, the isolated heart has to a great extent the power to oxidise fully to their gaseous end-products the same cell or plasma constituents, as the whole array of organs in the body has when they are working together in the normal way. Rohde's work also shows that the respiratory quotient of the isolated heart is distinctly higher when the animal has been previously fed on carbohydrates, than it is on a mixed diet, which may be considered as further proof in the same direction.

That glucose disappears from the fluid used to perfuse an isolated heart was discovered by Locke and Rosenheim(12) and has been confirmed by all subsequent investigators, the most recent work on the subject being that of Patterson and Starling(13). But the disappearance of the glucose may not mean that it is fully oxidised to carbon dioxide and water. There are other possibilities; thus it may be (1) converted into glycogen, or into a disaccharide, (2) conjugated with some other substance, so that the power of reduction is lost, (3) converted by oxidation into some intermediate product, the full oxidation of which is completed elsewhere in the body, (4) merely absorbed by the tissues. Locke and Rosenheim (*l.c.*) did not find any evidence that a disaccharide was formed, nor that glucose was mechanically absorbed. The latter possibility has also been rejected by Maclean and Smedley(14).

In order to obtain an answer to all these queries, it is essential to know the respiratory quotient of the heart before and after the addition of glucose to the circulating blood, and this is what has been done in the experiments here described. We have also carried out a few experiments on the influence of different diets on the respiratory quotients of the heart.

The effect of adding glucose to the circulating blood.

In the first place, the respiratory exchanges of a normal heart-lung preparation during three hours were taken in order to ascertain whether the respiratory quotients and total exchanges remained constant for this length of time. The heart-lung preparation in this and all the following experiments was made according to the method of Knowlton and Starling (15), and the respiratory exchanges were investigated by means of the apparatus described by the writer in a previous paper (10).

Exp. 1. Dog. Weight of heart 68 grams. Temperature of blood entering heart 36° C. throughout. Gaseous exchanges not corrected for metabolism of the lungs.

Duration of period	Art. press. mm. Hg.	Mean output of left ventr. L. per hr.	Work of left ventr. kgm. per hr.	C.c. O_2 per hr.	C.c. CO_2 per hr.	R. Q.	C.c. O_2[1] per kgm. work	C.c. CO_2 per kgm. work
1 hr.	100	21·1	27·4	309·5	253·0	·82	11·3	9·25
1 ,,	100	19·1	24·8	275·0	230·0	·835	11·05	9·25
1 ,,	130	21·4	36·2	344·6	275·0	·80	9·5	7·6

It is seen that the respiratory quotient has altered but little during the three hours over which it was taken. It is rather more difficult to form an opinion with regard to the total respiratory exchanges, since the work done by the heart varied somewhat from hour to hour. During the first hour these variations were due to alterations in the output of the heart, but it is seen that the amount of oxygen utilised to give 1 kgm. of work was the same in the first two periods, and similar relations held with regard to the carbon dioxide. We may therefore say that the metabolism is constant during these two hours. In the third hour, when the work was further increased by raising both the arterial pressure and the output, the metabolism per kgm. of work is much less, and it is not really comparable with the two preceding periods for this reason.

We may conclude, however, that if the blood-pressure, temperature and output be kept as constant as possible, the total gaseous exchanges will also be fairly constant, a fact which was indicated in a previous paper (10).

As regards the effect of glucose on the heart, the results may be divided into two classes, viz. those in which the R.Q. was lower than ·8 before the addition of the glucose, and those in which it was higher than this. We will first consider the cases in which the quotient was below ·8; these are given in the following experiments.

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[1] The columns showing the amount of oxygen consumed in the performance of a definite amount of work are given in order to eliminate the effects of variations of output, which in some of the experiments are considerable.

Exp. 2. Small dog. Heart weight 56 grams. An attempt was made to feed the dog on rice and meat, but the rice had been refused and the small quantity of meat alone eaten. No food at all had been eaten for 16 hours previous to the experiment. Arterial pressure in apparatus = 55 mm. Hg. Temp. of blood entering heart 36·0—36·2° C. Periods of 30 minutes each.

