1. Kagawa, C. M., Proc. Soc. Exp. Biol. and Med., 1958, v99, 705.
2. Liddle, G. W., Metabolism, 1961, v10, 1021.
3. Kagawa, C. M., Cella, J. A., Van Arman, C. G., Science, 1957, v126, 1015.
4. Noel, P. R., Leahy, J. S., Clin. Sci., 1962, v23, 477.
5. Ross, E. J., ibid., 1962, v23, 197.
6. Gantt, C. L., Dyniewicz, J. M., Metabolism, 1963, v12, 1007.
7. Snedecor, G. W., Statistical Methods, Iowa State College Press, Ames, 1956.

Received November 23, 1964. P.S.E.B.M., 1965, v118.

Experimental Analysis of the Rheoencephalogram (REG).* (29978)

FRANK GOLLAN AND RICHARD NAMON (Introduced by V. P. Popovic)
Veterans Administration Hospital and University of Miami School of Medicine, Coral Gables, Florida

The method of measuring blood flow by electrical impedance plethysmography has been investigated since 1907(1), and its development has tended to parallel developments in the electronics field(2,3,4). All plethysmographic systems for blood flow measurements are limited by their inability to detect non-pulsatile blood flow. If the heart were a continuous pump, there would be no volume change associated with blood flow. However, the hollow heart muscle with its valves, produces a highly pulsatile flow and pulse flow information for any part of the body can be recorded.

Polzer and Schuhfried(5) passed an alternating current of 20 kilocycle through electrodes on the head of 2 subjects and recorded pulsatile fluctuations of electrical conductivity. They also noted diminished amplitudes in a patient with carotid occlusion. With the recent interest in cranial plethysmography or rheoencephalography it has become important to prove the validity of assumptions used to study clinical abnormalities of cerebral blood flow. This latter situation is particularly challenging because the skull is a rigid container without measurable plethysmographic change associated with blood flow.

Methods. For analysis of hemodynamic factors influencing the rheoencephalogram, or REG, an artificial perfusion system was chosen which made the control of stroke volume, pulse pressure and pulse rate possible. Greyhounds weighing about 25 kg were anesthetized with sodium thiobarbital and injected intravenously with 100 mg heparin. Venous blood from the right atrium was drained *via* a jugular catheter into a pump-oxygenator system and returned under pressure into both common carotid arteries (Fig. 1). Stroke volume and rate of an elastic ventricle pump with ball valves could be regulated by compressed air(6). Before entering the common carotid arteries, blood flow was measured with an electro-magnetic flowmeter(7) and blood pressure with a strain gauge. Lead foil electrodes with silastic insulation were molded into the shape of contact lenses and inserted under the eye lids(8). The same results were obtained with circular aluminum foil electrodes of 6 cm in diameter placed on the dog's head. These monopolar electrodes and an indifferent electrode from the tongue of the animal, were connected with a rheoencephalograph.† The instrument measures impedance using a constant current of 0.002 amp at 30 kilocycles and approximately 0.7 volts are modulated by the pulse volume to a wide range of milliohms. Calibrations of 50 and 200 milliohms are available. Simultaneous tracings of the rheoencephalogram from both sides of the head, the blood flow and pressure in the outflow line of the pump were recorded on a Sanborn multichannel instrument. After adequate blood flow and oxygenation were established in the extracorporeal circulation, the cardiac output of the animal was stopped by externally induced ventricular fibrillation. Thus, the perfusion of the isolated dog's head

* Supported by a grant HE 06178-03 from Nat. Inst. Health, U.S.P.H.S.

