2. METABOLISM OF NORMAL AND TUMOUR TISSUE

19. THE METABOLISM OF INTESTINAL MUCOUS MEMBRANE

BY FRANK DICKENS AND HANS WEIL-MALHERBE

From the Cancer Research Laboratory, North of England Council of the British Empire Cancer Campaign, Royal Victoria Infirmary, Newcastle-upon-Tyne

(Received 30 December 1940)

STUDIES of the metabolism of intestinal mucous membrane are not numerous and seem to have been restricted to the mucosa of the large intestine [Warburg *et al.* 1924; Rosenthal & Lasnitzki, 1928; Bumm *et al.* 1934]. Dickens & Šimer [1930, 2] found the R.Q. of mucosa from the ileum to be low (0.85), but this result was not considered surprising in view of the low glycolytic activity reported by Warburg *et al.* [1924]. Weil-Malherbe [1938], however, observed with mucosa from rat jejunum a metabolism fundamentally different from that previously recorded for intestinal mucosa. All these various results are summarized in Table 1 from which it is seen that there is an extraordinarily great discrepancy between results obtained by different authors. Thus, while according to Warburg *et al.* mucous membrane belongs to the group of tissues with very low glycolysis, such as liver and kidney, Rosenthal & Lasnitzki as well as Bumm *et al.* found a high anaerobic glycolysis in their experiments with mucosa from the large intestine. Both groups of workers reported however a low aerobic glycolysis of this tissue, though occasionally high values were observed. Weil-Malherbe, on the other hand, found with mucosa from the jejunum very high values of aerobic glycolysis and a practically complete absence of the Pasteur effect. These observations seemed to us important enough to be followed up by a more detailed investigation in connexion with our previous studies on the significance of high aerobic glycolysis

Table 1. *Metabolism of intestinal mucous membrane: published data*

Average figures have been calculated, where possible, from the authors' results.

Part of intestine	Species	Medium*	No. of exp.	Q_{O_2}	$Q_{O_2}^a$	Q_G^N	R.Q.	Author
Not stated	Rat	BR	1	-12.4	1.6	3.5	—	Warburg <i>et al.</i> [1924]
Large intestine	Rat	BR	9	-14.6	4.2	15.1	—	Rosenthal & Lasnitzki [1928]
"	"	Serum	2	-9.9	1.1	10.3	—	"
"	Rabbit	BR	11	-11.1	2.7	14.2	—	"
"	"	Serum	10	-11.2	1.4	12.6	—	"
Ileum	Rat	PO ₄ -R	2	-9.4	—	—	0.85	Dickens & Šimer [1930, 2]
Large intestine	Guinea-pig	B & PO ₄ -R 95% O ₂ (10 or 15% O ₂)	18 (18)	-14.6 (-13.2)	4.2 (9.6)	15.7	—	Bumm <i>et al.</i> [1934]
Jejunum	Rat	BR	4	-14.6	18.3	20.4	—	Weil-Malherbe [1938]

* BR = bicarbonate-Ringer solution + glucose.
PO₄-R = phosphate-Ringer solution + glucose.
Serum = inactivated serum + glucose.

combined with low R.Q. in tumours [Dickens & Šimer, 1930, 2; 1931, 2]. Our results confirm and extend the earlier observations of Weil-Malherbe on the mucosa of jejunum. They show that this tissue differs in some respects from the mucosa of the large intestine. As in tumour, high aerobic and anaerobic glycolyses are combined with a low R.Q. Moreover, the Pasteur effect is completely absent, even if Ringer solution is replaced by serum.

EXPERIMENTAL

Preparation of tissue. The intestine was first rinsed out with a fine jet of water to remove the greater part of the contents. A length of about 1 in. was then cut open and spread on a glass plate with the mucous membrane facing upwards. After careful blotting with filter paper to remove adhering moisture and solid particles the mucosa was scraped off with the aid of a microscope slide. Another slide served to pin down the muscularis. With practice the mucosa can be stripped off entirely and without laceration. After weighing on a torsion balance the mucous membrane was transferred to the manometer vessel, and another piece was dried immediately for determination of the dry weight/wet weight ratio.

