HYPOGLYCAEMIC THERAPY IN THE PSYCHOSES.

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CONTENTS.

Introduction.

in this paper an attempt is made to evaluate the so-called Insulin Shock treatment of schizophrenia, the opinions expressed being based on experience with eighteen female psychotics, and on a survey of the literature.

Since its discovery in I922, insulin has been used in the therapy of mental disorder by various workers, however, deep and deliberate hypoglycaemia had not been described until I935, when Manfred Sakel of Vienna published the results of hypoglycaemic therapy in 50 cases of Schizophrenia. His description stimulated such interest that his treatment has been used all over the world.

It was Dr. Wilson's report to the Board of Control that led me first to practise this treatment, while later most help was obtained from the descriptions of Sakel (2), (I3) and (33), and Müller (3).

Essentially the treatment consists in the daily injection of increasing doses of insulin, until a dose is reached that causes insulin coma. This so-called shock dose is maintained daily thereafter until mental improvement occurs or lack of response determines the cessation of the treatment. Variations in the technique are advocated by various workers, and are mainly concerned with the criteria for interruption of the coma. These variations constitute the most difficult part of the technique.

Four phases of the treatment are described as follows:-

Phase I, the introductory phase.

In this phase an initial dose of I6 or 24 units of insulin is injected intramuscularly while the patient is still fasting. After a varying period, from 3 to 5 hours, the hypoglycaemia is ended by giving glucose to drink. On succeeding days the dose is increased by 8 units daily until a coma-producing dose is attained.

Phase 2, the Shock phase.

here the shock dose is given daily for a varying period. Sixty days treatment, or fifty comas is the optimum duration advocated now (December, I937).

Phase 3, the Stabilising phase.

In this phase, mild hypoglycaemia is induced daily for several days, until the curative effect of the treatment appears stabilised.

Phase 4, the Rest Phase.

This is represented by a respite from treatment on one day in the week, usually Sundays.

The Selection of Patients.

(A) Mental considerations.

the published results show that improvement is unlikely in cases of longer duration than two years, however, to obviate the confusing factor of a spontaneous remission, the patients were in most cases well established in their psychosis. Most of the cases were of schizophrenia, but wherever the diagnosis was in doubt, that doubt was discussed in the case-history. It is difficult, and sometimes impossible, to be sure when a case of schizophrenia has demented. Indeed, there must be few clinical psychiatrists of experiencewho have not seen at least one apparently demented schizophrenic recover, sometimes during an acute fever, sometimes for no apparent reason. It was taken therefore, that none of the cases selected were demented, and considerations of faulty habits, stereotypies, verbigeration, etc. were not allowed to influence the selection of cases.

It may be noted here, that one recent case of stupor was transferred to the insulin ward, and got ready to receive the therapy, when she spontaneously, or perhaps in response to the transfer, came out of her stupor, and had made a good recovery in a few days. Had she at that time undergone the treatment, and improved, I should have attributed the recovery to the treatment. This experience demonstrates the difficulty of evaluating any therapy applied to psychoses. Later, I had a second exactly similar case.

The classification of schizophrenia into the four types, of Simple, Catatonic, Paranoid and Hebephrenic is often difficult and not always helpful, so that in most cases, I have been content to give a short description of the mental phenomena and label the case as schizophrenia.

When it was first introduced, this form of therapy was applied only to cases of Schizophrenia, and especially the Praecox types, but recoveries have now been described in Paraphrenia, Paranoia, Menopausal psychoses, Manic-depressive conditions, and even in some severe Compulsion neuroses. It may be taken then, that there are no mental contra-indications to the application of this form of treatment in the functional psychoses.

(B) Physical considerations.

An ordinary physical examination was made of each patient. On the first few cases treated the glucose tolerance was estimated, but the results served only to support the present chaotic state of the literature regarding blood-sugar level in the psychoses, hence the estimation was discontinued. Blood cell counts and haemoglobin estimations were only performed where clinically indicated.

