OBSERVATIONS IN HYPOGLYCAEMIA III: C.S.F. SUGAR AND COMA.

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FINDING the blood-sugar level uncorrelated with the clinical symptoms of hypoglycaemia, Day and Niver (2) tried to establish the sugar level in the cerebro-spinal fluid as an indicator of the onset of coma. After examination of the sugar in both fluids every half hour from the injection of insulin until feeding of the patient, they found that coma began when the C.S.F. sugar reached a point between 30 and 15 mgm. per cent., whereas blood sugar was at its lowest point several hours before. The ratio C.S.F. sugar/blood sugar, normally between 10/8 and 10/6, was according to these authors " completely reversed " from the first hour after insulin injection onwards. They base their views on 43 observations of which only one was divergent, but no detailed figures are given. The four curves reproduced for illustration show the slow fall of C.S.F. sugar against the rapid falling blood-sugar level; but the alleged close correlation between coma and C.S.F. sugar can only be seen in one of the curves.

Zeghauser and Erb (5) came to the same conclusion after examining the C.S.F. of thirteen patients during the pre-comatose and the comatose stage of hypoglycaemia. They performed two, and in a few cases three lumbar punctures in each patient. They found the C.S.F. sugar always lower in coma than in the precomatose stage, and believe that it goes parallel with the increasing severity of clinical symptoms.

Day and Niver's observations have been accepted among others by McGregor and Sandison (4), who, however, observed that the sugar level of the C.S.F. did not rise for some time after intravenous glucose was given and the patient was out of coma.

METHOD.

We performed 14 lumbar punctures on six patients who were chosen because they were relatively quiet in the precomatose stage and had no motor symptoms during coma. It did not seem feasible to leave the needle in position through-

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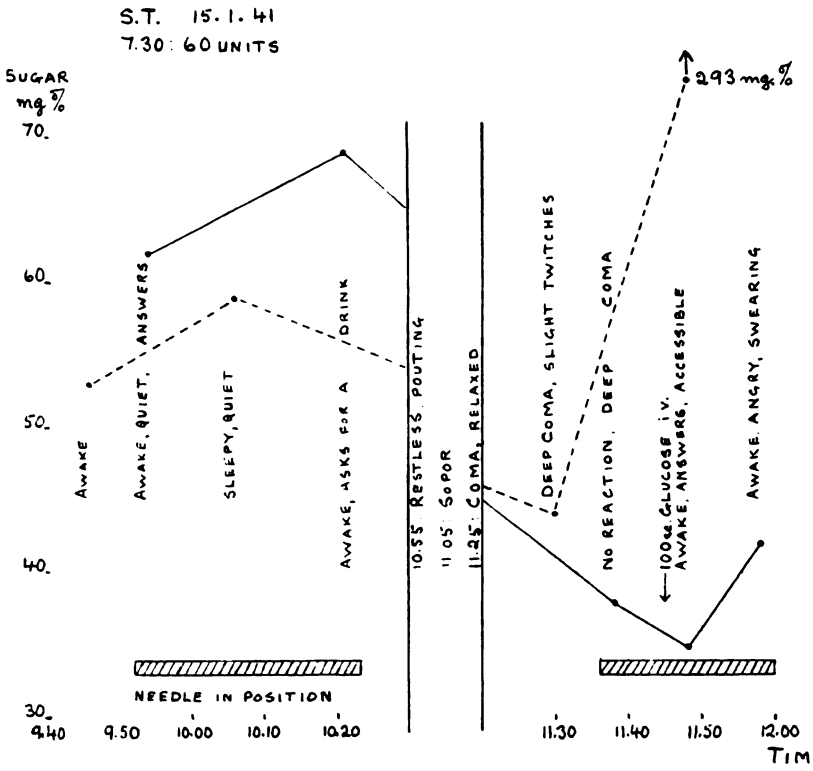


FIG. 1.—Precomatose and waking-up period. —— C.S.F. sugar ; - - - blood sugar.