Period No.	Output L. per hr.	Pulse rate	Kgm. work per hr.[1]	C.c. O_2 per hr.[2]	C.c. CO_2 per hr.[2]	R. Q.	Remarks	C.c. O_2 per kgm. work	C.c. CO_2 per kgm. work
1	14·4	152	10·2	149·4	155	1·04	—	14·6	15·2
2	13·9	152	9·9	233·2	143	·61	—	23·6	14·4
3	13·9	150	9·9	280·0	146	·52	—	28·2	14·7
4	12·9	140	9·2	174·0	145	·83	10 c.c. 10 $^0/_0$ glucose added[3]	18·9	15·8
5	13·2	143	9·4	166·8	147	·88	—	17·8	15·6
6	12·9	136	9·2	164·0	146	·89	—	17·8	15·9
7	12·4	133	8·8	166·6	151	·91	—	19·0	17·2
8	10·6	133	7·5	180·0	159	·88	—	24·0	21·2
9	7·5	125	5·3	179·0	161	·90	—	33·8	30·4
10	7·4	125	5·2	182·0	168	·92	5 c.c. 10 $^0/_0$ glucose	35·0	32·3
			Mean before glucose			·723		22·1	14·8
			Mean after ,,			·887		23·8	21·2
			Increase			·164	$^0/_0$ Increase	8·0	43·0

Exp. 3. Medium sized dog, given castor oil on Feb. 4th, '13, then fed with butter until Feb. 7th when exp. was made. One lung tied off. Gas values not corrected for lung metabolism. Arterial pressure 100 mm. Hg. Temperature 36° ± 0·3° C. Heart 89·5 grm.

Duration of period mins.	Output of left ventr. L. per hr.	Work of left ventr. kgm. per hr.	Pulse rate per min.	C.c. O_2 per hr.	C.c. CO_2 per hr.	R. Q.	Remarks	C.c. O_2 per kgm. of work	C.c. CO_2 per kgm. work
20	11·3	14·7	154	238	180	·76	—	16·2	12·2
20	10·6	13·8	157	245	186	·76	—	17·8	13·5
20	10·6	13·8	146	265	195	·74	—	19·2	14·1
43	10·9	14·2	145	273	204	·75	—	19·2	14·4
20	11·8	15·4	146	298	239	·80	10 grams glucose	19·3	15·5
26	8·9	11·6	146	376	228	·61	—	32·3	19·7
20	5·6	7·3	150	366	283	·80	—	50·0	38·8
21	4·6	6·0	150	368	297	·81	Level of blood raised	61·5	49·5
17	2·8	3·7	143	335	321	·96	—	91·0	87·0
20	1·7	2·2	146	300	262	·87	—	136·0	119·0
			Mean before glucose			·752		18·6	13·5
			Mean after ,,			·808		65·0	55·0
			Increase			·056		249 $^0/_0$	308 $^0/_0$

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[1] By left ventricle, obtained by product, output × pressure.

[2] Not corrected for lung metabolism. One lung was tied off, and therefore in order to correct for lung metabolism the oxygen values should be reduced by 28 c.c. per hour and the CO_2 values by 25 c.c. per hour. (Starling and Evans, This *Journal*, XLVI. p. 413. 1913.)

[3] This amount of glucose raises the glucose in the blood by about 0·3 $^0/_0$.

Exp. 4. Dog. Heart 68 grams. Temp. 36·2° C. Periods 20 mins. B.-P. 140 mm.

Period No.	Left ventr. output L. per hr.	Work of left ventr. L. per hr.	Pulse rate per min.	C.c. O_2 per hr.	C.c. CO_2 per hr.	R. Q.	Remarks	C.c. O_2 per kgm. of work	C.c. CO_2 per kgm. of work
1	15·6	?[1]	143	271	213	·79	—	—	—
2	12·9	23·5	146	369	279	·76	—	15·7	11·9
3	11·3	20·6	141	372	312	·84	1 gram glucose	18·1	15·2
4	6·4	11·7	143	366	300	·83	—	31·3	25·7
			Mean before glucose			·775		15·7	11·9
			Mean after ,,			·835		24·7	20·4
			Increase			·060		57 °/o	72 °/o

Exp. 5. Medium dog. Weight of heart not known. Art. press. 110 mm. Temp. 36° ± ·5° C. Periods 20 mins.