Methods. Measurements of respiration and of aerobic glycolysis at 37.5° were usually carried out simultaneously by Warburg's 2-vessel method in bicarbonate-Ringer [Krebs & Henseleit, 1932] or in inactivated sheep serum. A third manometer, filled with $N_2 + 5\%$ CO_2 , served for the measurement of anaerobic glycolysis. If not stated otherwise the medium contained 0.2% glucose. Retention in serum was determined by the method of Dickens [1939]. Aerobic glycolysis in the 2-vessel method was calculated on the basis of an R.Q. of unity. Measurements of R.Q. were carried out in phosphate-Ringer by the first method of Dickens & Šimer [1930, 1] and in bicarbonate-Ringer or serum by the second method of Dickens & Šimer [1931, 1]. Lactic acid was estimated by the method of Gordon & Quastel [1939].

Infection. Bacterial contamination, noticeable by the development of a faecal smell and a steadily rising metabolism, was encountered only in a few experiments with tissue from the lower part of the ileum or from the large intestine, and even then only in the second hr. of the experiment: such experiments were of course discarded.

Thickness of the tissue. The data collected in Table 2 show that the thickness (moist wt./area) of even the whole intestinal wall of the rat is well below the limiting thickness for complete O_2 -saturation, which, for a tissue with $Q_{O_2} = 15$, is 0.47 mm. in pure O_2 and 0.21 mm. in 20% O_2 [Warburg, 1923]. An adequate diffusion of O_2 was therefore assured in all experiments. The thickness of the mucosa is greatest at the upper end of the intestine and diminishes steadily towards the rectum.

Disintegration of the tissue. A considerable loss of weight is observed after pieces of intestinal mucosa have been shaken in Ringer solution at 37.5° for an hour. This disintegration varies greatly from one experiment to another, even with tissue from the same animal and the same part of the intestine, probably owing to the degree of success in stripping off an unbroken piece of mucosa in its entirety. The loss of wt. is usually higher in the small volume than in the large one, but there is no regularity. Our first experiments, which were carried out before this fact was sufficiently appreciated, were calculated on the final dry wt. as is the routine in tissue metabolism work. The results showed a considerable variation and the figures obtained were sometimes unusually high. Results of

Table 2. *Thickness of the intestinal wall and its components (rat)*

		Thickness in mm.		
		Whole wall	Mucosa	Muscularis
Jejunum		0.095	0.062	0.032
		0.105	0.069	0.024
		0.093	0.061	0.024
	Mean	0.098*	0.064	0.027
Ileum		0.086	0.048	0.026
		0.071	0.044	0.023
		0.078	0.046	0.025
	Mean	0.078	0.046	0.025
Colon		0.115	0.046	0.059
		0.112	0.023	0.067
		0.114	0.035	0.063
	Mean	0.114	0.035	0.063

Table 3. *Loss of weight after 1 hr. shaking at 37.5°*

				% Recovery ($\frac{\text{Final dry wt.}}{\text{Initial dry wt.}} \times 100$)		
Species	Tissue	Medium*	Initial dry wt. Initial wet wt.	In O ₂ + 5% CO ₂		In N ₂ + 5% CO ₂
				<i>v_F</i> = 2 ml.	<i>v_F</i> = 8 ml.	<i>v_F</i> = 3 ml.
Rat	Duodenum, mucosa	BR	0.199	59.0	49.1	64.8
		BR	0.197	48.5	67.5	78.0
Rat	Jejunum, mucosa	BR	0.211	61.6	52.1	61.3
		BR	0.239	68.5	76.0	59.3
		BR	0.226	—	—	65.6
		BR	0.198	29.4	44.6	19.6
				25.8	45.6	
				57.0	41.0	
		BR	0.188	49.0	36.0	—
				45.0	51.0	
		BR	0.197	23.0	55.5	61.5
		Serum		100.0	104.5	100.0
Rat	Ileum, mucosa	BR	0.195	27.0	70.0	28.0
		Serum		108	60.0(?)	85.0
		BR	0.193	36.1	38.3	39.4
		BR	0.184	28.4	26.5	31.8
		BR	0.170	27.5	32.4	36.0
		Serum		64.7	56.8	71.6
		BR	0.260	47.5	41.0	48.2
		BR	0.227	82.5	68.0	45.8
Rat	Jejunum, muscularis	BR	0.228	91.8	88.5	83.5
Mouse	Jejunum, whole wall	BR	0.234	90.5	89.8	78.0
		Serum		95.4	101	94.8