Almost as important as the physical examination is a thorough review of the patient's history regarding susceptibility to illness. An attempt was also made to discover any endocrine dysplasias.

As this therapy is rigorous, at the start at least, only cases of the soundest constitution ought to be treated. Nevertheless, one will often be surprised at the way in which unlikely cases stand up to the treatment, and conversely, apparently sound cases will display sometimes a circulatory weakness which had not been foreseen. In any patient whose condition gives rise to anxiety treatment should be stopped, for whereas Schizophrenia is not a lethal condition, Hypoglycaemia may be lethal.

Low blood pressure was considered a contra-indication to treatment because lowering of the arterial pressure is usual during shocks. Because of this, several otherwise suitable cases were not admitted to treatment. As those of my cases with raised blood pressure were all young, and without evidence of vessel-wall or other lesions, their hyper-tension was considered due to a benign endocrine abnormality, and so was not deemed to be a contra-indication. Unfortunately there exist no mental or physical criteria which help in deciding what will be the individ-

ual's shock dose. The chronicity of the psychosis, the physical condition, and the blood-sugar level are all alike in showing no obvious relation to the amount of the shock dose.

There is, however, general agreement that a relapse in the patient's mental state is associated with an increased resistance to insulin. Also, patients who are improving mentally show increased sensitivity to insulin (22). Increased sensitivity and increased resistance in the same patient have been described by Gillman and Parfitt and have also been noted by me on many occasions. (24).

The Method.

The patient is fasting. Before injecting, the pulse-rate, respiration-rate and temperature are noted, while the urine is tested for albumen and sugar. After the first few days glycosuria is the rule, but any other abnormality may be a contra-indication.

First Day.

at 7.I5 a.m. the initial dose of I6 or 24 units of quadruple strength insulin (80 units per c.c.) is injected intramuscularly in the gluteal region. Thereafter the pulse is palpated almost continually and its rate is charted every quarter-hour. It cannot be too strongly stressed that the state of the pulse, and through it of the heart, is of prime importance in estimating the reaction to insulin.

Ordinary hospital beds are used, and usually the patient lies without pillows.

The following features may require attention: the sweat is continually dried off, tongue-biting is constantly watched for, while hyper-salivation is treated by turning the head to one side or, if severe, by raising the patient on pillows. Should the patient become very restless she is laid on a floor mattress.

In the absence of danger-signs the hypoglycaemia is maintained usually until I2 noon, when interruption is performed by giving a cup of glucose tea containing from 3 to 5 ounces of glucose.

At I2.45 p.m. dinner is given, it is amply supplied with readily assimilable carbohydrate and sugars. After dinner the patient is occupied; she may be kept in bed or got up.

At the first institution of this treatment there is a tendency to give a superfluity of glucose so as to avoid the occurrence of after-shocks; laudable though this precaution may be it means that on the following morning the body still contains a quantity of glucose, and so the therapeutic effect of the insulin injected is lowered.

On the succeeding days the dose is increased by 8 units

daily until a shock dose or one producing insulin coma is reached. In one patient I5 units may be a shock dose, in another it may require 450 units or more. (33).

The duration of the treatment.

At first there was no agreement as to the duration of the treatment, periods of from 4 weeks upwards being advocated. But now (December, I937) there is general agreement that a period of 60 days treatment should be given before giving up hope of securing a remission. This involves usually 50 comas, and if no improvement has occurred after that number of shock doses then response is unlikely. Of course, if improvement occurs early then the treatment can be stopped so soon as the stabilising phase is complete. Some workers state that hope of remission need not be abandoned until 90 days of treatment have been given, but it is obvious that a spontaneous remission might have occurred by the end of this long period.

The duration of the stabilising phase also varies. It has been completely omitted by some, others continue it up to the time of discharge, while others give insulin for some IO days.

Combined insulin and Cardiazol treatment.

Cases I7 and I8 were treated with a combination of the insulin and Cardiazol treatments. I believe that such a combination is more useful therapeutically than either treatment alone. (see Appendix A).