In this experiment glucose was added during several periods in order to keep the amount more nearly constant in the circulating blood.

Gaseous volumes not corrected for lung metabolism.

						Remarks	R. Q.		
1	12·9	18·5	171	261	174	—	·67	14·1	9·4
2	12·9	18·5	150	252	186	—	·74	13·6	10·1
3	12·4	17·8	141	254	193	—	·76	14·3	10·9
4	12·0	17·2	171	258	223	10c.c. 10 °/o glucose	·86	15·0	13·0
5	12·1	17·4	150	285	210	0·5 ,,	·74	16·4	12·1
6	11·2	16·1	134	282	207	0·5 ,,	·73	17·5	12·8
7	12·2	17·5	133	278	219	0·5 ,,	·79	15·9	12·5
8	9·5	13·6	144	282	217	0·5 ,,	·77	20·8	16·0
9	7·5	10·7	143	276	226	0·5 ,,	·82	25·7	22·0
					Mean before glucose		·723	14·0	10·1
					Mean after ,,		·785	18·5	14·7
					Increase		·062	32 °/o	46 °/o

Exp. 6. Dog. Fed for 5 days on butter. Heart 75 grams. B.-P. 120 mm. Temp. 36° C. Periods of 20 mins.

1	12·8	20·0	133	312	246	—	·79	15·6	12·3
2	14·5	22·7	133	324	258	—	·79	14·3	11·4
3	13·2	20·7	120	324	259	—	·80	15·7	12·6
4	15·3	24·0	135	334	272	10c.c. 10 °/o glucose	·81	13·9	11·3
5	15·0	23·4	135	308	269	—	·87	13·1	11·5
6	10·7	16·7	141	318	270	—	·85	19·1	16·2
7	9·2	14·4	133	336	260	—	·77	23·3	18·1
8	—	—	133	384	321	—	·83	—	—
					Mean before glucose		·795	15·2	12·1
					Mean after ,,		·826	17·3	14·3
					Increase		·031	14 °/o	18·3 °/o

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[1] During part of this period the arterial pressure was only 100 mm., so that the work of the left ventricle is not known.

It will be seen on examination of these results that the output of the left ventricle varied considerably during the course of the experiment, especially after the addition of the glucose, which seems to have reduced it in most cases. For this reason, the figures in the column giving the volume of oxygen and of carbon dioxide per kgm. of work are not very constant, but the mean values given at the foot of the columns supply the necessary information with regard to the relative changes in the amounts of the two gases. There is some likelihood that the diminution in the output in the course of the experiments was due to an increase in the viscosity of the blood, possibly by the loss of plasma or water. Thus in the case of Exp. 6 the viscosity of the blood in the first period was 4·26 (water 1·0), and in the eighth period it had increased to 5·2. Whether the glucose is in any way responsible for this change in the viscosity I am not prepared to say, but as will be shown in a future communication, such a change in the viscosity can account for changes in output of the same order as those which have been observed in the experiments here recorded.

Of the experiments given above, the clearest result is that of Exp. 2, in which the addition of glucose raised the quotient from ·723 to ·887. In no other case has such a marked result been obtained. The effect of the glucose on the oxygen and carbon dioxide per kgm. of work is equally striking. The oxygen intake only increased 8 % while the CO_2 production increased 43 %. These results are similar to those of Magnus-Levy (*l.c.*) for the administration of glucose by the mouth in men and to those of Zuntz and v. Mering (*l.c.*) for introduction of glucose into the blood in dogs. The respiratory quotient is raised not by fall of the oxygen usage but by rise of the carbon dioxide production.

The results of the other four experiments given here are similar, but the rise of R.Q. is not so marked. The rises of quotient are in all cases due to the increase in the carbon dioxide production, and not to fall of oxygen usage; the latter in fact have increased greatly in some cases, though never so much as the carbon dioxide production, as a glance at the mean values at the bottom of the columns will show.