* BR = Bicarbonate-Ringer solution + glucose.

greater uniformity were obtained when the calculation was based on the initial dry/wet weight ratio. This method was used in most of the experiments to be reported; only a few of the earlier experiments have been retained where the differences within one and the same experiment serve to illustrate a point. Sometimes the results have been calculated by both methods to demonstrate the effect of the loss of weight on the calculation; it will be noticed that the figures based on the final dry weight are up to 5 times higher than those based on the initial dry/wet weight ratio.

In conformity with the decreasing thickness of the mucous membrane the disintegration is greater with material from the ileum and colon than with that from the jejunum.

There is very little loss of weight when the whole intestinal wall is used. If serum is used instead of Ringer solution the disintegration of the mucous membrane is greatly reduced; indeed the mucosa of the jejunum may be recovered almost intact after a 1 hr. experiment.

Results

Examples of the metabolism of the mucous membrane from different parts of the intestine of the same animal are given in Table 4 (cf. also Table 6). The metabolism is most active in the upper and middle parts of the jejunum though respiration was occasionally found highest in the duodenum. Usually respiration is steadier than glycolysis which is very unstable and falls to the same extent aerobically and anaerobically. This fall cannot be due to a mere mechanical breaking up of the tissue as it is also observed in serum where disintegration is

Table 4. *Metabolism of different parts of the intestine in bicarbonate-Ringer*

	Min.	Results based on initial dry/wet wt.			Results based on final dry wt.		
		Q_{O_2}	$Q_G^{O_2}$	$Q_G^{N_2}$	Q_{O_2}	$Q_G^{O_2}$	$Q_G^{N_2}$
		Exp. 1. Rat, mucous membrane					
Duodenum	0-20	- 8.8	11.1	10.4	-21.2	23.0	13.3
	20-40	- 8.1	7.8	6.9	-17.6	16.2	8.8
	40-60	- 6.0	4.7	4.9	-12.1	9.6	6.2
Jejunum (upper part)	0-20	-15.6	16.5	16.4	-23.1	24.0	27.8
	20-40	-14.8	12.3	13.3	-22.1	17.9	22.4
	40-60	-11.9	7.0	8.9	-16.8	10.1	15.0
Ileum (lower part)	0-20	- 5.3	5.5	4.0	-17.6	19.4	12.5
	20-40	- 2.1	2.0	2.2	- 7.3	7.0	6.8
	40-60	- 1.6	1.0	1.0	- 5.5	3.6	3.0
Colon	0-20	- 3.4	5.2	4.4	- 6.4	11.0	9.0
	20-40	- 3.2	3.5	1.9	- 5.0	3.2	4.0
	40-60	- 1.4	2.1	0.6	- 2.5	4.3	1.1
Exp. 2. Rat, mucous membrane							
Duodenum	0-60	—	—	—	-50.0	24.6	38.5
	60-120	—	—	—	-28.0	7.3	12.6
Jejunum	0-60	—	—	—	-22.8	35.1	39.0
	60-120	—	—	—	-13.8	11.1	18.5
Ileum	0-60	—	—	—	-13.7	14.3	15.7
	60-120	—	—	—	-10.6	11.0	11.0
Colon	0-60	—	—	—	-16.2	7.6	23.4
	60-120	—	—	—	- 7.4	4.7	—
Exp. 3. Mouse, whole intestinal wall							
Duodenum	0-60	—	—	—	-16.6	20.6	13.0
	60-120	—	—	—	-13.3	15.3	9.9
Jejunum	0-60	—	—	—	-28.2	32.1	23.3
	60-120	—	—	—	-21.0	23.0	15.9
Ileum	0-60	—	—	—	-10.7	4.5	9.3
	60-120	—	—	—	-10.8	4.4	6.3
Colon	0-60	—	—	—	-14.1	3.9	8.1

small. With mucosa from the ileum and colon, respiration, too, is unstable and this may well be ascribed to the greater disintegration of this tissue. If based on the initial dry weight the whole metabolism of these latter tissues is very low.

