INSULIN THERAPY.

A SHORT REVIEW OF THE WORK DONE IN GRANGEGORMAN MENTAL HOSPITAL.*

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As the title suggests, this paper is a review of insulin therapy in our hospital, and as such we shall discuss only actual cases with their results.

Treatment was begun in May of this year. Nineteen patients started the course, but of these two were withdrawn almost immediately, one for revised diagnosis and one for unmanageability. Six were discontinued at varying intervals for physical reasons, as follows: Persistent tachycardia (2), cardio-vascular collapse (1), staphylococcal septicæmia (1), aseptic meningitis (1), acute pulmonary œdema (1). Of the remaining 11, 5 have had a full course of insulin and 6 are still on treatment. In other words, we started with 19 cases —2 were dropped straight away, leaving 17. Six of the 17 fell out through complications. Of the remaining 11, 6 are still on treatment, and of the 5 who completed treatment 3 are recovered and have gone home.

We shall describe only the three recoveries and some others where complications arose.

CASE 1.—Miss M. K—, aged 26, clerk. Family history poor. Present illness—katatonic excitement—was of nearly three years' duration, six months of which was spent in a private institution. Treatment was begun May 4, and on that date her mental condition was as it was on admission nine months previously, viz., she was noisy, restless and impulsive. The initial dose was 15 units, and with 35 units, though not in coma, she was unable to drink glucose, and it was given intranasally. With 50 units she passed into coma. This dose had later to be raised and finally to be reduced. She went through the treatment quietly and without alarms. On two occasions there was a return of hypoglycæmic symptoms in the evening. She became restless, with spasmodic twitching of head and limbs, and perspired and salivated freely. All symptoms responded almost at once to ½ c.c. adrenaline. Physical betterment, increase in weight, clarity of complexion and improvement in the appearance of the hair were noted early. On June 3, i.e. four weeks later, a slight mental improvement was seen. She became quieter, answered an occasional

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question and appeared to take a certain interest in her surroundings. From now on there was a gradual improvement, which terminated in her recovery. She was discharged on July 4—just two months from the beginning of treatment. She has been to see us several times and is now back at work. She is apparently normal. (39 doses ; 34 comas.)

CASE 2.—Mrs. T. M—, aged 29, married. Formerly telephonist. Family history good. Patient had a mental breakdown five years ago—she was off work for seven months, but was not certified and apparently made a complete recovery. Present illness dates from the third day of her honeymoon, though her husband told me that she appeared to be worried and unlike herself for some days prior to the wedding. She was restless, resistive and at times violent. She believed everything people said or did had two meanings, one for her and one for the world in general. She was hostile towards her parents and teachers for having reared her in ignorance of the real meaning of things, and she later became exalted, considering she was rather a special person to have been so treated, until finally she stated she was God.

Therapy started June 22 with 15 units. Her first coma occurred with 50 units, which was later reduced to 45 units and again increased to 55 units. On July 23 treatment was suspended temporarily owing to the appearance of a bright red rash accompanied by gastric symptoms. It was resumed July 29 with 20 units, and worked up to 67 units before coma was again reached. To this date, August 17, there was no mental improvement. August 29 cardiazol 5 c.c. was given intravenously, and on the following day a slight change for the better was noted. Second injection was given September 1, and on September 3 there was a marked change. She was euphoric and told us she was losing her delusions—this was the first time she referred to her ideas as delusions. She laughed at the crazy notions she had and, indeed, from further information she gave us, we realized she was infinitely more insane than we had hitherto suspected. She stated also, " Though I am better, I am not all right yet. I still feel queer inside as though there were a great strain there ". She had a slight bilious attack, causing postponement of her third injection for a day. She then became restless, very talkative and slept badly. She objected to the cardiazol, and finally relapsed completely on September 12, with complete amnesia for her brief remission. She passed into a state of utter and complete confusion, during which symptomatic treatment only was employed. On October 6 cardiazol was resumed, and on October 12, following the second injection, she appeared to be perfectly normal. She was quiet and sensible, but the improvement did not last 24 hours. She is at present on cardiazol, but the prognosis, I fear, is doubtful. (32 doses ; 14 comas.)

CASE 3.—Miss D. K. B—, aged 26, tea-packer. Family history good. No previous mental trouble. Was treated for rheumatism in a Dublin hospital. Present illness dates from October, 1936. From the date of admission she was noisy, restless and suicidal. She made repeated attempts at self-destruction, tore out her hair in handfuls, tried to swallow her tongue and scoop out her eyes. She was artificially fed for months. Despite special nurses night and day, she twice all but succeeded in destroying herself. During this time also she suffered from eczema and frequently recurring septic spots. She was a dark-complexioned girl, with black hair and brown eyes, and as she went downhill she darkened further until it was impossible to believe she was not a coloured woman. All attempts to place her among the pigment-forming diseases were unsuccessful. She wasted considerably and, between the skin condition, the nearly denuded scalp and the emaciation, she presented a pitiable picture. She always refused to walk, and had to be carried to and from the grounds. When she spoke, which was only occasionally, she maintained she was dead and someone else was in her place. A very slow physical improvement set in, marked chiefly by a gradual increase in weight, but there was no coincident mental change.

