

administered intravenously would be without virucidal effect in the CNS.

These studies are being continued to include the effect of antiserum administered intrathecally.

Summary. Studies on the penetration of antiserum into the tissues of monkeys infected with poliomyelitis have shown that only a very small percent of circulating antibody is found in the spinal cord, thus suggesting little possible value in the use of antiserum in preventing the spread of poliomyelitis if such occurs other than by the blood stream.

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Effects of Insulin Treatment on the Cerebrospinal Fluids of Schizophrenics.

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Changes of the non-electrolyte/electrolyte ratio (INE/IE) in cerebrospinal fluids were observed in cases of spontaneous convulsions¹ and in schizophrenics in which convulsions had been induced by metrazol treatment.² A marked parallelism was found between the values of INE/IE and the intensity of the convulsions. Evidence has been given that the increases of the ratio are due to an increase of the non-electrolytes (cleavage products of proteins and lipoids) rather than to a decrease of the electrolytes. The increase in cleavage products after convulsions was explained as due, at least partly, to changes of the cellular and vascular permeability.

In order to test some of these conclusions it seemed of interest to extend these investigations to the cerebrospinal fluids of schizophrenics treated with insulin. Although insulin has in such cases therapeutic effects similar to the ones of metrazol, the occurrence of convulsions is not paramount.³ Moreover, observations have been reported indicating differences in the effects of the two methods of

¹ Spiegel-Adolf, M., *PROC. SOC. EXP. BIOL. AND MED.*, 1937, **37**, 92.

² Spiegel-Adolf, M., and Freed, H., 94th Meet. Am. Psych. Assn., San Francisco, June, 1938. Will appear in *Confinia Neurol.*, 1939, **2**.

³ Cobb, S., *Arch. Int. Med.*, 1937, **60**, 1098.

treatment on brain metabolism,⁴ with possible bearings upon the composition of the cerebrospinal fluids.

The method used in measuring the conductivity and interferometry values of the cerebrospinal fluids and in computing the INE/IE ratio was published previously.^{1, 5}

The material on which our observations were based consisted in 73 samples of cerebrospinal fluids from 25 schizophrenics in various stages of insulin treatment. Previous observations⁵ indicated that repeated tapping alone does not influence the INE/IE ratio. In all the cases, reports of the clinical symptomatology and in most of them data concerning the albumin and globulin content of the cerebrospinal fluids were available. Only a few sugar determinations have been made. The results were near the lower level of the average findings, confirming thus the results of Schretzmayr.⁶

Fifteen of our cases could be examined before the insulin treatment was started; 2 cases had undergone metrazol treatment before; in 8 cases, the measurements in the cerebrospinal fluids were made only after the patients had undergone insulin treatment. The average INE/IE ratios of these 3 groups were .27, .33, and .33 respectively. The first 2 figures check rather closely with similar figures reported in our studies upon the effect of metrazol treatment in schizophrenics; the third figure referring to possible effects of the insulin treatment will be considered later.

In 21 cases, complete reports as to the occurrence or non-occurrence of convulsions were available. Eleven cases of this group, which were observed before and during the whole course of insulin treatment never did show any convulsions. The average INE/IE values were .290 before the treatment and .292 after. Ten cases which all had shown convulsions of various intensity reached, after the insulin treatment, INE/IE values of .335 on the average.

Since, in the cases of epileptiform seizures, a certain parallelism could be observed between the severity of the convulsions and the height of the INE/IE ratio, an attempt was made to classify the cases which showed convulsions in the course of insulin treatment according to the number and the severity of these convulsions. If we order the material according to the number of convulsions, we find that 6 cases, which had between one and 4 convulsions, showed an average INE/IE value of .31. In 4 cases with 5-8 convulsions, the average INE/IE ratio was .38. If classified according to the

⁴ Himwich, H. E., Bowman, K. M., Farkas, T. F., and Orenstein, L. L., *PROC. SOC. EXP. BIOL. AND MED.*, 1937, **37**, 359.

⁵ Spiegel-Adolf, M., *Confinia Neurol.*, 1939, **2**, 1.

⁶ Schretzmayr, V., *Arch. f. Psych. u. Nervenkr.*, 1938, **108**, 680.

severity of the convulsions, in 5 cases the degree of the convulsions was recorded as moderate, the corresponding INE/IE value being .30. In the 5 other cases showing severe convulsions, an average INE/IE value of .376 was reached.

An attempt was made to correlate the changes in the INE/IE values to the clinical changes of the patients during the insulin treatment. In 8 of our cases, clinical improvements were reported while 16 showed relapses. The average INE/IE values for these two groups were .28 and .315 respectively. Although these figures seemed to indicate the possibility of prognostic value of the INE/IE ratios, it seemed necessary to ascertain how far the convulsions influenced the ratios in the improved cases as well as in the group with relapses. The material was divided into 4 groups: improvements without and with convulsions and relapse without and with convulsions. In the above sequence, the INE/IE ratios are .27, .33, .29, and .33 respectively. Only for the 2 groups without convulsions does there seem to exist a certain parallelism between the clinical findings and the changes in the INE/IE ratios. Nevertheless, it must be emphasized that even the value of .29, observed in cases showing relapses without convulsions, is somewhat below the ones observed in patients with organic lesions of the central nervous system.⁷ In the cases with convulsions, the psychiatric findings and the INE/IE ratios seem to be independent of each other. The ratios in the cases with convulsions, however, correspond closely to the ones observed in patients with epileptic seizures.

Since metrazol is used in the treatment of schizophrenics in convulsion-producing doses, it was not possible in the metrazol group to decide how far the composition of the spinal fluid is influenced by the convulsions alone, and how far by the brain changes associated with the alteration in the psychic behavior of the patients. This question could be studied in the insulin group, since we have here changes in the mental picture with and without convulsions. The above analysis of these various groups seems to confirm the hypothesis that the increase observed in the INE/IE ratios is mainly due to the effect of convulsions.

Summary. The non-electrolyte/electrolyte ratios (INE/IE) were measured by combined conductivity and interferometry methods in cerebrospinal fluids of schizophrenics treated with insulin. A marked parallelism could be observed between increases of INE/IE and occurrence and frequency and severity of the convulsions. These findings confirm previous observations in epileptics and in schizophrenics under metrazol treatment.

⁷ Spiegel-Adolf, M., *J. Nerv. and Ment. Dis.*, 1939, **89**, 311.