Respiration and aerobic and anaerobic glycolyses have about equal Q -values, especially if the calculation is based on the initial dry weight. This is at least true for the jejunum, whereas in the cases of the ileum and the colon the results are less consistent. Sometimes the glycolysis was as high aerobically as anaerobically (Table 4, exp. 1 for ileum and colon, exp. 2 for ileum); at other times the anaerobic exceeded the aerobic glycolysis (Table 4, exp. 2 for colon, Table 6 for ileum). In some experiments it was even observed that the glycolysis was higher aerobically than anaerobically, especially in the experiments with the whole intestinal wall of both rat and mouse (Tables 4–6). This is probably an artefact due to a more rapid autolysis under anaerobic conditions [cf. Macfarlane & Weil-Malherbe, 1941].

The high aerobic glycolysis of the isolated mucous membrane is not caused by the severance from its matrix as has been suggested for retina [Warburg *et al.* 1924]. If the whole intestinal wall is examined, the same type of metabolism is found as with the isolated mucosa. In fact the metabolism of the whole intestinal wall almost equals the average of the metabolisms of the isolated

Table 5. *Metabolism of mucosa, muscularis and whole wall of the upper part of the jejunum of the rat*

All results calculated on initial dry/wet weight basis.

	Min.	Q_{O_2}	$Q_G^{O_2}$	$Q_G^{N_2}$
Mucosa	0–20	– 11.3	14.8	12.6
	20–40	– 8.7	8.2	5.6
	40–60	– 4.8	3.7	4.0
Muscularis	0–20	– 6.3	4.8	6.8
	20–40	– 4.5	3.2	4.7
	40–60	– 3.9	2.4	4.0
Whole wall	0–20	– 7.8	10.6	8.1
	20–40	– 5.4	8.7	6.6
	40–60	– 3.2	8.0	4.9

mucosa and muscularis (Table 5). In the higher regions of the intestine the metabolism of the whole wall is determined by that of the mucous membrane owing to the higher metabolism and greater weight of the latter. The metabolism of the whole wall of mouse jejunum, especially, greatly resembles that of the isolated mucosa. In the lower regions of the intestine the influence of the muscular coat may be expected to be more marked owing to the decreasing thickness and low metabolism of the mucous membrane.

There is very little loss of weight during an experiment with whole intestinal wall and it therefore does not matter by which method the results are calculated as a comparison of the experiments published in Tables 4 and 6 will show.

Metabolism in serum. According to Negelein [1925] the aerobic glycolysis of normal growing cells such as embryo and the germinal epithelium of testis disappears in serum. This is not the case with intestinal mucosa or whole intestinal wall where aerobic glycolysis persists in serum to at least the same extent as in Ringer solution (Table 6). This result is similar to that obtained previously with the medulla of kidney [Dickens & Weil-Malherbe, 1936, 1] contrary to György *et al.* [1928].

Table 6. *Metabolism of intestine in bicarbonate-Ringer solution and in sheep serum*

All results based on initial dry/wet weight ratio.

	Min.	In serum			In Ringer		
		Q_{O_2}	$Q_G^{O_2}$	$Q_G^{N_2}$	Q_{O_2}	$Q_G^{O_2}$	$Q_G^{N_2}$
Jejunum, mucosa (rat)	0-20	-16.3	25.2	22.9	-10.3	13.3	13.5
	20-40	-15.4	17.7	13.6	-9.9	11.9	9.8
	40-60	-12.9	14.0	10.6	-8.4	9.7	8.4
Ileum, mucosa (rat)	0-20	-10.8	8.5	11.7	-2.1	4.4	7.7
	20-40	-5.0	3.1	4.7	-1.2	2.5	5.8
	40-60	-4.7	1.6	1.4	-1.6	1.5	4.0
Jejunum, whole wall (mouse)	0-20	-15.5	25.0	10.9	-19.0	25.8	10.6
	20-40	-16.5	20.8	6.6	-15.8	23.2	8.7
	40-60	-14.6	19.2	6.4	-14.8	18.9	7.5

Table 7. *Chemical control of lactic acid formation*

Jejunal mucosa of the rat.

