



Fig. 1

water; there might conceivably be no flux of water or a flux in either direction.

Since the activity of water in the guaiacol phase falls off as its concentration increases it would seem that we may draw the activity gradient of water in the guaiacol phase as shown by the broken line in Fig. 1.

These considerations may help to explain some of the puzzling cases met with in the living organism.

W. J. V. OSTERHOUT
J. W. MURRAY

THE LABORATORIES OF THE ROCKEFELLER
INSTITUTE FOR MEDICAL RESEARCH,
NEW YORK

CEREBRAL METABOLISM DURING FEVER¹

THE treatment of general paresis with hyperthermia, initiated by Wagner-Jauregg in 1887, is now an accepted form of therapy. In some manner fever facilitates the action of specific treatment in the cerebral form of syphilis. In an attempt to elucidate this question, the brain metabolism of patients with general paresis was studied before and during fever produced by injections of typhoid vaccine and inductotherm therapy. Samples of arterial blood and of the return flow of the brain obtained from the internal jugular vein were analyzed for oxygen, carbon dioxide, glucose and lactic acid. The changes of cerebral blood flow were estimated from the variations of blood pressure

¹ From the Department of Physiology and Pharmacology, Albany Medical College, Union University, and Bellevue Psychiatric Hospital, Department of Psychiatry, New York University Medical College. This work was aided by a grant from the Child Neurology Research (Friedsam Foundation).

and the velocity of the general circulation as determined by the objective cyanide method of Robb and Weiss.² The circulation rate through the brain is largely influenced by the changes of the general circulation.³

Complete studies were obtained on 7 patients after typhoid vaccine and 7 during fever therapy with inducto-therapy. Table I presents typical effects of

TABLE I

Experiment	Temperature (°F.)	Oxygen A-V difference (Vol. %)	Velocity of blood (Sec.)	Mean blood pressure Mercury millimeter
1.	98.0	5.15	17.6	132
	100.4	6.55	11.0	126
	102.0	6.63	10.0	113
	104.4	7.61	13.0	101
	106.0	9.14	7.4	103
2.	98.8	6.93	15	108
	105.4	7.88	11	79
	105.3	7.09	4	75
3.	98.6	7.75	20	110
	105.0	15.82	17	112

fever on the oxygen A-V difference, velocity of the blood and mean blood pressure. In 11 of 15 observations the oxygen A-V difference rose from 2.0 volumes per cent. to 8.1 volumes per cent. In 12 of 15 experiments the blood velocity was also increased, as may be seen in a typical result (Experiment I). In 3 other results (one of which is presented in Experiment II), the oxygen A-V difference remained unchanged within the error of the method. The velocity of the blood flow of the general circulation, however, was increased approximately 1½ and 3½ times. In these cases the more rapid blood flow was associated with the lower peripheral resistance, as indicated by a fall in blood pressure. One patient (Experiment III) reacted poorly and lapsed into a comatose condition. At this stage the oxygen A-V difference became huge, while the velocity of the blood revealed only a small acceleration. The small O₂ reserve in the venous blood indicated an insufficient O₂ supply to the brain. It is suggested that this relative anoxemia produced the coma.⁴

Thus in every instance an increase of cerebral metabolism during fever was indicated. This increase was evidence by a larger oxygen A-V difference, a faster blood flow, or both. The effect of the heightened metabolism of the brain on cerebral syphilis warrants further investigation.

HAROLD E. HIMWICH
KARL M. BOWMAN
W. GOLDFARB
JOSEPH F. FAZEKAS

² G. P. Robb and S. Weiss, *American Heart Journal*, 8: 1932-3, 650.

³ H. S. Forbes and S. S. Cobb, *Brain*, 61: 221, 1938.

⁴ Himwich, Bowman, Wortis and Fazekas, *Jour. Am. Med. Assn.*, 112: 1572, 1939.