Insulin was started June 24 with 15 units. Her first coma occurred with 70 units. This dose was later cut to 60 units. Treatment proceeded uneventfully. Twice there was a return of hypoglycæmic symptoms. She became excited and restless, and perspired freely. There were a few flickering muscular spasms. She complained of double vision, and pulse-rate increased to 132. The condition responded quickly to adrenaline and intranasal glucose. On another occasion, instead of wakening after the intranasal feed, she proceeded to become more deeply comatose. Intravenous sugar quickly brought her round. She was all the time very difficult with her food. We were afraid at one stage that we would have to suspend treatment altogether, fearing she was not getting sufficient carbohydrate, as both intranasal and intravenous glucose are quickly utilized by the tissues and must be speedily supplemented by intraoral food. The patient took liquids fairly well, but solids she held in her mouth, making spoon-feeding impossible. When coaxing failed she was artificially fed, the feeds containing the requisite amount of sugar. From the third day of treatment she appeared to brighten a little. On July 1, a week later, she gave us a reasonable account of the events leading to her admission. She still maintained she was dead. July 6 she spent some time drawing, which was a pastime of hers. July 16: Treatment was suspended temporarily, *B. coli* being found in a catheter specimen of urine. She was given a course of autogenous vaccine, ending July 27. During this time there was no further mental advance. She still refused to walk, stated she was dead and was difficult with food. She had put on 2 lb. in weight. On August 2 cardiazol 5 c.c. was given intravenously and repeated until she had seven injections. An immediate improvement set in, increasing day by day, until August 11, when she lost her idea of being dead, this being her most fixed delusion. She expressed the greatest anxiety to go home. She became very euphoric and displayed a hitherto unsuspected talent for crooning. She ate and drank with avidity and commenced to put on weight at once. Physically she changed beyond recognition. Her complexion lightened, all eczema disappeared and her scalp became quickly covered with a luxuriant glossy mane. She was discharged September 2, a healthy, clear-eyed young woman. We have seen her several times since, and her mental improvement continues to date. (16 doses, 5 comas, 7 cardiazol injections.)

CASE 4.—Miss S. R—, aged 26, waitress. No family history. Her present illness—katatonic excitement—is of over twelve months' duration, part of which time was spent in a private mental hospital. She has had a fairly thorough course of insulin followed by cardiazol injections. There is a slight improvement to date. (34 insulins, 29 comas; cardiazol injections.)

CASE 5.—Miss W. L—, aged 26, shop assistant. No previous mental trouble. Present illness—katatonic depression—was of more than twelve months' duration, part of which time was spent in a private mental institution. This girl was very suicidal, having made at least three attempts at self-destruction.

Insulin therapy was started July 12 with 10 units; 30 units gave her her first coma. July 19: She had a severe epileptiform convulsion lasting 60 seconds. Intranasal glucose was given at once and was as quickly vomited. With intravenous sugar she wakened practically at once. About one hour later she had a rigor lasting 20 minutes. That afternoon at 2.25 she relapsed into coma. Adrenaline ½ c.c. and intravenous glucose brought her round again, but she remained drowsy and disinclined to talk. There was a return of myoclonic spasms at 6.45 p.m. lasting about one hour. Everything given orally was vomited. Rectal wash-out followed by brandy and coffee *per rectum* was retained and she settled down to sleep. During the night she complained of abdominal pains and vomited once. She remained dull and drowsy, but was perfectly conscious for the next three days. Insulin was resumed six days later, July 25, with 15 units, and increased by 2 units daily until 25 units were given, when she passed into coma on a dose 10 units less than her original coma-producing dose—an occurrence one frequently

finds. On July 25 she voluntarily stated: " I am losing those awful ideas (suicidal). I feel great. You are curing me." From now on her mental condition improved and the insulin dosage was gradually reduced (stabilization phase). On August 4, with 23 units, she had another fit. Treatment concluded August 13, with a final dose of 5 units.

There is an interesting sequel to the case. She was due for discharge August 20, and on the morning of the 19th she complained of a pain in the left axilla, for which we could find no cause, whereupon she informed us, with some reluctance, that several months before admission she had inserted a needle there with suicidal intent. She was a little worried and feared we might consider her story was delusional. We believed her, however, and within a couple of hours we had her X-rayed and there the needle was. The report stated: " There is a needle lying below the left breast, either superficially or between the ribs." She was discharged as arranged on August 20, but we made an appointment for surgical examination some weeks later, and on September 9 the needle was finally removed. The operation, which the surgeon described as being long and tedious, was conducted under a local anæsthetic and finished with gas. It was an early and severe test for that delicate organism—the recovering psychotic—and we feared for the outcome, but she went through the ordeal magnificently, making an uneventful recovery, and making also, during her stay in hospital, a host of friends. We have seen this girl several times since and only as recently as yesterday, and she remains very well indeed. (Doses 21 ; comas 15.)