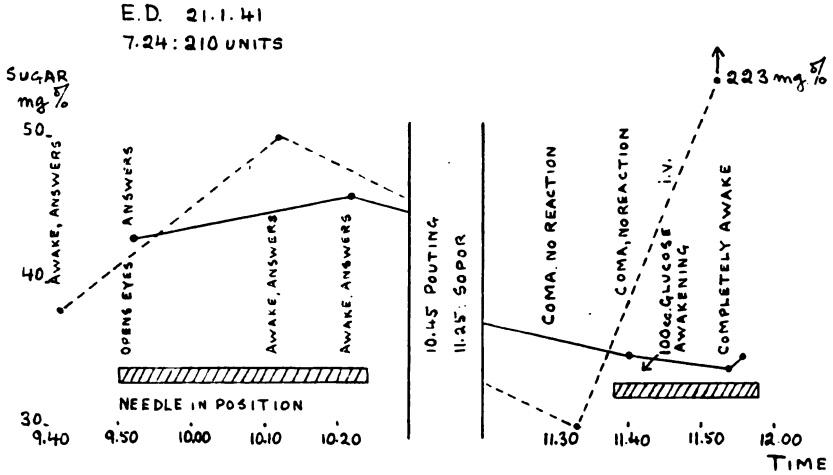


FIG. 2.—Precomatose and waking-up period. —— C.S.F. sugar ; - - - blood sugar.

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out the hypoglycaemia, the method used by Day and Niver; on the other hand, single lumbar punctures, as done by Zeghauser and Erb, could not furnish a clear picture of the movements in the C.S.F. sugar level. The needle was, therefore, left in position for approximately half an hour, during which time 2–4 specimens were taken. On four occasions we performed two lumbar punctures in the same patient on the same day; later we tried to eliminate the possible effect of the first on the second lumbar puncture, by testing the three periods (precomatose, comatose, and waking-up period) on different days. There was no essential difference in the results of this procedure and the earlier one. For testing the waking-up period the needle was inserted in coma, and while the patient received intravenous glucose it was left in position until one or two specimens were taken from the awakened patient. We thus collected 35 specimens of C.S.F. in which the sugar content was examined, using the Hagedorn-Jensen method, mostly in duplicate. Some of the parallel blood-sugar specimens were taken at the same time as the liquor specimens, but most of them were taken 10–20 minutes before in order to avoid the influence of the stimulus of the lumbar puncture on the blood-sugar level.

Results.

In six observations of the precomatose stage, we found the C.S.F. sugar value above that of the blood sugar approximately two hours after the injection of insulin. The C.S.F. sugar fell below the blood sugar in three observations within the next half hour, but this was obviously produced by the sharp rise of the blood sugar caused by the stimulation of the lumbar puncture. In all cases the two levels approached one another when the patient went into coma; but of eight observations during coma, only three showed C.S.F. sugar level lower than the corresponding blood-sugar level. Generally speaking, the two curves run parallel, and the increase in blood sugar produced by the stimulus of the lumbar puncture is repeated with some delay in a corresponding rise of the C.S.F. sugar. This holds true for the precomatose stage as well as during coma.

Our findings during the waking-up period (five observations) show that the return of consciousness is not related to a rise of the C.S.F. sugar level. While the blood sugar rose up to between 170 and 300 mgm. per cent. and the patient was completely awake, accessible and answering rationally, the C.S.F. sugar remained unaltered, in one case for 14 minutes (Fig. 2), and began to increase only after 10–20 minutes' delay.

In the following detailed survey of our observations, all numbers, not indicated otherwise, represent mgm. per cent. of sugar (total reduction); blood-sugar estimations are given in *italics*; C.S.F. sugar estimations in ordinary print. All times are a.m. Further observations are recorded in Figs. 1–4.

