Diastase determinations may therefore be of distinct help in the differential diagnosis of acute conditions of the upper abdomen, but it must be remembered that they only supplement clinical judgment.

9662

Effect of Insulin on Carbohydrate Tolerance of Nondiabetic Individuals.

J. T. MAHER AND MICHAEL SOMOGYI.

From the Laboratories of the Robert Koch Hospital and the Jewish Hospital of St. Louis.

One of us (Somogyi)[1] has shown that in diabetic patients the continued overdosage of insulin, *i. e.*, the administration of quantities sufficient to cause hypoglycemias, gradually diminishes the carbohydrate tolerance of the patient and aggravates the diabetic condition. In this paper we call attention to the fact that insulin when administered to nondiabetic individuals, exerts a similar effect.

This observation was made on nondiabetic tuberculous patients, who were treated with insulin with the purpose of inducing an increase in their body weight. The procedure in this work differed from others described in the literature in 2 respects. In the first place, the amount of insulin used was very small. In 2 cases only 10 units were given daily, injected in 5-unit doses before the noon and evening meals, while the remaining patients received at the beginning 10, and subsequently 20 units daily, always administered in 2 equal doses. In the second place, the duration of the treatment in this experiment was much longer than in others reported; the observations extended in 5 cases over a period of 6 months, and in one case over 12 months.

In each case glucose tolerance test was performed a short time before the beginning of the treatment and a second test after insulin injections had been continued for approximately 6 months; in one case a third test was carried out after 12 months of uninterrupted treatment. In the tolerance tests uniformly 100 gm. of glucose was given orally and the blood sugar was determined at hourly intervals by the Shaffer-Hartmann method, using copper reagent No. 50 of Shaffer and Somogyi.[2] The blood samples were depro-

[1] Somogyi, M., PROC. SOC. EXP. BIOL. AND MED., in press.

[2] Shaffer, P., and Somogyi, M., *J. Biol. Chem.*, 1933, **100**, 695.

teinized with Somogyi's zinc method[3] which removes nonfermentable reducing substances so that the analysis furnishes true sugar values (which are about 20 mg. % lower than the apparent sugar values obtained with the Folin-Wu method). The results are presented in Table I. It may be seen from these figures that following the insulin treatment the carbohydrate tolerance of all of the subjects has undergone marked deterioration, so that their response to glucose tolerance tests became identical with that of diabetic patients. It is noteworthy that the change in 2 of the 6 patients, Kate R. and Jessie H., who received only 10 units of insulin per day, was of the same order of magnitude as in the others.

TABLE I.
Deterioration of the Carbohydrate Tolerance of Nondiabetic Subjects as the Result of Insulin Injections.

Name and age of patient	Date of test	Time, hr. 0	0.5	1	2	3 Blood Sugar, mg.% (true sugar)	Daily dosage of insulin
Ella, 42	8/31/36	76	178	137	105	81	10 U., 10/22/36 to 2/20/37,
	4/26/37	80	191	191	116	60	20 U., from then on
Jessie, 33	9/11/36	101	153	97	71	54	10 U., 9/12/36 to date of
	5/3/37	100	167	218	178	95	tolerance test
Mary, 32	9/1/36	78	125	177	135	87	10 U., 10/22/36 to 12/10/36,
	5/3/37	85	204	253	182	101	20 U., from then on
Kate K., 38	9/1/36	74	142	97	67	62	10 U., 10/22/36 to 12/14/36,
	4/28/37	78	196	189	141	45	20 U. from then on
Kate R., 32	8/31/36	79	225	178	161	50	10 U., 10/22/36 to date of
	4/26/37	94	244	233	222	85	second tolerance test
Dorothy, 35	9/1/36	74	145	124	63	47	10 U. 10/22/36 to 1/22/37,
	4/28/37	74	176	318	218	107	20 U. from then on
	10/7/37	93	—	329	308	154	

The progressive character of the deterioration is well illustrated in the behavior of Dorothy M. Before subjected to insulin injections her response to the glucose tolerance test was definitely nondiabetic. After 6 months of treatment, during the first half of this period with 10, the second half with 20 units of insulin per day, her response became distinctly that of a diabetic, and after another 6 months of injections, with 20 units of insulin daily, her carbohydrate tolerance exhibited further deterioration.

Wilder, Smith and Sandiford[4] were the first investigators to ob-

[3] Somogyi, M., *J. Biol. Chem.*, 1930, **86**, 655.