Medium*	Gas phase	Time min.	μ l. lactic acid		% Chemic./manom.
			Manometrically	Chemically	
BR	$N_2=5\% CO_2$	120	251	197	78.5
Serum		120	238	206	86.5
Serum		120	460	471	102.5
Serum		150	226	225	100
BR	$O_2=5\% CO_2$	150	560	447	80
BR		150	687	484	70.4
BR		150	643	553	86

Table 8. *Effect of substrate on metabolism of mucous membrane of rat jejunum*

Medium*	Min.	Q_{O_2}			Q_{CO_2} No sub- strate	Appa- rent R.Q.	$Q_G^{N_2}$				$M/100$ hexosemono- phosphate
		No sub- strate	0.2% glu- cose	0.2% glyco- gen			No sub- strate	0.2% glu- cose	0.2% glyco- gen	0.2% fruc- tose	
Results based on final dry weight											
BR	0-30	-30.9	—	—	31.0	1.00	8.7	23.6	22.6	—	—
	30-60	-14.6	—	—	11.0	0.75	6.3	17.2	16.8	—	—
	60-90	-12.5	—	—	7.4	0.59	5.0	10.6	11.0	—	—
	90-120	-11.0	—	—	6.8	0.61	5.0	8.2	9.8	—	—
PO_4 -R	0-30	-26.4	-22.2	-21.6	—	—	—	—	—	—	—
	30-60	-23.7	-22.8	-23.7	—	—	—	—	—	—	—
	60-90	-19.7	-19.1	-19.4	—	—	—	—	—	—	—
	90-120	-20.8	-20.1	-19.5	—	—	—	—	—	—	—
BR	0-10	—	—	—	—	—	11.4	48.0	26.1	24.0	13.2
	10-30	—	—	—	—	—	7.0	27.7	15.2	14.7	12.9
	30-60	—	—	—	—	—	7.6	16.6	12.8	10.4	12.8
	60-90	—	—	—	—	—	8.2	9.8	8.2	9.0	8.8
Results based on initial dry weight											
BR	0-20	—	—	—	—	—	9.7	9.4	9.8	9.3	9.0
	20-40	—	—	—	—	—	5.4	6.1	6.2	5.7	4.5
	40-60	—	—	—	—	—	3.5	5.6	5.0	4.4	3.7
BR	0-20	—	—	—	—	—	7.3	7.7	11.0	4.7	5.3
	20-40	—	—	—	—	—	4.6	6.7	5.2	3.9	3.4
	40-60	—	—	—	—	—	2.6	4.7	3.2	2.7	2.8

* BR = bicarbonate-Ringer solution.

 PO_4 -R = phosphate-Ringer solution.

Nature of acid formation. That the acid formation by the intestinal mucosa is really due to glycolysis is shown by the fact that 70–100 % of the acid estimated manometrically is accounted for by chemical estimation of lactic acid (Table 7) and secondly by the disappearance of aerobic and, to some extent, anaerobic acid formation in absence of glucose or another suitable substrate (Table 8). Respiration, on the other hand, is not affected at all by the absence of a substrate.

The effect of addition of substrate on the anaerobic glycolysis seems to be variable. In experiments which were performed in early spring we repeatedly observed a strong effect of glucose and glycogen on the anaerobic acid formation which was increased 3–4 times. When we tried to repeat these experiments in November the only effect was a delay in the fall of glycolysis.

Respiratory quotient. For a strongly glycolysing tissue such as the intestinal mucous membrane one might have expected an R.Q. of about unity. In fact the R.Q. is low and decreases towards the ileal end of the jejunum (Table 9).