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S. T—	26.i.40	7.25	60 units insulin.
		9.25	Drowsy, *50*.
		9.35	First L.P., 55.
		9.55	*48*.
		10.05	54, needle removed.
		10.55	Sopor.
		11.12	In coma.
		11.30	*42*.
		11.40	Second L.P. 47.
		11.42	110 c.c. glucose i.v., waking up.
		11.46	42, needle removed.
		11.50	*237*.
E. D—	3.i.41	7.45	190 units insulin.
		9.43	*38*.
		9.50	Drowsy, stuporous, L.P. 53.
		10.15	*46*.
		10.24	29, needle removed.
E. D—	6.i.41	7.30	190 units insulin.
		9.35	Drowsy, *45*.
		9.43	L.P. 47, waking up.
		10.10	*48*.
		10.15	Still awake, 35; needle removed.
E. D—	7.i.41	7.32	190 units insulin.
		10.45	In coma.
		11.15	*20*.
		11.22	L.P. 17.
		11.28	70 c.c. glucose i.v., awake.
		11.30	*202*.
		11.34	22, needle removed.
L. B—	14.iii.41	7.30	100 units insulin.
		9.53	Drowsy, *34*.
		9.56	First L.P. 60.
		10.06	63.
		10.16	56.
		10.26	56, needle removed.
		10.28	*38*.
		10.35	In coma.
		11.04	*33*.
		11.10	Second L.P. 45.
		11.12	100 c.c. glucose i.v.; restless, needle removed.
K. A—	31.iii.41	7.30	150 units insulin, fasting b.s. *105*.
		10.30	In coma.
		10.45	*48*.
		10.55	L.P. 55.
		11.00	60 c.c. glucose i.v., awake.
		11.08	*173*, 48; needle removed.

Discussion.

Certain conclusions can be drawn from our investigations although they did not procure values of the C.S.F. sugar at the actual time when the patient went into coma. Attempts to obtain these were unsuccessful because we found it impossible in our patients to extend the duration of the lumbar puncture over more than half an hour. The rise in blood sugar brought about by the stimulus of the lumbar puncture regularly delayed the beginning of coma. In spite of a considerable decrease of C.S.F. sugar, which in one case fell to almost half of its value within 35 minutes, the patient remained awake and went into coma only about half an hour after the needle had been removed. This observation in itself is inconsistent with the idea of coma being dependent on the level of C.S.F. sugar. Further proof against this idea are the fluctuations of this level observed during coma parallel with blood-sugar fluctuations, but without concomitant clinical changes. Finally, from the absence of correlation between waking up and C.S.F. sugar it can be discarded as a fallacy.

One of the factors misleading the authors who promoted the idea was that they did not take account of the lumbar puncture acting as a stimulus, and raising the blood-sugar curve. This probably produced the "reversed ratio" found by Day and Niver, as well as the disproportionate high blood-sugar values as compared with C.S.F. sugar found by Zeghauser and Erb, who took their blood specimens simultaneously with the lumbar puncture.

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The influence of the lumbar puncture as a stimulus and of other factors interfering with the studies in C.S.F. sugar has been discussed by von Bothmer (1), who lately conducted a thorough investigation into the problem. He examined the relation between the two sugar levels in 105 normal persons and in a number of patients suffering from diseases of the nervous system. Under normal conditions, i.e. if the permeability of the meningeal barrier was normal,

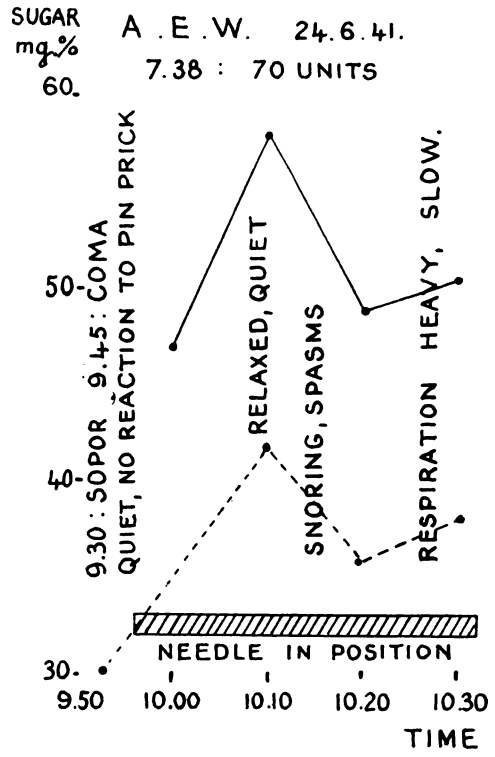


FIG. 3.

