CCLXXXIX. THE RESPIRATORY QUOTIENTS OF NORMAL AND TUMOUR TISSUE.

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THE respiratory quotients of slices of various tissues have been studied by manometric methods by a number of workers, and especially by Dickens and Šimer [1930; 1931]. In the course of work on other problems many of the results of the authors named have been confirmed, but in some cases important differences from their findings have been observed. A large number of experiments have therefore been made to confirm these agreements and differences and the results are reported in the present paper.

EXPERIMENTAL.

The differential manometric apparatus of Dixon and Keilin [1933] was used and the technique described by Elliott and Schroeder [1934] followed. Except where otherwise stated, the bicarbonate-containing medium used was that described by Krebs [1932] and it contained 0.24% glucose. The experimental period was 90 min. unless otherwise specified. The R.Q. is given by the expression

$$\frac{(h_1 - h_2) \cdot k_{\text{CO}_2}}{h_2 \cdot k_{\text{O}_2}},$$

where h_1 is the reading obtained when acid has been tipped into both vessels, killing the tissue and liberating total CO_2 , and h_2 is the reading given after all CO_2 has been absorbed by alkali, being a direct measure of the O_2 uptake. (In a normal experiment both h_1 and h_2 are negative.) k_{O_2} and k_{CO_2} are the vessel constants for oxygen and carbon dioxide. Small errors in h_2 have a negligible effect on the observed R.Q., but errors in h_1 can affect the value appreciably, especially when the oxygen uptake is not very large. For this reason a large number of blank experiments were made, *i.e.* experiments for the usual period but without tissue. It was found in the majority of cases that there was a negative h_1 reading, usually small but occasionally quite large, up to 2 mm., equivalent to 25 $\mu\text{l.}$ of gas. When the total oxygen uptake is 500 $\mu\text{l.}$, such an error would affect the R.Q. by about 0.05. In 33 blank experiments with various manometers, the h_1 reading varied from 0.0 to -2.0 mm., the mean being -0.9 mm., corresponding to 12 $\mu\text{l.}$ of gas. All our R.Q. values have been corrected for this mean error, and the limits of error are shown in the tables. (The actual uncorrected value obtained for the R.Q. is in each case the lower limit of the value given in the tables.) It is not understood why this error in h_1 should occur, or why it is always negative. Experiments in which anhydrous lanoline was placed on the bottom of the vessel showed that this grease absorbed a large amount of CO_2 , or it occluded bicarbonate, and the CO_2 was only slowly liberated by acid. Rubber grease (Lubriseal, A. H. Thomas Co.) did not do this and does not melt at 37° as lanoline does. The use of rubber grease throughout appeared to give slightly better results, though often an appreciable negative h_1 reading was still observed.

Terms.

We have employed the term, $-Q_{O_2}$, introduced by Warburg to express the rate of oxygen uptake, and the term, Q_A , as used by Elliott and Schroeder [1934] to express the rate of acid formation or glycolysis. $Q_A^{O_2}$ and $Q_A^{N_2}$ differentiate acid formations under aerobic and anaerobic conditions.

Chick embryo, brain, retina.

With these three tissues, Dickens and Šimer found R.Q. 1. For the chick embryo, Needham [1933] also found R.Q. 1, and we have confirmed this result. Thus, in two experiments with 4-day chick embryos the results shown in Table I were obtained.

Table I. *Four-day chick embryos.*

	Dry wt. mg.	$-Q_{O_2}$	R.Q.	Q_A
9 large embryos in each vessel	28.9	13.3	0.99 ± 0.02	+0.6
11 smaller embryos in each vessel	17.0	13.2	1.05 ± 0.04	-1.3

With brain cortex of rats and rabbits, we have not observed an R.Q. as high as 1.0 except in one abnormal experiment described below. Table II shows a number of the results. As far as possible, pure cortical matter was used and the slices were handled as gently as possible. In the last experiment on rabbit tissue, which was regarded at the time as the best experiment, a relatively large amount of tissue was used, and the slices, before introduction into the vessels, were drained, not on filter-paper, but on thin glazed perforated porcelain discs with filter-paper underneath the discs.

