

AN UNUSUAL COMPLICATION OF INSULIN SHOCK
(HYPOGLYCÆMIC) THERAPY.*

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INTRODUCTION.

SALM (1) has recently described stuporous conditions which developed in schizophrenic patients undergoing the insulin shock treatment. He concludes that such cases constitute a serious problem, because, if they do not yield to the repeated administration of sugar, one is at a loss in regard to specific treatment.

Recently, while giving this insulin shock treatment to six patients, we were surprised to find that one patient on the twenty-second day of treatment did not awake from the hypoglycæmic coma on being given food. Intravenous glucose and adrenaline also failed to revive her. Blood and spinal fluid sugars were then found to be excessive, and anti-diabetic treatment (including insulin) was administered with success.

PART I.

The patient a female, aged 36 years, was admitted to hospital on April 25, 1935.

The duration of the mental illness was 11 years. Treatment was begun on April 6, 1937. Patient, fasting, received 10 units insulin in the morning, and, a few hours later, received food. The amount of insulin was increased daily by about 5 units. For 21 days there was no major incident. Detailed notes were made each day. It will be sufficient to give the notes of one or two days during this period:

Second Day. April 7, 1937.

- (1) Time and amount of insulin: 10.30 a.m., 15 units.
- (2) Time of food: 1.30 p.m.
- (3) Blood sugar: 10.25 a.m., 65 mgrm. per 100 c.c.
- (4) *Clinical notes.*—No mental change; diarrhœa during the afternoon.

* A communication read at the Quarterly Meeting of the Irish Division, Royal Medico-Psychological Association, held at Kilkenny Mental Hospital, July 24, 1937.

Fourth Day. April 9, 1937.

- (1) 10 a.m. : 25 units.
- (2) 1 p.m. : Food given to terminate day's treatment.
- (3) 11.50 a.m. : Blood sugar, 45 mgrm. per 100 c.c.
- (4) *Clinical notes.*—Had an excited episode at 11 a.m., when she became restless, got out of bed and made it impossible to take blood for blood sugar estimation, which, however, was taken at 11.15 a.m., when she lay again quietly in bed. At 1 p.m. she was perspiring profusely; while taking her meal at this hour she was noticed to be drowsy, to doze off in such a way as to hinder the taking of food, so glucose D (1½ oz.) was administered in a glass of water at 1.10 p.m., and she quickly revived. Heart action good.

Fourteenth Day. April 19, 1937.

Prominal as usual (3 gr. had been given for some days previously, before the insulin injection, on account of a tendency to develop epileptic seizures during hypoglycæmia).

- (1) 8.30 a.m. : 40 units insulin.
- (2) 12.50 p.m. : Food given (glucose per nasal tube).
- (3) 12.35 p.m. : Blood sugar 35 mgrm. per 100 c.c.
- (4) *Clinical notes.*—10.15 a.m.: Perspiring; beginning to be drowsy; had much more peaceful coma than on previous days until 12.15 p.m. when she suddenly seemed to wake up and rolled around in the bed. Soon she dozed off again, but resisted a good deal and jerked herself all over the bed and gave a good deal of trouble in the taking of blood, at 12.35 p.m. She was like this—in a kind of “coma vigil”—until 12.50 p.m., when she was fed nasally with glucose. She then had shivering and tremors while awaking. She seemed more accessible for some time afterwards. She answered questions apparently quite normally, but without much initiative.

From April 6 to April 27 (21 days) patient had been given insulin on every day except 5 days. For the following reasons it seems certain that this insulin created hypoglycæmia every day that it was given :

- (a) (1) Blood sugar on April 7 = 65 mgrm. per 100 c.c.
- (2) “ “ “ “ 9 = 45 “ “
- (3) “ “ “ “ 19 = 35 “ “

(b) Glucose (given by tube) caused her to awake from the comatose state, day after day, in about 20 minutes.

PART II.

On the twenty-second day events took a different course, as the following record shows :

Twenty-second Day. April 27, 1937.

- (1) 8.30 a.m. : 40 units insulin.
- (2) 1.30 p.m. : Glucose per nasal tube.
- (3) *Clinical notes.*—11.20 a.m. : Very loud stertor; perspiring profusely; rapid pulse.

11.27 a.m. : Still some stertor, which increased, so she was turned well on side, and hung over edge of bed ; breathing improved.

11.35 a.m. : She was in quiet coma again. She remained in this quiet, comfortable coma until—

12.35 p.m., when she began to snore again. Held over bed and drained of saliva. This helped, but did not remove the stertorous breathing, which was still present at—

12.50 p.m., so she was again turned into bed and again went off into a quiet coma, with perfectly satisfactory pulse and respiration.

1.10 p.m. : Stertor, fairly rapid pulse and general trembling of muscles began.