he found the C.S.F. sugar following closely the variations of the blood sugar with a delay of 15 to 30 minutes. The ratio blood sugar/C.S.F. sugar, however, was not static, but variable ; it is relatively higher in cases of low blood sugar, and, conversely, relatively lower if the blood-sugar level is increased. It is, therefore, impossible to give a standard ratio which could be considered as normal, irrespective of the blood-sugar level. From von Bothmer's results, the increase of the ratio from 57 per cent. in the precomatose stage to 73 per cent. during coma, as observed in one of our patients, is not abnormal, because of the parallel decrease of both sugar levels. The closing-in of the two curves frequently observed in our cases is only what one would expect

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under normal conditions of permeability. In some cases, however, the ratio shows a definitely pathological increase and is even reversed (see Figs. 1 and 4). This is, according to von Bothmer, an unspecific symptom observed sometimes in diseases with diffuse and severe cerebro-spinal changes like tumours, cerebro-spinal syphilis, uraemia, carbon monoxide poisoning, etc. The explanation that the increased ratio may be due to alterations of per-

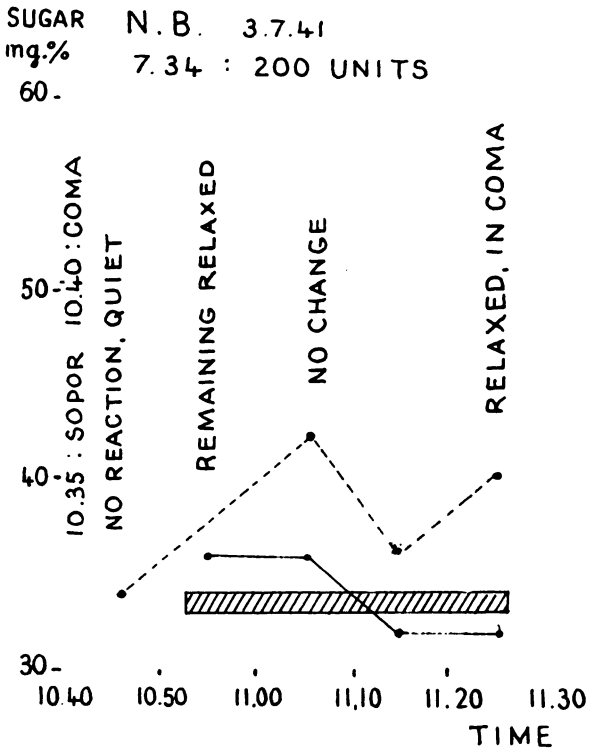


FIG. 4.

FIGS. 3 and 4.—Two examples of coma period. —— C.S.F. sugar ; – – – blood sugar.

meability in the barrier between blood and C.S.F. seems to be ruled out for hypoglycaemic coma by the findings of Forstmeyer (3), who discovered no demonstrable changes in the permeability during the insulin treatment. Further research on this point is wanted.

SUMMARY.

The results of parallel examinations of the sugar levels in blood and in cerebro-spinal fluid did not confirm the idea that the hypoglycaemic coma

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is correlated with a low C.S.F. sugar level, or that the clinical symptoms of hypoglycaemia are more dependent on the C.S.F. sugar than on the blood sugar. The two levels run a parallel course with a certain temporal delay of the C.S.F. sugar ; this corresponds to results obtained under physiological conditions. The " reversed ratio " found in some cases during coma cannot be explained from our present knowledge.

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