HYPOGLYCAEMIC THERAPY IN THE PSYCHOSES

BY

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In 1935 Manfred Sakel of Vienna published a book describing his new insulin shock treatment of schizophrenia. Since then his method has been used in many parts of the world, and in this country reports have been published by Russell (1937), Larkin (1937), and James and co-workers (1937). Up to now I have administered this therapy to sixteen female psychotics, the majority of whom were cases of schizophrenia. Two of these cases are described later, as they present features that have not been fully recorded in the English literature. The first case showed status epilepticus in the course of treatment, and the other laryngeal spasm on two occasions. It happens that in the first case the series of convulsions was apparently responsible for a remarkable improvement in the mental condition, but it would be premature to draw conclusions from this, and my purpose is rather to point out certain of the dangers associated with this treatment. A complication which demands no description is the lessened resistance to infection that is sometimes seen in these patients. In my series there have been two cases of pyelitis, which quickly responded to mandelic acid.

Details of the technique will not be given here as they have been well presented in the recent article by James and his co-workers. Essentially the treatment consists in the daily injection of increasing amounts of insulin, until a dose is reached which causes hypoglycaemic coma. On succeeding days this dose is maintained until mental improvement occurs or there is a lack of response to the treatment. In practice, however, few patients receive the routine treatment. The variations are mainly concerned with the criteria for interruption of the hypoglycaemia, and constitute the most difficult part of the technique.

Case I

A woman aged 32 years was admitted as a temporary patient on May 28, 1935, with a history of mental disorder of three weeks' duration. She was in a state of acute confusion, being completely disorientated, and was restless, insomniac, resistive, and impulsive, and had aural hallucinations. It was stated that she had suddenly developed this condition on the night of May 5. After about four weeks in hospital she showed some clearing of consciousness. However, a silly fatuous element was then noticed in her speech and appearance. She began to have grotesque delusions of little depth and of a grandiose nature, and the affective reaction was observed to be shallow and did not co-ordinate with her expressed thoughts. A diagnosis of paranoid schizophrenia was made. On May 7, 1936, she was certified after two extensions of her temporary status.

The hypoglycaemic treatment was begun on February 13, 1937, with the intramuscular injection of 24 units of insulin. The insulin used was Messrs. Boots' quadruple strength—that is, 80 units per c.cm. The dose was increased by 8 units daily until on February 18 with 64 units she became comatose. This dose was continued daily, except on Sundays, until February 23, when she developed status epilepticus. At 7.25 a.m. on that day she had received 64 units of insulin. At 9 o'clock she was drowsy, and at 9.15 sweats appeared on the face and chest. At 10.20 she became comatose, and an oesophageal tube was passed by the nasal route. Further progress in the coma was uneventful, and as usual her degree

of unconsciousness was light—that is, she was insensible to painful stimuli, the conjunctival reflex was absent, the corneal reflex on both sides and the knee and ankle reflexes could just be elicited, while the plantar responses were bilaterally extensor. She was fed at 12.10 p.m. with 150 grammes of glucose in half a pint of water, and had regained normal consciousness by 12.35. At 12.40 she had a typical major epileptic fit with well-marked tonic and clonic stages. By 12.44 she had recovered full consciousness and appeared none the worse. At 12.50 a second major convulsion occurred. From this she recovered in four minutes, and as she appeared well no intravenous glucose was given. She was occupied until 3.10, when she had a third major fit, from which she did not regain consciousness. Identical convulsions occurred at twenty-minute intervals until 5.40, making a total of ten convulsions that day. Treatment was as follows:

3.15 p.m.—30 c.cm. of 25 per cent. glucose in saline given intravenously.

3.20 p.m.—Glucose 5 ounces, calcium lactate 20 grains, and prominal 1 grain in half a pint of water, given per oesophageal tube.

3.40 p.m.—Soap-and-water enema given with fairly good result.

3.50 p.m.—Adrenaline 1/2 c.cm. injected subcutaneously.