Table 9. *Respiratory quotient of mucosa from rat jejunum*

Medium*		Time min.	Q_{O_2}	$Q_{O_2}^2$	R.Q.
Based on final dry weight					
PO ₄ -R		150	- 13.4	—	0.92
PO ₄ -R		150	- 16.6	—	0.89
		100	- 28.5	—	0.86
		150	- 20.8	—	0.84
Based on initial dry/wet weight ratio					
BR	Duodenal end	150	- 5.7	7.0	0.93
	Middle part	150	- 5.6	8.6	0.86
	Ileal end	150	- 12.5	9.7	0.78
Serum		90	- 5.4	9.1	0.89
		90	- 7.4	10.3	0.83

* BR = bicarbonate-Ringer solution + glucose.

PO₄-R = phosphate-Ringer solution + glucose.

Effect of acetylcholine. In view of the work of Deutsch & Raper [1936; 1938] on the effect of acetylcholine on the *in vitro* metabolism of the salivary glands of the cat it was of interest to examine whether this substance would cause a similar stimulation of metabolism in intestinal mucous membrane, this being largely a glandular tissue controlled by sympathetic and parasympathetic impulses. Experiments were carried out with acetylcholine (1–5 μ g./ml.), with eserine (20 μ g./ml.), with atropine (40 μ g./ml.) and with acetylcholine + eserine. No effect was observed whether the addition was made before or during the experiment.

Nucleic acid-phosphorus. It has been suggested by Berenblum *et al.* [1939, 1] that the measurements of tissue metabolism should be related to the content of nucleic acid rather than to the dry weight. For the conversion of our figures to the nucleic acid standard we have estimated the nucleic acid-P in intestinal mucosa by the method of these authors. We found the following values:

	Nucleic acid-P, % of dry weight
Jejunum: Proximal part	0.34
Distal part	0.40
Ileum: Proximal part	0.44
Distal part	0.53

DISCUSSION

It is surprising that the exceptional features of the metabolism of intestinal mucous membrane should have been entirely overlooked by previous workers in the field of tissue metabolism. For some reason their attention was turned almost exclusively on the mucosa of the large intestine, yet the experimental difficulties and hence the variation of the results are much less with jejunal mucous membrane which is thicker, less fragile and free from bacteria. It can easily be stripped off from the smooth surface of the small intestine, whereas the surface of the large intestine is undulated owing to ridges of longitudinal muscle fibres which make it difficult to strip off the mucosa without laceration.

The mucous membrane of the jejunum shows the highest metabolic activity of all parts of the intestinal tract. It belongs to the most actively respiring tissues of the body. Its glycolysis in nitrogen is at least of equal activity. Yet this active glycolysis is not depressed by the respiration; it persists at the same rate in oxygen. This complete absence of the Pasteur effect is the most remarkable and indeed unique property of this tissue. There is no reason to assume that the high aerobic glycolysis which we constantly observed is an artefact which does not exist *in vivo*, since it is due neither to the separation from the intestinal wall, nor to incomplete O_2 -saturation, nor to bacterial contamination, nor to a toxic effect of saline, nor to a sudden stimulus caused by liberation of acetylcholine.

Although we have never observed a glycolysis which was smaller aerobically than anaerobically in jejunal mucous membrane, the converse was occasionally seen. This was probably due to a more rapid autolysis under anaerobic conditions. It has been shown for brain tissue that there is a rapid fall of the P_2O_7 fraction anaerobically even in presence of glucose with a corresponding fall of glycolysis [Macfarlane & Weil-Malherbe, 1941].

The metabolism of the isolated mucosa of the ileum and colon is low, especially if allowance is made for the disintegration of the tissue during the experiment. Though it was sometimes observed by ourselves as well as by earlier workers that the aerobic glycolysis reached the level of the anaerobic glycolysis, a definite Pasteur effect was found in other experiments. Some of our experiments with colonic mucous membrane agree in fact very well with the figures of Rosenthal & Lasnitzki [1928]. This variation does not seem to recommend the colonic mucous membrane as a suitable subject for the study of the Pasteur effect. Yet it was used for this purpose by Bumm *et al.* [1934] who claimed to have shown that if the O_2 -tension is lowered to 10% the Pasteur effect is inhibited without respiration being affected (cf. Table 1).