Table II.

	Dry wt. used mg.	$-Q_{O_2}$	R.Q.	Q_A	Remarks
Rat brain cortex.					
1	25	10.9	0.81 ± 0.03	2.5	—
2	21	14.4	0.88 ± 0.02	3.2	—
3	14	15.5	0.91 ± 0.03	1.3	Krebs medium
	14	13.1	0.93 ± 0.04	3.0	Warburg medium
4	22	14.9	0.86 ± 0.02	1.3	Krebs medium
	22	16.6	0.78 ± 0.02	6.1	Warburg medium
5	13	14.0	0.93 ± 0.03	0.9	Krebs medium
	13	16.4	0.90 ± 0.03	5.3	Warburg medium
6	28	13.6	0.87 ± 0.02	1.4	—
7	22	15.6	0.84 ± 0.03	2.0	1½-hour experimental period
8	22	15.1	0.85 ± 0.02	1.9	—
9	22	13.6	0.83 ± 0.03	2.8	1½-hour experimental period
a	24	13.2	0.89 ± 0.02	1.9	1½-hour experimental period
10 b	12	13.3	0.93 ± 0.02	2.5	5-hour experimental period
c	19	7.9	1.00 ± 0.04	4.5	Last 2 hours only of 5 hours' incubation
Mean of all except 10b and 10c: 0.86.					
11	19	5.4	0.95 ± 0.06	0.0	Glucose absent
12	24	8.2	0.72 ± 0.04	2.2	Glucose absent
13	41	5.4	0.87 ± 0.04	0.2	Glucose absent
14	16	—	—	13.0	Anaerobic, glucose present
Rabbit brain cortex.					
15	16	8.2	0.89 ± 0.06	4.2	—
16	19	8.5	0.83 ± 0.05	4.4	—
17	25	8.9	0.95 ± 0.04	1.8	—
18	28	8.9	0.85 ± 0.04	1.8	Best experiment
Mean		0.88			

Ashford and Holmes [1931] obtained results similar to those in Table II with rabbit brain in ordinary Ringer solution using the rather crude method described by Dixon and Elliott [1929]. With rat brain Himwich *et al.* [1934] found the R.Q. to be 0.92 using the method of Warburg with phosphate-containing medium.

Dickens and Šimer [1931] mention that older rats tend to have a lower brain R.Q.; all animals here used were young and healthy. The Krebs medium generally used in this work contains traces of Mg, PO_4 and SO_4 as well as the other salts present in the bicarbonate medium of Warburg [1926] which was used by Dickens and Šimer in their later work [1931]. Several duplicate experiments with the two media showed that differences in medium could not account for the different results. It is interesting to note however that the aerobic glycolysis or acid formation, Q_A , is in every case higher in the less complete medium of Warburg.