1.20 p.m. : A similar attack with shivering (mild rigor) set in, with, however, a pulse-rate of 110 per minute only. This eased off, but it was thought better to give glucose at—

1.30 p.m.

2.50 p.m. : She was not awake, but had stertorous breathing, and at—

2.55 p.m. : Cyanosis.

3.5 p.m. : Patient was given $\frac{1}{100}$ gr. adrenaline subcutaneously.

3.25 p.m. : 30 c.c. 50% solution of glucose was given intravenously.

3.30 p.m. : Nasal tube was passed, and it was noticed that the glucose given at 1.30 p.m. returned almost in full quantity. Reaction of fluid from stomach was neutral or slightly alkaline.

3.30–4 p.m. : Another nasal feed (4 oz. glucose) was given ; more intravenous glucose was administered—in all 90 grm.

Neither this nor subsequent nasal feed of glucose (about 5 p.m.) revived the patient, who, most inexplicably, remained in coma.

5.30 p.m. : *Blood sugar—280 mgrm. per 100 c.c.*

Later a salt solution, per nasal tube, was given, to influence the pseudo-tetanic condition which had, by then, set in.

6.45 p.m. : Salt solution, together with glucose previously administered, was vomited.

7.45 p.m. : Respiration seemed to be failing, and artificial respiration was done for a few minutes, and $\frac{1}{60}$ strychnine given hypodermically.

7.50 p.m. : In view of the high blood-sugar found at 5.30, 10 units of insulin were tentatively given.

8 p.m. : Temperature (under arm)— 102.2° F. She vomited again. Any relieving of the coma noticed after the insulin was temporary—for instance she coughed forcibly over the side of the bed, but soon lapsed into coma again.

9 p.m. : Temperature (under arm), 102° F.

8.30 p.m. : *Blood sugar—200 mgrm. per 100 c.c.*

9.30 p.m. : In view of above a further 10 units of insulin were administered—without much effect on the coma, but—

10.50 p.m., *blood sugar* was down to 85 mgrm. per 100 c.c., but she was not very appreciably less comatose.

12, midnight : Anxiety, lest the drop of blood sugar to 85—1 hour and 20 minutes after the second dose of insulin—might continue progressively during the night and lead to dangerous hypoglycæmia, dictated the administration of 3 oz. of glucose per nasal tube.

This did not affect the prevailing coma very much, and she was reported as having slept from 2 to 5 a.m., and been “restless” thereafter. She was sufficiently conscious, however, in this restless period to drink half a pint of tea.

April 28, 1937.

- 8 a.m. : Temperature (under arm)—98.4° F.
 8.45 a.m. : Took $\frac{1}{2}$ pint tea, in small mouthfuls.
 9.15 a.m. : Asleep ; breathing naturally.
 10 a.m. : Restless ; tossing about.
 10.45 a.m. : Pupils small and fixed.
 10.50 a.m. : 3 oz. glucose given per nasal tube ; pupils dilated to half the normal size.
 11.40 a.m. : Fed 1 pint milk, 2 eggs, and ostomalt (1 tablespoon).
 12.20 p.m. : Coughing forcibly ; tossing about and yawning.
 12.25 p.m. : Pupils began to react to light (sluggishly) for the first time in 20 hours. Abdominal reflexes were absent ; plantar reflexes were normal.
 12.30 p.m. : Catheter specimen urine taken : Reaction, acid ; sugar (Benedict's solution), .1% ; albumen, a trace ; acetone, small amount ; diacetic acid, none ; sp. gr., 1.022 ; occasional pus-cells and hyaline casts.
 1 p.m. : Sweating ; yawning.
 1.45 p.m. : Temperature (under arm), 98.6° F.
 2 p.m. : Asleep.
 2.45 p.m. : *Lumbar puncture.* C.S.F. under marked pressure, dropping to normal pressure when 30 c.c. had been removed ; *sugar* (Folin and Wu's method), 360 (at least) mgrm. per 100 c.c. ; Benedict's test—10 drops reduced 5 c.c. to a brick-red colour—that is, the sugar content was *over 2%*.
 2.55 p.m. : Catheter specimen urine—sugar present—about .25%.
 3.30 p.m. : *Blood sugar, 154 mgrm. per 100 c.c.*
 4.0 p.m. : Enema—stools looked normal in colour and consistency.
 4.20 p.m. : Temperature (under arm), 99.2° F.
 4.50 p.m. : 10 units insulin given intramuscularly ; this did not seem to ameliorate the stuporous state ; but there was no longer present the perspiration which had been noticeable when she was in the hypoglycæmic condition.
 5.25 p.m. : Corneal reflex present, but sluggish ; abdominal reflexes absent ; plantar reflexes normal in type, but sluggish.
 5.30 p.m. : Stomach washed out ; old milk curds and egg remnants returned in washing ; 1 pint normal saline left in stomach.
 5.45 p.m. : Much more wakeful ; restlessly throwing her arms about.
 7.10 p.m. : 1 pint cold saline per nasal tube.
 7.15 p.m. : Moved limbs around bed ; yawned naturally ; opened her eyes.
 7.35 p.m. : Relapsed into drowsiness, breathing heavily, and perspiring ; pulse-rate was 104 per minute—this seemed like a *hypoglycæmic reaction*.
 7.50 p.m. : 6 oz. glucose given by nasal tube.
 7.56 p.m. : Trembling all over ; vomited a little of the glucose solution.
 8.30 p.m. : In coma ; no perspiration ; quiet breathing ; slow pulse-rate.
 11.0 p.m. : Given 1 pint saline by nasal tube.
 11.30 p.m. : *Blood sugar, 190 mgrm. per 100 c.c.*
 11.45 p.m. : Catheter specimen urine showed a trace of sugar.
 At this stage the impression grew that something must have gone wrong with her carbohydrate metabolism—that insulin could still reduce the blood sugar (this had been proved biochemically, the previous evening, by the reduction, as the result of 2 injections of 10 units each of insulin, of the blood sugar progressively from 280 (at 5.30 p.m.) to 200 (at 8 p.m.) and to 85 (at