As we have previously pointed out [Dickens & Weil-Malherbe, 1936, 1, 2] a high aerobic glycolysis is not specific for either malignant or normal growth. On the other hand a tendency has recently been noticeable [Berenblum *et al.* 1939, 2] to dissociate the high aerobic glycolysis completely from the tumour problem. In experiments to be published one of us has observed examples where there is little change of the metabolism of a normal tissue with low glycolysis during its transformation to a benign tumour or to a precancerous condition, while the development of malignancy is accompanied by a definite increase in the aerobic and anaerobic glycolysis. Thus while aerobic glycolysis is not limited to tumours—and as the present paper shows may even reach the level of the anaerobic glycolysis in a normal 'resting' tissue—it is not correct to assume that the glycolysis of tumour is always merely that of the tissue of origin.

Formerly tumour was considered to be the only tissue where a high glycolysis was accompanied by a low R.Q. We interpreted this [Dickens & Šimer, 1930, 2] as

meaning a defective carbohydrate metabolism, and regarded it as a specific property of tumours. Meanwhile, Bywaters [1937] showed that synovial membrane has a similar type of metabolism, but the low activity of this tissue makes comparison difficult. The mucous membrane of the intestine provides another and more satisfactory example, showing clearly that combination of active glycolysis with low R.Q. is not a specific property of tumours. Another interesting similarity is the occurrence of aminoethylalcohol phosphoric ester in both tumour [Outhouse, 1937] and intestine [Colowick & Cori, 1939].

SUMMARY

The metabolism of mucous membrane from the various parts of the intestine has been measured in Ringer solution and in serum. It is found that the jejunal mucous membrane possesses a high respiration, a high glycolysis, aerobically and anaerobically, and a low R.Q.; acetylcholine was without effect. Jejunal mucous membrane is unique among tissues hitherto studied in that the Pasteur effect is absent. These results are not due to toxic action of Ringer solution, as they are also observed in serum; nor are they due to severance of the mucosa from the matrix as the metabolism of the whole intestinal wall is that expected from the summation of its parts.

The metabolism of mucous membrane from ileum and colon is less active and more variable, probably owing to greater fragility. It resembles in general that of the jejunum, but the Pasteur effect was often evident.

These results are discussed in relation to the problem of tumour metabolism.

REFERENCES

- Berenblum, Chain & Heatley (1939, 1). *Biochem. J.* **33**, 68.
——— (1939, 2). *Amer. J. Cancer*, **38**, 367.
Bumm, Appel & Fehrenbach (1934). *Hoppe-Seyl. Z.* **223**, 207.
Bywaters (1937). *J. Path. Bact.* **44**, 247.
Colowick & Cori (1939). *Proc. Soc. exp. Biol. N.Y.*, **40**, 586.
Deutsch & Raper (1936). *J. Physiol.* **87**, 275.
——— (1938). *J. Physiol.* **92**, 439.
Dickens (1939). *Biochem. J.* **33**, 230.
——— & Šimer (1930, 1). *Biochem. J.* **24**, 905.
——— (1930, 2). *Biochem. J.* **24**, 1301.
——— (1931, 1). *Biochem. J.* **25**, 973.
——— (1931, 2). *Biochem. J.* **25**, 985.
——— & Weil-Malherbe (1936, 1). *Biochem. J.* **30**, 659.
——— (1936, 2). *Nature, Lond.*, **138**, 125.
Gordon & Quastel (1939). *Biochem. J.* **33**, 1332.
György, Keller & Brehme (1928). *Biochem. Z.* **200**, 356.
Krebs & Henseleit (1932). *Hoppe-Seyl. Z.* **210**, 33.
Macfarlane & Weil-Malherbe (1941). *Biochem. J.* **35**, 1.
Negelein (1925). *Biochem. Z.* **165**, 122.
Outhouse (1937). *Biochem. J.* **31**, 1459.
Rosenthal & Lasnitzki (1928). *Biochem. Z.* **196**, 340.
Warburg (1923). *Biochem. Z.* **142**, 317.
——— Posener & Negelein (1924). *Biochem. Z.* **152**, 309.
Weil-Malherbe (1938). *Biochem. J.* **32**, 2257.