† Physical Instruments, Inc. (Model 450B-1A)

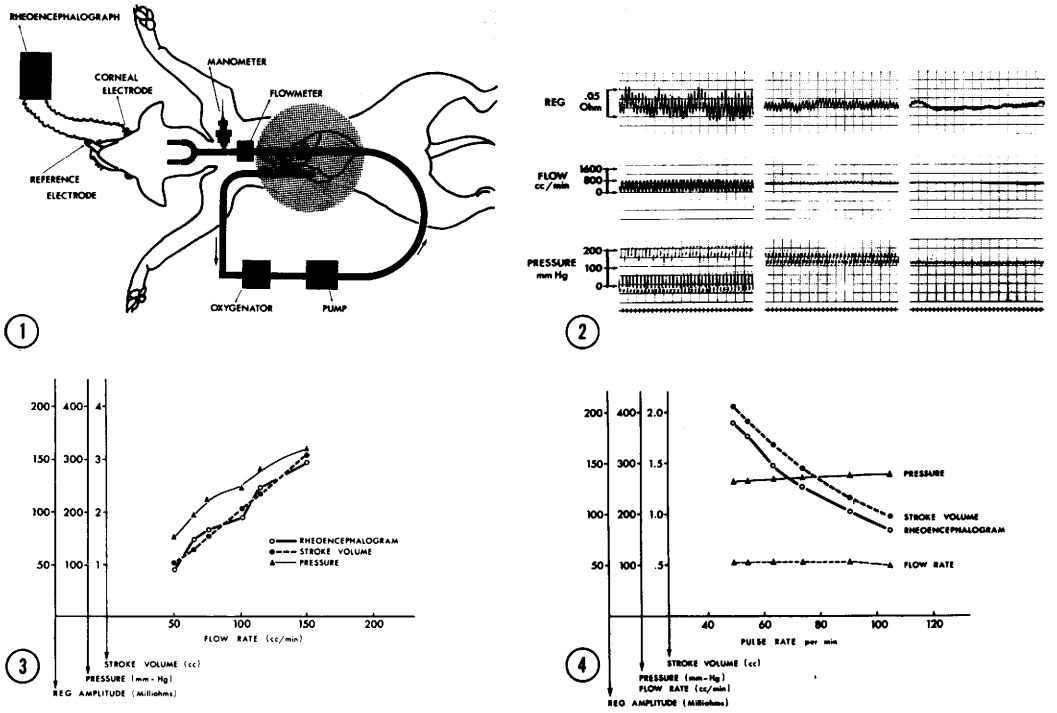

FIG. 1. Pump-oxygenator system for perfusion of the head after external induction of ventricular fibrillation.
FIG. 2. Effect of pulsatile, semi-pulsatile and continuous flow on rheoencephalogram.
FIG. 3. Effect of flow rate at constant pulse rate on rheoencephalogram.
FIG. 4. Effect of pulse rate at constant flow rate on rheoencephalogram.

through the common carotid arteries could be controlled and measured.

Results and discussion. One can demonstrate the causative effect of pulsation on the rheoencephalogram by gradually converting pulsatile into continuous flow. This can be accomplished by inserting elastic chambers of increasing size into the arterial outflow line (Fig. 2). As the stroke volume and the pulse pressure diminish during semi-pulsatile flow the amplitude of the rheoencephalogram is reduced proportionately and when flow and pressure reach their mean values the amplitudes of the rheoencephalogram become too small for evaluation. By changing the flow rate within the physiological range of carotid blood flow and blood pressure, a direct relation between the amplitude of the rheoencephalogram and pulsatile blood flow could be established. This relation held true when blood flow was increased from 50 to 600 ml/min and when pulse rate was increased from 50 to 104/min. In the intact animal the amplitude of the rheoencephalogram occurs simultaneously with the amplitudes of the stroke volume and pressure, and therefore it is difficult to decide which of these parameters affect the rheoencephalogram. With an artificial perfusion system we can change the flow rate, stroke volume, pressure and pulse rate at will and establish their causal or temporal relationship to the rheoencephalogram. If the pulse rate is kept constant and flow rate is being changed by increasing the stroke volume (Fig. 3) with more gas presture compressing the ventricle, then the flow rate is directly related to the peak amplitude of the rheoencephalogram, the stroke volume and the pressure. This experiment does not lend itself to a separation of the hemodynamic factors which influence the electrical impedance changes. However, if we keep the flow rate constant and change the pulse rate of the pneumatically driven ventrical (Fig. 4) then the rheoencephalogram reflects the stroke volume only and is independent of pressure.

