Studies on Gas Metabolism of Tissue in Vitro. VII.

On Kidney Tissue. II.

Tissue respiration under various carbon dioxide concentrations.

By

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There is little doubt that the kidney is the chief place where the hydrogen ion concentration of the blood is regulated to maintain a certain limit. This suggests that the kidney may be very sensitive to a change of the hydrogen ion concentration of the blood, and that when the tissue is kept alive in some artificial media with various hydrogen ion concentrations, it may change its respiration as a reaction to the media. So far as we know, there are very few who have investigated tissue respiration of the kidney in vitro in various hydrogen ion concentrations. Especially we know no report which tells us the tissue respiration on the cortex and the medulla of a kidney separately. We tried thus to approach a problem of the buffer action of the kidney from the stand point of the tissue respiration.

Method.

General arrangements and the experimental materials were the same as in our first report on the tissue respiration of the kidney (Okabe, 1934). Warburg's second method (1924) was used. Rabbits were used. Respiration of liver tissue was also examined and compared with that of kidney tissue. Tissue respiration of the medulla was calculated as in the first report after ammonia correction.

Hydrogen ion concentrations were prepared according to Hasselbalch's principle (1917), that is, by varying the carbon dioxide concentration in the experimental vessel against a certain sodium bicar-

bonate concentration (0.0136 mol in 1 liter) in Ringer's solution. The various carbon dioxide concentrations were 14, 7, 3.5 and 1.5% in oxygen gas. These concentrations give to Ringer's solutions pH of 6.72, 7.02, 7.32 and 7.68 respectively, pK_1 being taken as 6.1.

Results.

Results were summarised in table and figures. Q_o and Q_c in the table are the means of those during two hours.

TABLE.

Oxygen consumption and carbon dioxide output of cortical and medullar tissue of kidney and liver tissue of rabbit under various carbon dioxide concentrations.

Concentration of CO_2 (% in O_2)		14			7			3.5			1.5		
		6.72			7.02			7.32			7.68		
Calculated pH		Number of exp.	Q_o	Q_c	Number of exp.	Q_o	Q_c	Number of exp.	Q_o	Q_c	Number of exp.	Q_o	Q_c
Cortex	Observed	6	6.3	2.0	6	7.0	3.8	19	9.2	6.9	10	12.3	9.3
			± 0.2	± 0.4		± 0.4	± 0.5		± 0.2	± 0.3		± 0.6	± 0.8
Medulla	Calculated		5.7	1.9		7.6	4.2		9.5	6.7		11.8	9.4
	Observed	5	2.6	4.9	6	5.7	8.4	23	7.1	11.9	6	10.7	16.1
Ammonia (mg) per mg of tissue			± 0.2	± 0.6		± 0.4	± 0.3		± 0.1	± 0.5		± 0.6	± 1.5
	Calculated		2.8	4.9		5.2	8.4		7.6	11.9		10.5	16.1
			0.0001			0.0004			0.0005			0.0007	
Liver	Observed	7	2.4	1.0	7	4.6	3.2	6	5.9	5.3	7	8.9	7.8
			± 0.1	± 0.0		± 0.3	± 0.0		± 0.3	± 0.4		± 0.4	± 0.2
			2.4	1.0		4.4	3.2		6.3	5.3		8.7	7.8

Calculated Q_o and Q_c were obtained from the equation of the straight lines of Q_o and Q_c drawn by the method of least squares.

All the tissues experimented on showed increased gas metabolism, both oxygen consumption and carbon dioxide output in proportion to increase of pH within the limits we applied. Degrees of the increase of the metabolism were similar in the case of the cortical and the liver tissue, but that of the medulla tissue was much greater than the other two.

Reinwein and Singer (1927) found with marmot kidney that oxygen consumption increased slightly with increase of pH between 4.5 and 8.4 and decreased at the larger pH . Radzimovska, Odrijna and Vjdro (1928) found the optimum pH to lie between 7.8 and 8.4. Kisch and Leibowitz (1930) and

Kisch (1932) found the optimum pH of oxygen consumption to be between 7.1 and 7.4 in rat, at 7.4 in cat, between 7.7 and 8.1 in rabbit and hare and 7.2 in ox. Yamaguchi (1932)

Figure 1. Oxygen consumption of cortical and medullar tissue of kidney and liver tissue of rabbit in various hydrogen ion concentrations.