In none of the above cases has the respiratory quotient been raised over ·9 by the addition of glucose to the circulating blood, and in this respect the results differ from those of the observers quoted above for experiments on the entire animal. It may be that the isolated organ is deprived of some accessory factor by means of which it is normally enabled to more fully oxidise the sugar which is offered to it, or, on the other hand it may be that the heart does not readily relinquish the oxidation of other constituents such as protein and fat, even in the presence of excess of carbohydrate. The fact that glucose does rapidly disappear from the circulating blood seems to be opposed to the latter hypothesis, while the fact that the hearts of some dogs without treatment with glucose will show a respiratory quotient higher than ·9 seems opposed to the first idea.

It is of interest in this connection to calculate roughly the relative amounts of protein, carbohydrate, and fat consumed by the heart. In order to do this, it is necessary to make certain provisional assumptions. Thus we must assume that only proteins, carbohydrates, and fats are being oxidised; we must further assume that the oxidation of all these constituents is *complete*. Finally, in default of direct knowledge we must make an assumption as to the relative share of protein in metabolism. We can then calculate the proportion of the energy which is derived from the oxidation of fat and carbohydrate, according to the method of Schumburg and Zuntz(16). These workers believe that about 15 % of the oxygen used goes to oxidise protein.

It may be objected that this figure, which relates to the metabolism in man, cannot be applied to the case of carnivorous animals such as the dog. It has been shown by Rubner(17), however, that in well-fed and in fasting dogs from 8 to 25 % of the total energy is derived from protein break-down, the mean being about 14 %. Benedict also (18) has shown that in fasting men from 13 to 17 % of the energy is derived from protein.

It is moreover not essential to know the protein figure more than approximately for the purposes of the present calculation. The results of such a calculation are given in the following table.

			Percentage of energy derived from oxidation of				
Exp. No.		R. Q.	Protein	Fat		Carbohydrate	
2	Before glucose	·723	15	85	Mean 74·4 %	0	Mean 10·6 %
3	,, ,,	·752	15	75		10	
4	,, ,,	·775	15	66		19	
5	,, ,,	·723	15	85		0	
6	,, ,,	·795	15	61		24	
2	After glucose	·887	15	29	Mean 48·6 %	56	Mean 36·4 %
3	,, ,,	·808	15	55		30	
4	,, ,,	·835	15	46		39	
5	,, ,,	·785	15	64		21	
6	,, ,,	·826	15	49		36	

These figures are of interest in showing to what extent the metabolism of the carbohydrate is changed when glucose is present in the circulating liquid. Of course, if glucose is only partially oxidised by the isolated organ the case is quite a different one.

It has been shown by Cruickshank(19) that under conditions similar to those which obtained in these experiments the heart does not draw to any very great extent on its store of glycogen. Thus he gives ·463% as the average content of the fresh heart (seven experiments), while hearts which had worked for about two hours after isolation gave ·494 % as the mean of six experiments. Under the influence of adrenalin, however, much of the glycogen disappears even when the glucose content of the blood is kept high. Patterson and Starling (*l.c.*) find that the glucose consumption of the heart-lung preparation, when adrenalin is not added, does not on the average exceed 2 mg. per gram of heart per hour. Taken in conjunction with Cruickshank's determination given above, this would mean that a heart weighing 50 grams would, together with its lungs utilise 100 mg. of carbohydrate per hour. It is immaterial to our present purpose to discuss whether such a heart uses 100 mg. of glycogen, which it replaces from the blood-sugar, or whether it uses the 100 mg. of sugar direct from the blood and leaves the glycogen store intact. Since 1 mg. of glucose requires ·75 c.c. of oxygen for complete oxidation, such a heart-lung preparation would utilise 75 c.c. of oxygen per hour for oxidation of carbohydrate. I have shown (*l.c.*) that the oxygen requirement of a heart-lung preparation is about 4 to 5 c.c. per gram of heart per hour. Thus a heart-lung preparation in which the heart weighed 50 grams would use 200 to 250 c.c. of oxygen per hour, and if we then allow 75 c.c. of this as the amount used in oxidation of carbohydrate, this gives us about 27 to 33 % of the oxygen utilised for the oxidation of carbohydrate. This agrees fairly well with the calculation made above from the respiratory quotient in the similar condition where glucose was added to the blood. Until we know definitely, however, to what extent the working heart draws upon its own store of glycogen, it is not possible to decide whether the glucose which is attacked is fully oxidised or not. There is moreover the possibility that the glucose may be attacked but only partially oxidised, the intermediary product formed being still capable of reducing Fehling's solution.