A possible explanation of the results of Dickens and Šimer lies in the fact that their experimental period was 5 hours. This is suggested by Exp. 10, Table II. For this experiment, slices were obtained from four rat brains and fair samples taken for each of three manometers. One of these manometers was run for the usual 90 min., using a large amount of tissue to minimise the relative effect of experimental errors. The second manometer ran for 5 hours and it is seen that the average R.Q. is definitely higher over the longer period. The tissue for the third manometer was kept for 3 hours at 37° in Krebs medium with O_2/CO_2 gas mixture bubbling through the medium. The tissue, after having been rinsed in bicarbonate-free Ringer solution in the usual way, was then introduced into the vessels of the manometer, and a 2-hour run was made. In this case the R.Q. was unity. A further interesting observation was made in this experiment. With the short period manometer the glycolysis was small and the movement of the manometer fluid during the experimental period was very small. In the 5-hour experiment the manometer fluid scarcely moved for the first 3 hours and then started a movement in the positive direction, indicating the onset of glycolysis. With the third manometer, the tissue for which had already been incubated aerobically for 3 hours before introduction, the manometer fluid started moving at once and the glycolysis was quite considerable. It appears therefore that when the tissue is kept for some time, abnormal metabolism sets in with higher R.Q. and aerobic glycolysis. Rosenthal [1931] observed an increased anaerobic glycolysis after a preliminary period of aerobiosis. Experiments with rat brain in the absence of glucose showed that the oxygen uptake was much decreased and the R.Q. was variable but not necessarily lowered. These results agree with those of Loebel [1925] and of Dickens and Greville [1933, 1]. Exp. 14 illustrates the well-known high anaerobic glycolysis of brain tissue [Warburg *et al.*, 1924; Loebel, 1925].

For the experiments with retina, the room was darkened and the retinas extracted under the least possible light. For two experiments (Nos. 4 and 6) the manometer vessels were painted black with a suspension of lamp-black in shellac. After removing the eyes from the animals they were cut equatorially by one snip with fine scissors, the lens was removed and the retina carefully dislodged with a thin flattened glass spatula and dropped into Krebs medium through which O_2/CO_2 was passing. Immediately before the experiment, the tissue was rinsed in ordinary Ringer solution, drained on thin glazed perforated discs, and equal amounts, as judged by eye, were introduced into the two vessels. In Table III, results of the experiments are shown and again it is seen that R.Q. values of less than unity were obtained. The discrepancy between these

results and those of Dickens and Šimer may be explained, as with brain, by the longer experimental period used by the latter authors. A very high aerobic glycolysis was found, as was first observed by Warburg *et al.* [1924]. In Exp. 3, where both Krebs and Warburg media were used, the R.Q. were not significantly different, nor were the oxygen uptakes, considering the high probability of error in determining such small dry weights. The glycolysis in the simpler medium however was considerably higher than in the more complete medium of Krebs. Warburg *et al.* [1924] and Kubowitz [1929] consider that the aerobic glycolysis found with retina is not normal but is produced by damage; in this case it would seem that use of the Krebs medium results in less of this damage. The same would apply to the effects mentioned above with brain tissue. In the first three experiments of Table III, the movement of the manometer fluid followed an

Table III. *Rat retinas.*

	Approx. no. of retinas in each vessel	Dry wt. mg.	$-Q_{O_2}$	R.Q.	Q_A	Remarks
1	5	4.7	26.4	(0.70 ± 0.05)	49.5	2 hours; O_2 uptake too small for reliable R.Q.
2	8	6.6	23.3	0.89 ± 0.03	37.0	Krebs medium Warburg medium } $2\frac{1}{2}$ hours
3	8	4.7	26.7	0.93 ± 0.04	49.8	
4	10	6.1	32.6	0.92 ± 0.03	43.8	2 hours
5	11	8.0	26.7	0.91 ± 0.03	29.7	2 hours
6	20	13.6	27.9	0.96 ± 0.02	22.1	2 hours
	25	18.6	27.5	0.87 ± 0.02	20.7	$1\frac{1}{2}$ hours
Mean			0.91			

almost linear course showing that the rate of glycolysis was almost constant. In Exp. 4 the glycolysis fell off somewhat and in Exps. 5 and 6, where larger amounts of tissue were used, the rate of glycolysis fell off continuously and considerably; in the last 30 min. with Exp. 4 the manometer moved only about $\frac{1}{4}$ as much as in the first 30 min. This falling off is reflected in the lower average acid formation (Q_A) with Exps. 4 and 5. This change in the rate of glycolysis can scarcely be explained by a decrease in the concentration of glucose since in all experiments 7.2 mg. glucose were present initially and the total glucose that would be removed by glycolysis varied between 2.1 mg. for Exp. 1 and 2.7 mg. for Exps. 4 and 5. A further 0.4–1.2 mg. might have been removed if only carbohydrate or lactate were oxidised, but the low R.Q. does not indicate this. The glycolysis therefore falls off much more rapidly than the glucose concentration. Further, the bicarbonate concentration in the medium was more than sufficient to maintain a normal p_H . Possibly there is some glycolysis-inhibiting substance in the retina which becomes effective when there is a greater amount of retina in the 3 ml. of medium.