Figure 2. Carbon dioxide output of cortical and medullar tissue of kidney and liver tissue of rabbit in various hydrogen ion concentrations.

found that oxygen consumption of the kidney tissue of marmot increased parallel to increase of pH between 5.1 and 7.3 but decreased at 8.1 of pH.

It seems to be a general process that oxygen consumption increase with increase of pH of the medium in narrower limits not far from physiological, not only in the case of the kidney but also in other tissue.

Thus Reinwein and Singer found increase of oxygen consumption of liver tissue of marmot between 4.5 and 8.4 of pH, and Ellinger and Landsberger (1922) in goose erythrocytes between 5.8 and 8.25. Warburg, Posener and Negelein (1924) found also increased glycolysis of rat cancer with increase of pH of the medium between 6.66 and 7.83 (6.40 and 7.57 at our calculation). Their experiment is the only one known to us in which the hydrogen

ion concentration of the medium in the respiratory vessel is modified by changing the concentration of carbon dioxide with constant bicarbonate.

As can be seen from the inclinations of the straight lines in the figures drawn by the method of least squares, the sensitivity to decrease of the hydrogen ion concentration of the medium within the experimental range was more marked in the case of carbon dioxide output of the tissues, especially of the medullar one. Increase of carbon dioxide in a medium favours an increase of hydrogen ion concentration of the latter. Whether the increase of the carbon dioxide output in our experiment be an expression of a mechanism of buffer action of the tissue or not, is hard to answer. At any rate it is sure that the medium of our experiment had to become more acid in the experimental time in cases of lower hydrogen ion concentration than at the beginning of the experiment, if the alkaline reserve was kept at constant. If this be true, the medullar region of kidney can be regarded as having the most powerful ability to buffer against lowering the hydrogen ion concentration of the medium in which tissue is bathed.

Amount of ammonia liberated in the gas space of the experimental vessel was found to be the smaller, the larger the carbon dioxide concentration was. In the case of 14% of the carbon dioxide it was very difficult to detect ammonia with our experimental technique. If this ammonia be an expression of the production in the tissue and proportional to the amount in the tissue, it seems to be inconsistent with our views with regard to the buffer action of the medulla.

At present we do not know how this inconsistency should be explained. It is necessary to make more experiment, especially with much more elaborate technique in regard to ammonia determination both on the gas and liquid medium.

While it can not be decided whether the increase of the carbon dioxide output was due in the cases of the liver and kidney cortex to an increase of a respiratory carbon dioxide or to that of an aerobically glycolytic one or to that of both, as the respiratory quotient was smaller than unit, there is little doubt that the increase in the case of the medulla was partly due to an increase of an aerobically glycolytic one, as the respiratory quotient was in this case larger than unit.

It may therefore be concluded that the buffer action of the medullar tissue against lowering of the hydrogen ion concentration of the medium would be partly attributed to a glycolysis on the tissue though we do not know as to whether this be taking place *in vivo*. On the

other hand we know that the kidney has a means of guarding against increasing the hydrogen ion concentration of the blood both by excreting acid radicals and by increasing ammonia production (Henderson, 1909; Wilson, 1923).

We have seen in the first report (1934) of our experiment that the ammonia is found much more in the medullar tissue than in the cortical. We know also that the kidney is one of the chief places where ammonia is produced (cf. the next report). It may be thus concluded that the medullar part of the kidney be the place of ammonia production in the kidney.

With these considerations it may be said that the kidney acts as a buffer against changing of hydrogen ion concentration of the body fluid by means of excreting acid or basic radicals on one side, and of glycolysis and ammonia production on the other side, the latter two factors taking place chiefly in the medullar part of the kidney.

Summary.

Oxygen consumption and carbon dioxide output of the cortical and the medullar tissue of kidney and the liver tissue of rabbit were measured under various carbon dioxide concentrations (14, 7, 3.5 and 1.5% in oxygen), which should modify the hydrogen ion concentration of the medium. Calculated *pH*-values were 6.72, 7.02, 7.32 and 7.68.

Oxygen consumption and carbon dioxide output of all the tissue experimented on increased with increase of *pH* within the above range.

Increase of carbon dioxide output was more marked than that of the oxygen consumption, especially in the case of the medullar tissue of the kidney.

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