

TABLE I.  
Respiratory Metabolism of Cerebral Cortex.

Animal	$\frac{\text{CO}_2 \text{ mm}^3/\text{mgm}/\text{hr}}{\text{O}_2 \text{ mm}^3/\text{mgm}/\text{hr}}$	R. Q. of excised cortex	R. Q. of brain <i>in situ</i>
Pigeon No. 1	$\frac{0.68}{0.89}$	0.76	
Pigeon No. 2	$\frac{0.88}{1.02}$	0.86	
Pigeon No. 3	$\frac{0.63}{0.96}$	0.66	
Dog	$\frac{1.13}{1.30}$	0.87	0.89
	$\frac{1.10}{1.33}$	0.83	
	$\frac{1.06}{1.39}$	0.76	

lactic acid,<sup>3</sup> the determination of the respiratory quotient of the cortex during B<sub>1</sub> avitaminosis is of importance.

Three pigeons and one dog were fed on diets deficient in vitamin B<sub>1</sub> and were studied after they showed definite signs of polyneuritis. The respiratory metabolism of the cerebral cortex of the pigeons was examined in the Warburg apparatus. The respiratory quotient of the brain of the dog was determined in 2 ways: (1) directly from the arterial-venous difference of CO<sub>2</sub> and O<sub>2</sub>, and (2) the brain was then excised and studied in the Warburg apparatus. The results presented in Table I indicate respiratory quotients below unity probably caused by a diminished ability of the brain to oxidize lactic acid.

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### Effect of Methylene Blue and Cyanide on Respiration of Cerebral Cortex, Testicle, Liver and Kidney.

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The respiratory metabolism of tissues of various organs was studied in the Warburg respiration apparatus. The tissues were suspended in a phosphate medium buffered at pH 7.4 with lactate as the

<sup>3</sup> Holmes, E. G., *Biochem. J.*, 1930, **24**, 914.

substrate. Three different samples of methylene blue were used and, with each, a diminution of  $O_2$  uptake was observed in 47 experiments on the cerebral cortex of rat, dog and cat. Whenever methylene blue was added to the solution the  $CO_2$  production of the surviving brain tissue was decreased to a greater extent than the  $O_2$  consumption; the respiratory quotient therefore fell.

Cyanide, on the other hand, caused a diminution in the  $O_2$  uptake of excised cortex in each of 66 observations. The decrease in  $CO_2$  output was usually similar for equal concentrations of cyanide and varied inversely with the concentration of cyanide. However, the decrease in  $O_2$  consumption varied from observation to observation even if the concentration of cyanide was kept the same. Since the  $O_2$  uptake varied, the respiratory quotient after treatment with cyanide fluctuated.

Even though cyanide and methylene blue separately decreased  $O_2$  uptake, in the presence of both substances the oxygen consumption tended to return to the normal value. The fact that the  $CO_2$  consumption is so small is evidence that the oxidations activated by methylene blue do not proceed in the usual manner. A characteristic experiment is presented in the table (Exp. 1).

The results of 6 observations of the testicle are similar to those found on the brain (Exp. 2).

TABLE I.  
Effects of Methylene Blue and Cyanide on Respiratory Metabolism of Excised Organs ( $mm^3/mgm/hr$ ).

Exp. No.	Organ	Control		0.005% MB		0.006% NaCN		MB + NaCN	
		$CO_2/O_2$	R.Q.	$CO_2/O_2$	R.Q.	$CO_2/O_2$	R.Q.	$CO_2/O_2$	R.Q.
1.	Cortex of brain	$\frac{0.86}{0.85}$	1.01	$\frac{0.28}{0.52}$	0.54	$\frac{0.26}{0.27}$	0.97	$\frac{0.14}{0.76}$	0.19
2.	Testicle	$\frac{0.47}{0.49}$	0.96	$\frac{0.15}{0.30}$	0.50	$\frac{0.13}{0.15}$	0.87	$\frac{0.12}{0.28}$	0.43
3.	Kidney	$\frac{2.77}{3.47}$	0.80	$\frac{1.20}{1.67}$	0.75	$\frac{0.22}{0.58}$	0.38	$\frac{0.34}{0.71}$	0.48
4.	Liver	$\frac{0.77}{1.15}$	0.66	$\frac{0.49}{0.97}$	0.51	$\frac{0.32}{0.42}$	0.76	$\frac{0.39}{0.87}$	0.45
5.	Liver	$\frac{0.84}{1.19}$	0.70	$\frac{1.25}{1.74}$	0.72	$\frac{0.43}{0.85}$	0.50	$\frac{0.72}{1.33}$	.054

In 16 experiments on the kidney, methylene blue produced a diminished oxygen consumption without any constant effects on the R.Q. Similarly cyanide decreased the oxygen uptake, but, in those experiments in which methylene blue was added, this was raised again toward the normal value (Exp. 3).

The effect of methylene blue on oxidations in the liver varied in different experiments. Five times, oxygen consumption decreased; once no change was observed and 5 times oxygen uptake increased. Cyanide, however, always diminished respiration and the diminution was reversed by methylene blue (Exps. 4 and 5).

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## Effects of Methylene Blue on Respiratory Metabolism of the Rat.

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Methylene blue exerts definite effects in the metabolism of excised tissue.<sup>1</sup> It is therefore of importance to determine the action of methylene blue in the intact animal. The respiratory metabolism of 6 rats was studied by means of a Haldane open circuit apparatus after various periods of fasting. Then 0.5 cc. M/100 methylene

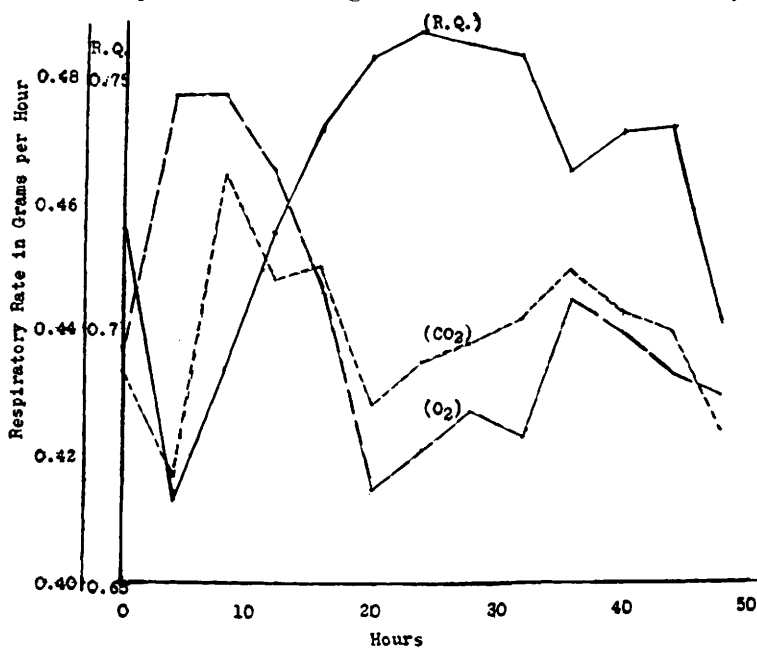


Fig. 1.  
Effect of Methylene Blue. Composite of 4 experiments.

<sup>1</sup> Himwich, H. E., Fazikas, J. F., and Hurlburt, M. H., *Proc. Soc. Exp. Biol. and Med.*, 1933, **30**, 904.