The following experiments in which glucose was added to the blood when the primary R.Q. of the heart without treatment with sugar was above ·8 were made in order to ascertain whether in those hearts the sugar was more readily oxidised than in those having a low quotient. If the R.Q. is originally lower than ·8 there is an indication that fat is

Exp. 7. Dog. Heart 48·5 grams. One lung tied off. Arterial pressure 88 mm. Temp. 37·5° C. 20 min. periods. Values not corrected for lung metabolism.

Period No.	Output of left ventr. L. per hr.	Work of left ventr. kgm. per hr.	C.c. O_2 per hr.	C.c. CO_2 per hr.	R. Q.	C.c. O_2 per kgm. of work	C.c. CO_2 per kgm. of work	Remarks
1	15·6	17·9	66·8	62·3	·93	3·7	3·5	—
2	10·0	11·4	68·0	57·2	·84	5·9	5·0	—
3	9·0	10·3	59·0	54·7	·93	5·7	5·3	—
4	10·1	11·6	60·2	53·2	·89	5·2	4·6	0·5 gram glucose in 5 c.c. water added.
5	9·7	11·1	58·3	51·5	·88	5·3	4·6	—
6	10·0	11·4	60·2	52·5	·87	5·3	4·6	—
7	9·7	11·1	57·8	49·7	·86	5·2	4·5	—
8	10·3	11·8	57·3	52·4	·91	4·9	4·4	0·5 gram glucose in 5 c.c.
9	9·1	10·4	58·2	49·2	·85	5·6	4·7	—
		Mean before glucose			·900	5·1	4·60	
		Mean after ,,			·875	5·25	4·57	
		Difference			− ·025	+3 %	−1·0 %	

Exp. 8. Dog. Heart 33 grams. Arterial pressure 80 mm. Temp. 37·2° C.

1	12·0	12·5	162	139	·85	13·0	11·1	
2	11·3	11·8	158	141	·89	13·4	11·4	
3	11·7	12·2	158	143	·90	13·0	11·7	10 c.c. 10 % glucose.
		Mean before glucose			·87	13·2	11·25	
		Mean after ,,			·90	13·0	11·7	
		Difference			+ ·03	− 1·5 %	+4 %	

Exp. 9. Dog. Heart 50·5 grams. Arterial pressure 30 mm. Hg.[1] Temp. 36·4° C.

1	10·6	17·9	158	140	·89	8·8	7·8	—
2	9·7	16·4	174	165	·95	10·6	10·1	—
3	10·0	16·9	182	165	·91	10·8	9·8	10 c.c. 10 % glucose.
4	9·5	16·1	191	178	·94	11·8	11·1	—
		Mean before glucose			·920	9·7	8·95	
		Mean after ,,			·925	11·3	10·45	
		Difference			+ ·005	+16 %	+17 %	

Exp. 10. Dog. Diet of meat and fat. One lung tied off. Arterial pressure 55 mm. Heart 67 grams. Temp. 36·5° C. Half hour periods.

1	12·0	8·6	192	169	·88	22·4	19·7	—
2	12·0	8·6	212	185	·88	24·6	21·5	—
3	11·3	8·1	204	180	·88	25·3	22·2	10 c.c. 10 % glucose.
4	11·1	7·9	219	194	·88	27·8	24·6	—
		Mean before glucose			·88	23·5	20·6	
		Mean after ,,			·88	26·55	23·4	
		Difference			0	13 %	14 %	

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[1] At a higher pressure beats were dropped.

being oxidised to supply some of the energy, and it might be urged that such a tissue will not immediately turn over to an exclusive consumption of carbohydrate and protein. But when the R.Q. is higher than ·8 it might be assumed that the further supply of glucose might result in a much greater usage of carbohydrate, in a heart already accustomed to this mode of metabolism.

It will be seen from these experimental results that in these cases where the R.Q. was above ·8 to begin with, the increase of oxygen usage per kgm. of work is much less than it was in the previous series in which the initial R.Q. was low. The reason for this is that the output of the heart remained much more constant in these cases, since the experiments were of shorter duration.