[4] Wilder, R. M., Smith, F. H., and Sandiford, I., *Ann. Int. Med.*, 1932, **6**, 724.

serve this phenomenon when studying the influence of insulin upon the body weight of nondiabetic, obese individuals. Two patients of these authors received 55 units daily, one for 12, the other for 25 days. At the end of the treatment it was found in both cases "that responses to glucose tolerance tests were obtained typical of diabetes mellitus."

Clark, Gibson and Paul[5] employed insulin injections on a number of nondiabetic patients with the purpose of increasing their subnormal body weight. They injected gradually increasing doses, starting with 15 units daily and raising it frequently to 75 units. In 3 cases glucose tolerance tests were performed immediately before the beginning of the treatment and the day after discontinuation of the injections. One of the patients received 15 to 45 units daily over a period of 20 days, the second 15 to 54 units for 20 days, and the third 15 to 75 units over a period of 45 days. All 3 cases showed deterioration of their carbohydrate tolerance, and in one case the progressive aggravation of the process also was illustrated.

Both groups of workers point out the temporary character of this condition caused by insulin. After discontinuation of the injections the tolerance tests show a gradual return in the direction of normal, but after 8 days of recovery (the changes were not followed longer) the glucose tolerance still was distinctly inferior to that before treatment. We intend to follow the changes in our patients over longer periods of time after stoppage of the treatment; it is of interest to observe the course of recovery after the prolonged action of insulin to which our patients were subjected.

On the basis of these findings it is only to be expected that schizophrenic patients, treated often with very large quantities of insulin, should respond with diminished carbohydrate tolerance. Studies in progress show this to be the case. (This report was presented before the Missouri Section of the Society for Experimental Biology and Medicine last October. Since then Looney and Cameron[6] published observations made on schizophrenic patients which agree with ours.)

This phenomenon, in our opinion, is closely related to that observed on diabetic patients who are treated with excessive doses of insulin.[1] In the case of the diabetic any amount of insulin that

[5] Clark, B. B., Gibson, R. B., and Paul, W. D., *J. Lab. Clin. Med.*, 1935, **20**, 1008.

[6] Looney, J. M., and Cameron, D. E., PROC. SOC. EXP. BIOL. AND MED., 1937, **37**, 253.

depresses the blood sugar below the fasting level represents an overdose which entails high degrees of hyperglycemia, *i. e.*, a further diminution of carbohydrate tolerance. In the case of the non-diabetic subject, whose pancreas supplies adequate amounts of insulin, any added quantity of extraneous insulin represents an excess and leads to deterioration of the carbohydrate tolerance just as overdosage does in the diabetic.

9663

Blood and Spinal Fluid Magnesium and Calcium Levels in Epilepsy and Convulsive States.*

DAVID M. GREENBERG AND ROBERT B. AIRD. (With the assistance of Muriel Boelter.)

From the Division of Biochemistry and the Department of Surgery, University of California Medical School.

Certain of the constituents of blood and spinal fluid in cases of epilepsy have been subjected to analysis by a number of investigators in order to test the hypothesis that the incidence of convulsions in this condition is associated with a disturbance of the ion balance of the body. No significant variation from normal has been found in the calcium content of the blood and spinal fluid in epileptics.[1-4]

Some time ago Hirschfelder and Haury[5] reported that they observed low magnesium and high potassium levels in the blood plasma in a high percentage of epileptic subjects during convulsive attacks.

To our knowledge virtually no information is available on the magnesium content of the spinal fluid and red blood corpuscles in epilepsy.

Since the blood and spinal fluid of epileptic subjects were available to the authors, a series of analyses was undertaken on the composition of the blood and spinal fluid of subjects afflicted with epilepsy

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1 Hamilton, B., *J. Biol. Chem.*, 1925, **65**, 101.

2 Osnato, M., Killian, J. H., Garcia, T., and Mattice, M. R., *Brain*, 1927, **50**, 581.

3 Katzenelbogen, S., *J. Nerv. and Ment. Dis.*, 1931, **74**, 636.

4 Scott, M., and Pigott, A. W., *Arch. Neurol. and Psych.*, 1936, **36**, 596.

5 Hirschfelder, A. D., and Haury, V. G., PROC. SOC. EXP. BIOL. AND MED., 1935, **33**, 40.