Testis.

For this tissue Dickens and Šimer [1931] found R.Q. about 0.9 and results shown in Table IV are similar or a little higher. In the absence of glucose the respiration is decreased and the R.Q. lowered, and similar results are given by Dickens and Greville [1933, 1]. The high anaerobic glycolysis [Warburg, 1927] is shown in one experiment.

Liver.

Dickens and Šimer [1931] found that the R.Q. of liver tissue in bicarbonate-Ringer solution varied between 0.55 and 0.76, the lower values being obtained with fasting animals, and recently Gemmill and Holmes [1935] gave values

Table IV. *Testis.*

Dry wt. mg.	$-Q_{O_2}$	R.Q.	Q_A	Remarks
14	12.4	0.91 ± 0.05	4.8	—
31	11.8	0.96 ± 0.02	4.3	—
18	11.1	0.92	6.0	1 hour. O_2 uptake too small for accuracy
27	11.9	0.95 ± 0.03	4.9	—
13	6.5	0.69 ± 0.09	2.1	Glucose absent
33	4.7	0.69 ± 0.05	1.1	Glucose absent
33	6.6	0.57 ± 0.04	1.7	Glucose absent
17	—	—	13.4	Glucose present, anaerobic

between 0.61 and 0.87 for rats on a normal diet. Results obtained in this laboratory with well-fed animals are in general higher than these figures and very frequently R.Q. values of 1 have been obtained. Out of 78 experiments with rats on the normal diet, or especially well-fed, 42 gave R.Q. values between 0.95 and 1.15 and the remainder varied between 0.95 and 0.70. The animals used were all of the Germantown albino strain between 3 and 12 months old, and they were fed on a standard diet of lettuce, bread, boiled mixed cereal grains and some milk. It may be mentioned that at first it appeared that a very high R.Q. was associated with cancer in other parts of the body, with pregnancy and with the healing of wounds, since a long series of R.Q. values of unity were obtained with the livers of rats in such conditions. This now seems to have been simply coincidence, and no consistent differences between normal and tumour-bearing animals in the Q_{O_2} , R.Q. or Q_A of their livers were found. Such high R.Q. values could not be regularly and deliberately induced by special feeding. The difference between these results and those of the above authors makes it seem possible that the metabolism of rat liver tissue may depend to some extent on the strain to which the animal belongs, although Dr M. Dixon (private communication), working in the same laboratory as Gemmill and Holmes, has found liver R.Q. values of 1. The R.Q. was not affected by using the Warburg bicarbonate medium in place of the usual Krebs medium.

The anaerobic glycolysis of a number of livers was measured. In the case of livers with high R.Q. the anaerobic glycolysis was rapid, as high as that of testis or brain, but usually it fell off very quickly. This falling off may be associated with the disintegration of the tissues under anaerobic conditions. It should be emphasised that the glycolysis of liver tissue takes place at the expense of its glycogen stores [Rosenthal and Lasnitzki, 1928; Rosenthal, 1929]. The rate of glycolysis is usually even higher when glucose is absent from the medium than when it is present. Similarly the R.Q. is independent of the presence of glucose in the medium [see also Dickens and Greville, 1933, 1]. In fasting rats both the R.Q. and the glycolysis are low and the livers contain practically no glycogen. With fasting rats the R.Q. values observed by us are lower than those of Dickens and Šimer. In 11 experiments with livers of normally fed mice one value of 0.99 and one of 0.93 were found, the remainder being between 0.49 and 0.81. A few of the numerous results obtained are shown in Table V.