4.15 p.m.—Stomach washed out with normal saline solution, and ammonium chloride 40 grains left in the stomach.

4.20 p.m.—Lumbar puncture was performed and 20 c.cm. of cerebro-spinal fluid removed. It was under greatly increased pressure.

5.20 p.m.—1 c.cm. of 20 per cent. luminal solution injected intramuscularly.

6.20 p.m.—Lumbar puncture was repeated and 20 c.cm. of fluid removed. The pressure was less this time, although still raised.

There were no further fits after 5.40 p.m., and at 9 p.m. the coma lightened and she became restless. At that time morphine sulphate 1/4 grain was injected subcutaneously. At no period during the day did the cardiac condition give anxiety. The need for constant medical attention during the hypoglycaemic treatment is shown by the fact that her bedside was hardly quitted the whole of that day.

All the next day the patient was drowsy, but on the morning of February 25 she was found to be pleasant and coherent in speech. As recovery might be hindered by a psychological investigation no questions were put to her, but from her spontaneous utterances it was obvious that she had lost her psychotic signs and symptoms. She was no longer deluded or hallucinated, and was coherent, relevant, rational, and pleasant in conversation. In her affective, conative, and cognitive responses she appeared normal. On April 5 she was discharged on trial. On the 26th she reported back and appeared so well that she was discharged altogether.

On June 9 she reported again for a more complete mental investigation, and showed entire disappearance of schizophrenic symptoms, with normal affective relationship and ability to return to her normal sphere of work. It was felt, however, that she did not fully appreciate the serious nature of her illness, and so her case had best be recorded as an incomplete remission according to the standards of Müller (1936).

Discussion

Typical major epileptic fits are common in this treatment, and other convulsions may occur that show a preponderance of tonic or clonic stages but are still to be looked on as major epileptic fits. These fits may appear at any stage in the hypoglycaemia, even when this has apparently been relieved by glucose. The latter occurrence may be due to the hydration of an already irritable cortex.

The epileptic fit is not now regarded as a catastrophe, and it does not depend on the blood-sugar level. It is of interest that Meduna (1936), by the use of various con-

vulsive agents, especially camphor and metrazol (cardiazol), has claimed to have had good results in the treatment of schizophrenia. He believes that the likelihood of cure with his treatment is proportional to the liability to convulsions. It is reasonable to suppose that in the case described above a similar therapeutic result would have been achieved by the use of cardiazol, and my experience in the use of this drug shows that it is simpler and safer than the hypoglycaemic treatment.*

For status epilepticus the treatment is the administration of glucose intravenously and by the oesophageal tube, along with repeated lumbar puncture. A soap-and-water enema and the injection of 1/4 grain of morphine may also be indicated.

It may be added that in the case described the personal and family histories contained no reference to epilepsy or other nervous or mental disease. It was the patient's first psychotic attack, there were no apparent exciting factors, and there had been no evidence of remissions during her stay in hospital. It remains to be seen how long the present mental improvement will last.

Case II

A woman aged 27 years was admitted as a temporary patient on March 5, 1935, and was certified on March 10, 1936. Throughout her stay she has shown mutism and apathy, but without katatonic features; hence benign stupor appeared to be the most appropriate diagnosis.

Hypoglycaemic treatment was begun on April 7, 1937, with a dose of 24 units of insulin. By April 23 she was having 104 units, and on that day, three hours after the injection and while still awake, she suddenly showed inspiratory stridor, and at once became cyanosed and unconscious. The pulse was 40 beats per minute and was intermittent. She was immediately given 1 c.cm. of coramine intramuscularly, 1 c.cm. of adrenaline intramuscularly, and 5 c.cm. of 25 per cent. glucose in saline intravenously. By this time she had stopped breathing, was quite blue, and was pulseless. Artificial respiration was also begun and simultaneously she received 150 grammes of glucose per the oesophageal tube. She recovered almost at once, and gave no further anxiety that day.