Thus, the fact that the experimental impedance changes which look like volume

curves, correlate with stroke volume, may give rise to the verbal interpretation that the electrical impedance plethysmogram, just like the mechanical plethysmogram, is caused by volume changes. At this point it is well to remember Thomas Henry Huxley's words: "The tragedy of science is the shattering bereavement of seeing a beautiful hypothesis slain by an ugly fact." Some such ugly facts were brought to light by Sigman, Kolin, Katz and Jochim(9) who discovered in 1937 that the conductivity of blood flowing by gravity into rigid tubing changes linearly with velocity and that even a transitory decrease in electrical resistance occurred when blood was agitated in a beaker. Actually the correlation between "specific" resistance (ohms/cm) and velocity (cm/sec) is so striking that one may mistake Fig. 1 in their publication for a calibration of an electromagnetic flowmeter. They also observed that pressure changes were without effect but that there existed a temperature coefficient of about —1.5 ohm-cm per each degree rise. These authors believed that the changed electrical resistance of blood in motion is dependent in some unknown fashion on the direct interaction between the electrodes and the changing configuration and orientation of moving red cells. Liebman, Pearl and Bagno(10) elaborated on these findings in a circulatory model which incorporated a fixed volume of blood and a pulsatile blood pump. They observed that in rigid tubing the impedance pulse was synchronous with the velocity pulse and that their amplitudes were directly proportional. With the present availability of a great variety of blood pumps for extracorporeal circulation such impedance pulses can be reproduced easily and, if one so desires, used as a flow measurement. Liebman, Pearl and Bagno believe that the impedance pulses can be explained by the gyroscopic behavior of moving red cells and their calculations show that the conductivity changes as a function of the angle of the axis of symmetry of the cell to the applied electrical field. Although model experiments and calculations cannot serve to establish the cause of the impedance pulses *in vivo,* they show that a change in motion and not in volume of blood can give rise to proportional changes in electrical conductivity. Thus the term electrical impedance plethysmography (11) may be misleading because it implies that only volume changes may cause the impedance pulses. As long as unequivocal experimental evidence for this or any other assumption is lacking, it is more appropriate to use the noncommital term of electrical rheography.

Summary. 1. Controlled perfusion of the head of dogs through the common carotid arteries by means of a pump-oxygenator, produces electrical impedance changes. 2. If pulsatile flow is made continuous, these electrical impedance changes disappear. 3. The electrical impedance pulses are independent of pressure and directly related to stroke volume. 4. Since changes of electrical conductivity occur in blood moving in rigid tubing or in a beaker, pulse volume changes may not be the cause of the observed electrical impedance pulses. Therefore, it is suggested that instead of the misleading and cumbersome name of electrical impedance plethysmography, the more general and shorter name of electrical rheography be used.

1. Cremer, H., Münch. Med. Wchnschr. 1907, v54, 1629.

2. Horton, J. W., Van Ravenswaay, A. C., J. Franklin Inst., 1935, v220, 557.

3. Mann, H., Proc. Soc. Exp. Biol. and Med., 1937, v36, 670.

4. Nyboer, J., Bagno, S., Barnett, A., Halsey, R. H., J. Clin. Invest., 1940, v19, 963.

5. Polzer K., Schuhfried, F., Wiener Z. für Nervenheilkunde, 1950, v3, 295.

6. Hufnagel, C. A., McAlindon, J. D., Vardar, A., Vencia, N., Reed, L., Trans. Am. Soc. Art. Int. Organs, 1958, v4, 60.

7. Spencer, M. P., Green, H. D., Circ. Res., 1955, v3, 39.

8. Bishop, S., Nyboer, J., Harper Hosp. Bull., 1962, v20, 142.

9. Sigman, E., Kolin, A., Katz, L. N., Jochim, K., Am. J. Physiol., 1937, v118, 708.

10. Liebman, F. M., Pearl, J., Bagno, S., Physics in Med. & Biol., 1962, v8, 177.

11. Nyboer, J., Electrical impedance plethysmography, Charles C Thomas Publ., Springfield, Ill., 1959.

Received November 4, 1964. P.S.E.B.M., 1965, v118.