10.50 p.m.); but that the administration of glucose, to check the resultant hypoglycæmia from going too far, while doing so effectively, did not wake the patient, but caused persistent *hyperglycæmia* with what looked like pseudo-diabetic coma.

12.40 a.m. : 1 pint saline by nasal tube.

During the day the fundi were examined occasionally, and seemed normal. The blood-urea was normal.

Kahn test on C.S.F. was normal.

April 29, 1937.

11.10 a.m. : *Blood sugar, 130 mgrm. per 100 c.c.*

12.10 p.m. : *C.S.F. sugar : 300 mgrm. per 100 c.c.*

No food all day except saline.

April 30, 1937.

12.50 p.m. : *Blood sugar, 154 mgrm. per 100 c.c.*

No food all day except saline.

May 1, 1937.

10.50 a.m. : *Blood sugar, 130 mgrm. per 100 c.c.*

May 2 and May 3, 1937.

No food except saline during these days.

May 4, 1937.

11.45 a.m. : *Blood sugar, 95 mgrm. per 100 c.c.*

12.10 p.m. : *C.S.F. sugar, 180 mgrm. per 100 c.c.*

Patient now began to make an uneventful recovery on a diabetic regime. During the next 10 days the carbohydrate content of her food was gradually increased.

Some highly interesting features of the induced disturbance of carbohydrate metabolism from which this patient suffered over a period of some days seem to merit discussion.

For instance at 11.10 a.m. on April 29 her blood sugar was 130 mgrm. per 100 c.c.; but the really striking feature was the extraordinarily high level of the cerebro-spinal fluid sugar, which, estimated an hour later, was no less than 300 mgrm. per 100 c.c. This persisting discrepancy between the blood and C.S.F. sugar content would appear to be unique, and we have failed to find any like instance recorded in the literature.

Ordinarily as blood passes through the choroid plexuses some sugar is passed over to the C.S.F. Apparently in this case so much sugar passed over or accumulated in the C.S.F. that at one time (April 28) her C.S.F. sugar at 2.45 p.m. was 360 mgrm. per 100 c.c., and at 3.30 p.m. on the same day the blood sugar was only 154 mgrm. per 100 c.c.

At 12.50 p.m. on April 30 the blood sugar was again 154 mgrm. per 100 c.c.,

i.e., even higher than it had been 24 hours earlier, and this in spite of the fact that she meantime had had no food whatever. At 10.50 a.m. on the following day the blood sugar was 130 mgrm., and it was only 3 days later, i.e., at 11.45 a.m. on the morning of May 4, that her blood sugar had dropped to the normal level—it was then found to be 95 mgrm. per 100 c.c.

During all these days she was given no food whatever, her life being maintained entirely by normal saline solution administered by the nasal tube.

Yet, in spite of this starvation, the C.S.F. sugar level was still abnormally high on that morning (May 4), namely 180 mgrm. per 100 c.c.

SUMMARY.

This patient, for 21 days, underwent the ordinary insulin shock treatment for schizophrenia without untoward incident. Then rather suddenly, on the twenty-second day, she did not awake from the hypoglycæmic comatose state on the administration of glucose. On examination she was now found to be in a state resembling diabetic coma ; and it required persistent anti-diabetic treatment to bring her back to normal.

We are indebted to Dr. P. J. Irwin, Medical Superintendent, Limerick Mental Hospital, for permission to undertake this therapy and to publish the clinical notes on this case ; and to Miss Mai M. O'Brien for her help with the technical side of the investigations.

Reference.—(1) Salm, *Munch. med. Wochenschr.*, Munich, July 2, 1937, lxxxiv, pp. 1046-9 (abstract in *Brit. Med. Journ.*, August 28, 1937).