CASE 6.—Miss M. O'K. L—, aged 27, children's governess. No previous mental trouble. Family history bad. Present illness was of about 18 months' duration when she came to us. She was quiet but voluble. She had numerous delusions of a bizarre and persecutory type. She was erotic, exalted and actively hallucinated. Insulin was started on August 22 with 10 units, and on the fifth day, 25 units, she had her first coma, from which she wakened quickly with intranasal glucose. She felt very well and was up and out that afternoon. Her appetite was good and she slept well. The following morning at 7 a.m. she complained of feeling cold and of a slight dryness in her throat. Temperature was 99°. In view of the latter insulin was not given that morning, as even the mildest pyrexia is looked upon as a contra-indication to this therapy. Temperature rose during the morning to 102° and pulse to 120. She complained of headache, vomited and perspired freely, and at 6.15 p.m. she had a rigor. On the 27th and 28th these symptoms persisted and she had a rigor each day. Laboratory tests up to this date were negative, including agglutination test for enteric, *abortus* and *melitensis* infections. Blood and urine cultures were negative. The only positive finding was some tenderness on deep palpation in right lumbar region. Prontosil album was given on this and succeeding days, but symptoms continued unchanged. On September 9 spinal puncture was performed. The cerebro-spinal fluid was not under pressure, and was normal in appearance and content. The patient was seen next night by an outside consultant, who agreed with our tentative diagnosis of pyelitis and septicæmia, despite negative urinary findings. He advised soluseptasine injections, which were commenced and given intramuscularly for the next three days in doses of 10 c.c., and later in doses of 8 c.c. and 6 c.c., when temperature rose above 102°. Prontosil by mouth was continued and she was also taking large doses of alkalis. Though the pyrexia lessened somewhat at this stage, her symptoms in general remained unchanged. On September 3, 10 and 14 staphylococci were present in the urine and in the blood. In view of this the consultant advised a trial of the product known as M. & B. 693. We did not obtain the drug until the 24th. The patient at this stage was in her fifth week of illness. She was cadaverous, worn and exhausted. Staphylococci were still in the blood and a fatal outcome appeared imminent. On September 24, 10 M. & B. 693 tablets were given in the first 24 hours, four tablets in the first dose and the remainder in doses of two tablets at intervals. Patient had a rigor that night. She vomited and perspired profusely,

and suddenly collapsed. She responded, however, to restoratives. One tablet was given three times daily for the next two days. On the third day, through a misunderstanding, the drug was withheld. On the fourth and fifth day three tablets were given, and on the sixth day two tablets. The temperature, which had fallen dramatically on the night of the 24th, now showed signs of rising again, so four tablets were given on the 7th, three on the 8th, 9th, 10th, 11th and two on the 12th day. On October 5 the blood-culture was negative. The patient, who had been more or less prostrate, now proceeded to make a complete recovery. There were no further rigors. Her appetite improved and she slept soundly. She is now physically recovered, and is up for some hours daily. One point of interest in the previous history only recently obtained was that the patient suffered from a whitlow and several boils before she came to us. The question at once arises: Had the insulin anything to do with the illness? Were the staphylococci, present but quiescent in the body, suddenly whipped into activity by the weakened resistance induced by insulin? If such be so, it emphasizes the necessity for exacting physical examination for each patient prior to treatment. The mental condition of the patient described did not change during her long illness. Since recovery she has become very depressed.

CASE 7.—Miss G. B—, aged 27, shop assistant. This girl was not a good subject for insulin, as her illness was of several years' duration. The family history also was bad. Mentally she was dull and depressed, disinclined to talk, and very easily upset. On admission she had been restless, actively hallucinated, and had numerous bizarre delusions.

Therapy was started September 15 with 5 units and worked up to 15 units on the 17th. On this date she refused to drink the glucose, which was given intranasally. Shortly afterwards she was noticed to be looking ill. She commenced to cough and to expectorate, at first a frothy fluid which, quickly becoming blood-stained, presented the text-book salmon-coloured sputum. Her respiration and pulse quickened alarmingly. She became cyanosed, and on listening over the chest rales and rhonchi were heard all over. She was, at this time, critically ill. Atropine $\frac{1}{100}$ gr. was given, also digitalin, and after about half an hour the acute symptoms subsided. The cyanosis disappeared. The pulse and respiration slowed, and when the chest was re-examined a little time after all adventitious sounds were completely absent. She was our first and, we trust, our last case of acute pulmonary œdema. It is mentioned in the literature as one of the most dangerous complications. Following on the attack the patient developed pneumonia in the left lower lobe, which extended to the upper. Resolution was considerably delayed. On October 17 she again became pyrexial, and X-ray disclosed formation of a small abscess in the left lower lobe, with delayed resolution in the upper. Postural treatment was immediately adopted, and sulphanilamide, which had been stopped, was resumed by mouth. She is now improving, but her progress is slow. She resents all treatment, is difficult with food, and in general tries in every way to frustrate our efforts.