The treatment was begun again after two days' rest, using smaller doses of insulin, and on May 5 she was receiving 64 units. On that day she again showed laryngeal spasm three and three-quarter hours after the injection, and almost at once became pulseless, cyanosed, and unconscious. She was given the same treatment as before, and quickly recovered. The treatment was permanently discontinued after this, as it was felt to be unwise to risk a third occurrence of the complication. She was said to have suffered much from bronchitis in childhood, and this may be associated with her laryngeal susceptibility.

Little more need be said about this complication. It is not very common, it is easily and quickly recognized, and it responds quickly to the appropriate treatment. So soon as the first stridor is noticed treatment by adrenaline, repeated coramine, artificial respiration, and the administration of glucose should be instituted. The intravenous route will probably be useless because of collapse of the veins. As recommended by James, a cylinder of 95 per cent. oxygen and 5 per cent. carbon dioxide would be an advantage, and this has been added to the equipment of my insulin ward.

Summary

Two cases are described which show at the same time the dangers and the potentialities of Sakel's hypoglycaemic treatment in the psychoses. The first case was that of a female psychotic who had suffered from a schizophrenic insanity for one and three-quarter years. After developing

status epilepticus as a result of the insulin treatment she showed such improvement mentally that she was discharged.

The second case illustrates the occurrence of laryngeal spasm during the insulin treatment.

The treatment of both these complications is described, and the necessity for constant medical attention is emphasized.

I am indebted to Dr. J. Harvey Cuthbert, medical superintendent of West Ham Mental Hospital, for permission to report these cases. My warmest thanks are due to Sister Mackenzie and the staff of Ward 6, West Ham Mental Hospital, for their skilful nursing and continued enthusiasm. For a translation of Meduna's paper I am indebted to Knoll Ltd. of Welbeck Street.

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Clinical Memoranda

Marked Febrile Erythematosis During Treatment with Mandelic Acid

Since Rosenheim's articles dealing with the treatment of urinary infection by means of mandelic acid have appeared in medical papers many thousands of such cases have been successfully treated by this drug and very few complications have occurred. It is possible, however, that with its use some practitioners may have noted results similar to those experienced recently in a patient of mine who was undergoing mandelic acid medication, and the following case record may therefore prove of interest.

CASE REPORT

A woman aged 42, who gave a long history of cystocele and associated urinary symptoms, consulted me on account of urgent frequency of micturition. A bacteriological examination of her urine showed *Bacillus coli communis* and pus cells to be present in considerable quantities.

Treatment was begun with large doses of alkalis, and when after a week this afforded no relief cystopurin, two tablets four-hourly, was substituted. This likewise failed to relieve her discomfort, and the bacteriological findings in the urine remained as before. As no albumin had been found in the urine the patient was considered to be a suitable case for mandelic acid therapy, and this was instituted forthwith, the urinary pH being kept at 5.3 by the coincident administration of ammonium chloride by mouth. Methyl-red was used as the indicator. This treatment was started on February 10, and was continued uneventfully until February 24, when the patient complained of a generalized pruritus, although there was no sign of a rash. As at this time the bacteriological findings were still positive the treatment was continued. On February 27 the suboccipital and submaxillary glands showed some enlargement and were slightly tender. On March 3, besides the pruritus and lymphadenitis, the patient complained of a persistent acid taste in the mouth resembling that of the medicine. On March 6 the first negative bacteriological report was obtained, but the mixture was continued.

On March 10, in addition to the previous symptoms, there was soreness of the gums (the patient was edentulous), and these were found to be injected and swollen. The mixture was then stopped, and large quantities of alkaline fluids and glucose were substituted. On March 14 the patient had a marked nocturnal sweat, and on the morning of the 15th her temperature was found to be 102.2° F. and there were small red papules on her chin, neck, shoulders, and the front of her chest. By

* It should be stressed that cardiazol only produces convulsions when used in very large doses, and according to a special technique. In the doses used ordinarily it acts only as a respiratory and circulatory stimulant.