In these four experiments it is seen that the effect of adding glucose to the circulating blood is but small; in experiments 9 and 10 we may say that there is no effect, either as regards the respiratory quotient or the total exchanges, since the oxygen intake and the CO_2 formation increased together to the same extent. Of the other two experiments, No. 7 showed a slight fall, due to increase of oxygen absorption, while No. 8 showed a similar small rise in R.Q. due to increased CO_2 production.

In one or two cases in which larger amounts of glucose were added (10 grams), there was a marked fall in the R.Q. due to increased oxygen intake, but it was not thought to be necessary to give these results in detail, as the amounts of glucose added were so large that there was a possibility of it having interfered with the normal processes of metabolism, in some such manner as was found to be the case by Verzár(20) when sodium chloride was injected into the circulation of the intact animal.

The effect of previous diet on the respiratory quotient of the heart.

Rohde has found that after feeding cats with a rich carbohydrate diet, the amount of sugar burned by the heart was much increased in relation to the "reserve substances" (fat) used. This fact has not been directly tested, but I have taken the respiratory quotients of some dogs' hearts after the animals had been fed on carbohydrate. The results of four such experiments are given below.

In these four experiments the respiratory quotients are high, though not remarkably so. The quotients obtained in these cases are similar to those which Rohde obtained in his experiments with the carbohydrate feeding of cats. They are not so high as most of the published

Exp. No.	Weight of heart	Duration of observation	C.c. O_2 per hr.	C.c. CO_2 per hr.	R. Q.	Remarks
11	41	3½ hrs.	137	128	·935	Dog fed on rice and minced beef 4 days.
12	70	2 ,,	192	165	·855	Biscuit 3 days.
13	58·5	1½ ,,	203	164	·81	Biscuit and sugar 3 days.
14	—	¾ ,,	203	186	·915	50 grams glucose by stomach tube for 6 days previously.

figures which show the effect of carbohydrate feeding on man (and which are usually well over ·9), although they are in two cases higher than any of those given here in which glucose was added to the blood.

The converse experiment of deprivation of carbohydrate was also tried. Experiments 2, 3, 6 and 10 are examples of the results obtained. The respiratory quotients obtained were ·723, ·752, ·795 and ·88 respectively, from which it may be seen that in cases where proteins as well as carbohydrates were withdrawn (the first three cases) the R.Q. can be decidedly low, but that when plenty of meat is given, as in Exp. 10, the quotient may be as high as it often is when a heavy carbohydrate diet is given. This can probably be explained as being due to the production of glycogen from the protein. It seems therefore that the heart will utilise some glucose or other carbohydrate if any is available, as is seen in the fact that the R.Q. is raised on the addition of glucose to the circulating blood, even after prolonged deprivation of carbohydrate. But, on the other hand, the carbohydrate consumption of the isolated heart is not great, since it is not easy, by the administration of carbohydrate to the heart direct in the form of glucose, to raise the respiratory quotient of the heart to such an extent as that of the entire animal is raised by similar treatment. In this connection it is interesting to note that Cruickshank (*l.c.*) finds that it is not easy, either to increase the glycogen content of the heart to a very marked extent, or, even by feeding with fat, or by starvation, to entirely, or even greatly, reduce the glycogen content.

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CONCLUSIONS.

1. When glucose is added to the circulating blood of a heart-lung preparation, the respiratory quotient of the preparation is raised.

2. This result is of importance as indicating that the isolated organ has the same power as has the entire organism to carry out to full completion the oxidative processes which it commences.

3. The addition of glucose does not raise the respiratory quotient beyond a certain maximum, which usually lies below ·9.

4. The respiratory quotient of the heart is markedly increased by previous carbohydrate diet, and it is then often decidedly higher (above ·9) than that which is obtained after the addition of glucose to the blood.

5. Although both the oxygen intake and the carbon dioxide production are in most cases increased when glucose is added to the blood, the rise of the respiratory quotient is due to a greater increase in carbon dioxide formation relative to the oxygen intake.

6. It is calculated that the normal heart of the dog obtains about one third of its energy supply by oxidation of carbohydrate. But in animals deprived of carbohydrate for some time previously the amount may be, and usually is, much less than this.

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