CASE 8.—E. O. C—, school-girl, aged 16. Had a previous breakdown twelve months ago and was treated in Grangegorman, whence she was discharged "not improved" at her parents' request. She was then in katatonic stupor. This time she was admitted in katatonic excitement.

Insulin was started on September 13 with 5 units. She reached 55 units without showing any appreciable effect, physical or mental. Pyrexia started September 20, continuing to October 14, with signs of cerebral irritation, including irritability, positive Kernig, *tache cérébrale*, tenderness of hair and scalp, drowsiness and photophobia. There was occasional screaming and vomiting. A noticeable symptom was marked hyperæsthesia of the toes. Lumbar puncture was negative beyond a slight increase of cells—16, all lymphocytes. On October 1 she had one epileptiform seizure, lasting four minutes. There is a history of a previous illness of like

nature two years ago, when, according to her mother, patient was undiagnosed by six doctors. From October 6 she began to improve gradually. The treatment, we may state, was entirely symptomatic. The negative findings in the cerebro-spinal fluid suggest that this may have been a case of acute sterile meningitis. Against this is the very poor increase in cells. It may have been merely an attack of meningism. At any rate the patient recovered completely.

CASE 9.—Miss M. S—, aged 20, no occupation. Family history poor. No previous mental trouble. Certified as being restless, troublesome and uncontrollable. With us she was idle, lazy and mischievous. She heard voices, and her language was obscene. Insulin was started September 12 with 5 units, and worked up to 140 units without effect beyond some perspiration and a little facial pallor. We decided to supplement the insulin with cardiazol. It was given twice weekly, three hours after the insulin dose. With the first dose, 3 c.c., she had a severe fit, lasting 60 seconds. On the next two occasions with 3 c.c. and 5 c.c. there was a " missed fit ", but beyond some pallor and perspiration she seemed little the worse for this. There was complete absence of the terror and distress said to be associated with a " missed fit ", due no doubt to the depressing effect of the insulin, which is given as one of the advantages of the combined treatment. There is a considerable mental improvement in this case, but she has not finished treatment.

As stated at the beginning of this paper, therapy was started six months ago, and doing the same work daily for six months various aspects of the work impress us. We noticed (1) the unexpectedness, or better, the individuality of the treatment. To-day in hypoglycæmia the patient behaves in a definite way. Next day, with the same dose, one might expect the same behaviour, but it is utterly different, and though successive days might resemble one another, one could not trust them to do so. (2) A case which has returned to hypoglycæmia can be easily missed. We have seen more than one patient, who had received and retained intranasal glucose, waken, sit up, smile and talk, then quietly lie down and compose themselves for sleep, and within a few minutes of doing so facial pallor, lost corneal reflexes and double extensor responses can be demonstrated, and coma quickly deepens unless sugar is at once given. This is but another instance of the unexpected results of the treatment. (3) Where intravenous glucose was given it was followed in nearly all cases by pyrexia and malaise a few hours later, which frequently persisted into the following day. (4) Where recovery takes place the contrast between the patient ill and the patient well is utterly amazing. We all know these schizoid people with their strange behaviour, their aloofness and inaccessibility and their indifference to surroundings. We have been baffled by the irrelevant reply and chilled by the slow inscrutable smile. We have seen such patients within less than three weeks of therapy waken up, as it were, and shake their illness from them. They become bright and cheerful. They look about and, unasked, help with the ward work. They become interested in their recovery and take a friendly interest in their neighbours' welfare. Again, our insulin recoveries come back to see us, not with the air of performing a duty, but as if they were glad to come. They report their progress and inquire without fail for one's

own health, for the nurses in the insulin ward and for those under treatment. This complete reversal of behaviour has to be seen to be believed.

As well as gaining impressions during the six months' work, one is bound also to form some opinions as to the value of the treatment. Does it justify the expense entailed on any hospital adopting it? Is it dangerous? Are the results permanent? Time only will answer the last. Is it dangerous? I do not hesitate to say it is dangerous—for the unwary. A treatment that may carry in its wake such complications as laryngeal spasm, recurring convulsions, protracted coma and acute pulmonary œdema is a treatment to be taken seriously. Does it justify the expense and trouble entailed? Most sincerely we say it does.

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