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**Clinical, Electroencephalographic, and Biochemical Changes
During Insulin Hypoglycemia.***

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The present report is concerned with further investigation on the insulin treatment of schizophrenia. This work was done at the Harlem Valley State Hospital, Wingdale, New York, where patients with schizophrenia are receiving Sakel's insulin treatment. Ten observations were made on 5 patients. An attempt was made to correlate the clinical, biochemical, and electrical changes occurring as a result of insulin. It was hoped that such studies would establish a physiological basis for this treatment.

Clinical observations were made before insulin was injected. Brain waves were recorded at this time and samples of blood, drawn from the internal jugular vein and femoral artery were analyzed for oxygen¹ and glucose² in order to estimate cerebral metabolism. All these observations were repeated during various stages of hypoglycemia and after sugar was administered to terminate the coma.

The typical results here published were obtained on E.B. during hypoglycemia caused by a dose of insulin adequate to produce coma. The symptoms exhibited by the patient are presented and divided in 4 groups; the first including somnolence, perspiration, and hypotonia developed during the first 2 hours after the injection of insulin. Loss of consciousness, primitive movements, and forced grasping formed the second group. The third group is characterized by tonic and torsion spasms and occurred chiefly during the fourth hour. The final group in the fifth hour includes deep coma with depressed tendon reflexes and respiratory disturbances which necessitated termination of the hypoglycemia with sugar. Table I contains the results of the arterial-venous oxygen differences of the cerebral blood and values for arterial blood sugar, alpha frequency and delta index, as well as the time after the injection of insulin that these observations

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¹ Van Slyke, D. D., and Neill, J. M., *J. Biol. Chem.*, 1924, **61**, 523.

² Folin, O., and Wu, H., *J. Biol. Chem.*, 1920, **41**, 367.

TABLE I.

Min. after insulin injection	Arterial-Venous O ₂ Difference Vol. %	Blood Sugar mg %	Alpha Frequency per second	Delta-Index, cm
0	9.0	89	9.5	0.5
70	—	—	7.0	16.0
90	2.8	22	0.0	21.0
175	—	—	0.0	22.0
252	1.6	23	0.0	20.0
10 (After sugar)	4.5	45	7.0	—
30 " "	6.3	57	8.8	2.0

were made. The first group of symptoms appeared while the oxygen uptake fell from 9.0 volumes % to 2.8 volumes %. The second, third, and fourth groups developed in turn as oxygen uptake decreased further to 1.6 volumes %. The administration of sugar was followed by a rapid reversal of the symptoms and the blood picture. In view of the fact that there may be no significant change in cerebral blood flow during hypoglycemia uncomplicated by convulsions³ it may be concluded that (a) there is a progressive decrease in cerebral metabolism as indicated by the diminution in the arterial-venous oxygen difference, (b) this decrease in oxygen consumption may be correlated with a lessening frequency and final disappearance of the alpha waves as well as an augmentation of the delta index, and (c) the progress of the symptoms through the 4 stages is also associated with an ever-deepening depression of cerebral metabolism. Thus a parallelism is revealed in the metabolic, electrical, and clinical changes resulting from the injection of insulin.

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An Indirect Method for Repeated Determinations of Blood Pressure of Rats.

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A frequently used method for recording approximate mean blood pressures in rats is the insertion into the aorta, or other large vessels,

³ Leibel, B. S., and Hall, G. E., *PROC. SOC. EXP. BIOL. AND MED.*, 1938, **38**, 894.

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