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An Improved Capillary Microrespirometer.

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Instruments for the measurement of tissue and cell respiration have steadily moved, since the introduction of Warburg's convenient manometer, in the direction of smaller volume and greater sensitivity. Gerard and Hartline[1] took advantage of the greater stability afforded by reducing the tissue chamber of a volumeter to capillary dimensions (0.5 to 1.2 mm diameter) and having this inside the relatively large "differential" chamber. Index drop movements, followed with an ocular micrometer, were consistent over 5-minute intervals, even when corresponding to volume changes of about 0.01 cmm. The diver technique, introduced by Linderström-Lang,[2, 3] is of the same order of sensitivity and consistency; and the electrical method[4] gives promise of superior performance.

We have further developed the capillary method so that it is convenient to follow the respiration of 10 tissue samples at once, and it is possible to measure absolute gas volume changes of 0.001 cmm, minute by minute, with an error of some 8% minute by minute, under 1% for longer intervals. The respiration even of bits of frog sciatic nerve weighing a fraction of a milligram can thus be followed at half-minute intervals.

The tissue chamber, also containing filter paper bits soaked with acid or alkali and separated from each other and the tissue by dry paper guards, is a short length of capillary of 1.2-1.5 mm internal diameter. The "open" end of this, after the insertion of materials, is plugged with plasticine. Into the other end has been cemented a fine drawn capillary of about 0.2 mm diameter. At the close of the experiment, this capillary is broken off and its end diameters accurately measured by end on examination with an ocular micrometer. Several such units are mounted on a central rod extending from a glass stopper, which ultimately fits into a glass container to provide a completely closed system. This is then immersed in a thermostat with the capillaries horizontal, and the whole is rotated about its long axis so that one or another capillary is brought into

[1] Gerard, R. W., and Hartline, H. K., *J. Cell. and Comp. Physiol.*, 1934, **4**, 141.
[2] Linderström-Lang, K. L., *Nature*, 1937, **140**, 108.
[3] Boell, E. J., Needham, J., and Rogers, V., *Proc. Roy. Soc.*, Series B, 1939, **127**, 322.
[4] Davies, P. W., and Brink, F., *Proc. Am. Physiol. Soc.*, 1941, 69.

the field of a long focus horizontal microscope. A droplet of synthetic isodecane (2,7 dimethyl octane kindly given us by Dr. Goldsby) is placed at the open end of each small capillary before the system is closed. While the system is reaching temperature equilibrium the droplets are drawn well in from the tube tip, where they otherwise tend to be held.

With such fine capillaries the usual index fluids—purified kerosene, mineral oil, xylol, and Ringer solution—proved unsatisfactory, although with capillaries of about 1 mm diameter Ringer solution serves well. (Incidentally, several samples of kerosene showed considerable evaporation and attendant pressure changes.) To control possible constant errors, an absolute calibration of amount and speed of response was made by altering the pressure in the outside chamber in a known manner. The drop movement was found to measure the theoretical volume change within the accuracy with which this latter was known (5%); and to reach its final position, even after large movements, within a few seconds.

In each experiment, capillaries, with and without reagents, served as thermometric controls; but their droplets rarely moved after the initial attainment of temperature equilibrium. The other tubes, containing tissue, manifested a steady and smooth oxygen consumption which usually fell slowly and continuously with time. Over time intervals of 10 minutes or more, the accuracy of readings was better than 1%; and variations in Q_{O_2} from one tissue sample to another are attributable to differences in the samples. Actually the reliability of Q_{O_2} values is limited by the accuracy of estimation of

TABLE I.

Tissue	Amount	Micrometer divisions moved in successive intervals (1 div. = 0.004 mm)	Q_{O_2}	
Whole blood	4. cmm	7.8, 7.9, 7.1, 5.5, 7.2 (60 sec. inter.)	30	
Sciatic	0.62 mg	3.6, 2.4, 2.3, 2.6 (60 sec.)	70	
Brain	0.69 "	11.0, 13.0, 12.0, 13.0, 15.6, 14.4, (30 sec.)	442	
	No. exp. averaged		90 min.	150 min.
Primordium Palii	16		530	449
Cerebellum	11		462	359
Ant. Olfactory Nuc.	8		440	352
Ventral Off. Bulb	6		457	378

the amount of respiring material. Weighing a half milligram of tissue, even on a semi-micro balance, permits a considerable percentage error; but forcing the tissue into a capillary and measuring its volume gives promise of greater accuracy. That the injury attendant upon the initial dissection is not a constant source of error is shown by the essentially similar values obtained from samples of large and small fragments of the same type of tissue. Such tests likewise indicate an adequate gas diffusion and absorption.

Some actual respiration values obtained on frog blood and nervous tissue, and the reliability of individual readings, are indicated in the tables.

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Anti-sulfapyridine and Anti-sulfathiazole Effect of Local Anaesthetics Derived from p-Aminobenzoic Acid.

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It was shown by Woods[1] that the bacteriostatic effect of sulfanilamide or sulfapyridine on hemolytic streptococci *in vitro* could be blocked by small concentrations of p-aminobenzoic acid. Also the diethylaminoethyl ester of p-aminobenzoic acid, used as a local anaesthetic under the names 'Novocaine' or 'Procaine,' was almost as strongly anti-bacteriostatic as p-aminobenzoic acid itself; in concentrations of 5.8×10^{-8}M these compounds could suppress the effect of 3.03×10^{-4}M sulfanilamide.

Owing to the increasing local and systemic use of sulfonamides in treatment of wounds and in surgery where local anaesthetics are concurrently employed, it appeared of interest to determine first, whether or not the anti-bacteriostatic effect of 'Novocaine' could be obtained with other local anaesthetics and, secondly, whether or not local anaesthetics which were not p-aminobenzoic acid derivatives would exhibit an anti-bacteriostatic effect similar to that of 'Novocaine.' To this end, 7 local anaesthetics derived from p-aminobenzoic acid and 9 local anaesthetics not derived from p-aminobenzoic acid have been tested *in vitro* for their ability to

[1] Woods, D. D., *Brit. J. Exp. Path.*, 1940, **21**, 74.