Kidney.

For rat kidney (cortex *plus* medulla) Dickens and Šimer [1930; 1931] gave R.Q. values from 0.76 to 0.92, and the results given in Table VI for cortical tissue agree well with this. In the absence of glucose the oxygen uptake and R.Q. are slightly decreased, which is in agreement with the observations of Dickens and Greville [1933, 1]. Results very similar to these were also obtained by Shorr

et al. [1930] using phosphate-Ringer solution as medium. Crabtree [1929], using phosphate-free Ringer solution, also found a slightly higher Q_{O_2} in the presence of glucose.

Table V. *Metabolism of liver tissue.*

Exp.	Glucose	$-Q_{O_2}^*$	R.Q.†	$Q_A^{O_2}$	$Q_A^{N_2}$	
					1st 30 min.	3rd 30 min.
Normal rat	{ -	14.0	1.00	1.4	7.7	2.6
	{ +	12.3	1.04	1.4	8.5	3.7
Normal rat	{ -	11.8	1.05	2.5	12.2	10.7
	{ +	12.0	1.03	3.0	9.9	8.2
Normal rat	{ -	12.2	1.04	0.8	11.8	3.5
	{ +	10.5	1.07	2.2	6.4	2.6
Normal rat	-	12.0	1.05	0.6	13.4	2.9
Normal rat (pregnant)	-	12.6	0.90	0.6	10.4	3.1
Normal rat	+	9.9	0.80	2.5	2.7	1.1
Normal rat { Krebs medium	+	17.0	0.79	3.2	—	—
	+	15.7	0.77	3.9	—	—
Normal rat { Warburg medium	+	14.2	0.78	1.1	—	—
	+	14.1	0.71	1.9	—	—
Normal rat	{ +	13.0	0.77	1.4	4.2	3.4
	{ -	—	—	—	2.0	1.4
Rat starved 20 hours	-	9.8	0.46	2.5	2.6	1.2
Rat starved 20 hours	-	4.9	0.48	1.6	0.2	2.2
Rat starved 24 hours	{ -	12.7	0.53	2.8	—	—
	{ +	11.1	0.56	2.3	—	—
Normal mouse	-	16.3	0.99	1.8	—	—
Normal mouse	-	15.4	0.82	1.0	—	—
Normal mouse	-	13.6	0.64	1.8	—	—
Normal mouse (pregnant)	-	14.8	0.49	3.5	—	—

* These values for Q_{O_2} appear higher than those of Gemmill and Holmes [1935]. This is probably due to the fact that the dry weights of tissue actually used were determined after each experiment. Gemmill and Holmes followed the perhaps more rational method of deducing the dry weight from the initial moist weight of the tissue used and the wet weight/dry weight ratio of a separate sample.

† Corrected values given. Limits of error due to blank error ± 0.02 in all cases.

Table VI. *Kidney cortex.*

Animal	Glucose	No. of exps.	$-Q_{O_2}$			R.Q.*		
			Highest	Lowest	Mean	Highest	Lowest	Mean
Rabbit	Present	9	15.5	11.8	14.1	0.92	0.85	0.88
Rabbit	Absent	18	14.7	10.4	12.0	0.80	0.72	0.77
Rat	Present	7	24.3	19.0	22.5	0.90	0.78	0.85
Rat	Absent	7	21.5	17.0	19.3	0.84	0.75	0.78

* Corrected values given. Limits of error due to blank error ± 0.03 in all cases.

Tumours.

The tumours studied were the Philadelphia No. 1 rat sarcoma [Waldschmidt-Leitz *et al.*, 1933] and the Walker No. 256 carcinoma. The tumours were taken 16–28 days after implantation and the slices used showed little or no necrosis. In Table VII are summarised the results of a large number of experiments, and results of specific experiments on the effect of glucose on the metabolism are given in Table VIII.

With Jensen rat sarcoma and a slow-growing carcinoma, Dickens and Šimer [1931] obtained mean R.Q. values of 0.78 and 0.77 in bicarbonate medium. The results here shown are, on the average, distinctly higher and our results differ sharply from theirs in that we have found a number of tumours with R.Q. values of about 1. The tumours showing this type of metabolism appeared quite normal,

Table VII. *Metabolism of rat tumour tissue.*

Tumour	Glucose	No. of exps.	$-Q_{O_2}$			R.Q.*			$Q_A^{O_2}$		
			Highest	Lowest	Mean	Highest	Lowest	Mean	Highest	Lowest	Mean
Phila.	Present	28	12.7	9.9	10.8	1.06	0.72	0.89†	17.6	11.3	14.7
No. 1	Absent	20	14.1	10.6	12.0	0.92	0.77	0.82	+0.6	-1.5	-0.5
Walker	Present	2	12.5	11.3	11.9	0.89	0.84	0.87	15.9	13.2	14.6
No. 256	Absent	4	11.9	10.3	11.4	0.86	0.80	0.83	+0.2	-0.7	-0.2

* Corrected values given. Limits of error due to blank error ± 0.03 .

† The distribution of the results was as follows:

R.Q.	Over 0.95	0.95 to 0.90	0.90 to 0.85	0.85 to 0.80	0.80 to 0.75	0.72
No. of exps.	7	5	6	8	1	1

Table VIII. *Effect of glucose on the metabolism of Phila. No. 1 sarcoma.*

Glucose	$-Q_{O_2}$	R.Q.	Q_A	
Absent	12.5	0.80 ± 0.02	0.0	
0.24 %	{ 10.2	0.91 ± 0.03	14.7	Duplicates
	{ 10.0	0.94 ± 0.03	16.5	
1.20 %	8.2	1.00 ± 0.03	12.5	
Absent	{ 11.3	0.82 ± 0.03	-0.6	Duplicates
	{ 11.6	0.83 ± 0.02	-0.9	
0.24 %	{ 10.8	0.84 ± 0.03	13.8	Duplicates
	{ 9.9	0.88 ± 0.04	12.9	
0.24 %	11.9	0.86 ± 0.04	17.6	
1.20 %	11.3	0.92 ± 0.03	16.6	

had been growing rapidly and showed the usual high aerobic glycolysis. Further, one such tumour was used in the work reported in the preceding paper [Elliott *et al.*, 1935, Table VIII] and the deficiencies in metabolism seemed the same as with tumours with a lower R.Q. High values of R.Q. for tumour tissues have recently been reported by Jares [1935]. Using phosphate-buffered Locke solution as medium he found R.Q. 0.99 for a slow-growing Jensen sarcoma, 0.97 for a No. 180 mouse sarcoma, and for the No. 256 carcinoma he gives results up to 0.95 with a mean value of 0.89. Dickens and Šimer [1930] themselves observed quite high values of R.Q. in phosphate-Ringer medium with a slow-growing rat sarcoma (0.97), with the Rous chicken sarcoma (0.92), with a spontaneous mouse tumour (0.91) and with a human tumour (0.86).

It is interesting to note that with Phila. No. 1 tumour the respiration is slightly greater in the absence of glucose than in its presence, but that glucose does cause a slight rise in R.Q. These points are shown in Table VIII and in the average results in Table VII. Crabtree [1929] also showed increased O_2 uptake in the absence of glucose with tar carcinoma 2146 and Jensen rat sarcoma, though Dickens and Greville [1933, 1] did not find this. Crabtree drew "the tentative conclusion that glycolytic activity exerts a significant checking effect on the capacity for respiration of tumour tissue". The effect of glucose on R.Q. would suggest that to a certain extent the sugar also replaces other substances as respiratory substrate.

DISCUSSION.

A summary of the R.Q. of the various tissues in the presence of glucose is given in Table IX.

The results here reported agree with those of Dickens and his co-workers in many details but in the following important respects the observations differ from those of Dickens and Šimer [1930; 1931]. For brain and retina they gave R.Q. 1 while our results are lower than this. For liver R.Q. 1 has frequently been found which is higher than any reported by other authors. For tumour also

Table IX. *R.Q. in presence of glucose.*

Animal	Tissue	No. of exps.	R.Q.		
			Highest	Lowest	Mean
Rat	Brain—grey matter	13	0.93	0.78	0.86
Rat	Retina	5	0.96	0.87	0.91
Rat	Testis	4	0.95	0.91	0.94
Rat	Kidney cortex	7	0.90	0.78	0.85
Rat	Liver of fed animals	78	1.15	0.70	0.94
Rat	Phila. No. 1 sarcoma	28	1.06	0.72	0.89
Rat	Walker No. 256 carcinoma	2	0.89	0.84	0.87
Rabbit	Brain—grey matter	4	0.95	0.83	0.88
Rabbit	Kidney cortex	9	0.92	0.85	0.88
Mouse	Liver of fed animals	9	0.99	0.64	0.78
Chick	Embryo	2	1.05	0.99	1.02

many of the results here given are higher than those of Dickens and Šimer and again several values of *R.Q.* of about 1 have been found. Consideration of their results led Dickens and Šimer to make the generalisation that all normal tissues which showed high glycolytic activity anaerobically respired in the presence of oxygen at *R.Q.* 1. The main respiratory activity of such tissues appeared therefore to consist in carbohydrate combustion, or oxidation of the lactic acid or some precursor, whilst under anaerobic conditions lactic acid accumulated. They found that tumour tissue, in spite of having a very high glycolytic activity, respired at a moderately low *R.Q.* and this was adduced as evidence that a failure to oxidise carbohydrate (or lactate) was characteristic of tumour tissue. The foregoing paper [Elliott *et al.*, 1935] shows that there is a definite failure by tumour tissue to oxidise carbohydrate by way of lactate and this fits in well with the conclusion of Dickens and Šimer. Nevertheless the findings of this paper show that consideration of *R.Q.* gives no evidence of abnormal failure of tumour tissue to oxidise carbohydrate. Though the *R.Q.* of most tissues seems to vary considerably, Table IX shows that there is no significant difference between the mean values for tumour and any other type of adult tissue. Further, in several cases with apparently typical tumours, *R.Q.* values of about 1 were obtained which would indicate carbohydrate oxidation. Oxidation of protein, with NH_3 as end product instead of urea, involves *R.Q.* about 1, but consideration of the determinations of Q_A and Q_{LA} of Elliott *et al.* [1935] makes it seem unlikely that appreciable amounts of a base are being produced, and estimations by Dickens and Greville [1933, 2] of NH_3 formation by the Jensen rat sarcoma indicated that very little protein is oxidised when glucose is present. The fact that the *R.Q.* of tumour is somewhat higher in the presence of glucose than in its absence also indicates that tumour tissue does oxidise carbohydrate. Nevertheless, if carbohydrate is oxidised by tumour, the course of breakdown must follow a route other than that involving lactic acid [Elliott *et al.*, 1935].

SUMMARY.

A study of the metabolism of various tissues has been made with particular reference to the *R.Q.*, and the results obtained differ in important respects from those of Dickens and Šimer [1930; 1931]. In particular, the *R.Q.* values of brain (grey matter) and retina have been found to be less than 1, whilst with liver and tumour tissue *R.Q.* values of unity have frequently been observed. The main results are summarised in Table IX. It is concluded that there is no significant difference between the mean *R.Q.* of the different tissues of well-fed adult animals and that no evidence for defective carbohydrate oxidation by tumours can be adduced from consideration of *R.Q.*

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