Phenomena during hypoglycaemic therapy.

(A) Psychic phenomena.

During the introductory phase the individual may show her usual psychotic traits, but more usually, she is quiet and her hallucinations tend to lessen in frequency and intensity. Usually in proportion to the dose of insulin, drowsiness comes on and increases. It is usually first evident about one hour after the injection. If left alone she may sleep.

At any time, however, the quiet behaviour may be interrupted by outbursts of psychomotor excitement, sometimes in obvious response to hallucinations, at other times, apparently of impulsive nature.

In the pre-comatose period of the hypoglycaemia, lucidity and remarkable clearing of consciousness may be seen, and the patient may exhibit evidence of mentation that had previously seemed impossible for her. These lucid periods may perhaps be identical with the similar periods described as a result of inhalation of mixtures of carbon dioxide and oxygen (4) i.e. the stimulating effect is perhaps due to increased blood-supply. These lucid periods are usually of very short duration and merge into the insulin coma; in my series such lucid periods have been rare.

Hunger-excitement has been described by Sakel, but I have seen no case of this type. On wakening signs of regression were common.

In those patients capable of response, an amnesia for the events of the hypoglycaemia was almost invariable.

During the shock phase the depth of the coma varies almost continually, and reasonably enough, excitement of any kind is usually followed by a lightening of the coma, this being due to the adrenalinaemia caused by the excitement.

(B) Physical phenomena.

In most of my cases the pulse-rate increased about 40 minutes after the injection. Later in the hypoglycaemia the tachycardia may become extreme e.g. 150 beats per minute. Less frequently, there was bradycardia. Irregularities of the heart's action are common. Sinus arrhythmia often occurs and is not a danger-signal. Extra-systoles may occur and in conjunction with the general clinical picture may be a danger-signal. Similarly

as regards an alternate slowing and quickening of the pulse. The volume and force of the pulse vary within wide limits, and like the rate, they may vary every few minutes. The bradycardia seen by the Vienna workers was unusual in my series, hence their belief that tachycardia is a toxic effect of insulin does not apply to English patients and English insulin as an invariable law. However, tachycardia of high degree, occurring late in the hypoglycaemia is almost certainly a danger-signal, and was taken as such by me. The systolic blood pressure rises, the diastolic falls. The face usually flushes about half-an-hour after the injection but later becomes and remains pale. This effect and the changes in pulse-rate are probably due to variations in the secretion of adrenalin (5). Cameron states that most of the symptoms of hypoglycaemia are probably traceable to disturbances having their origin in the central nervous system, because the latter is peculiarly susceptible to glucose starvation from low blood-sugar, since it has no store of carbohydrate.

The blood-sugar level at which hypoglycaemic symptoms occur varies greatly. Hill and Howitt state that symptoms are usual when the amount of blood-sugar is less than 75 milligrammes per 100 c.c., but they cite a case in which the level fell to 32 milligrammes per 100 c.c. without the onset of symptoms (6). Among insulin shock therapists there is general agreement that the degree of hypoglycaemia bears little relation to the severity of the symptoms, for example, a patient may become comatose when his blood-sugar level is actually rising above what it had been when he was yet conscious. Hence, the value of blood-sugar estimations during the treatment is slight, except in the case where the patient has failed to come out of coma after the administration of enteral and parenteral glucose. In this case, a blood-sugar estimation will avoid the error of continuing the administration of glucose when the blood holds the normal or a greater than normal amount of glucose, an error, moreover, that will perhaps involve flooding an already waterlogged circulation with additional fluid.

Cyanosis of the face and extremities is described by the Vienna

workers as being common, but apart from the occurrence of laryngeal spasm, I saw it on one occasion only.

Sweating occurs in all cases at some time, and in many cases is abundant and constant. It is usually most marked on the face and chest, but may run in streams from the body. The associated thirst may be relieved by copious draughts of tepid water. I have been unable to confirm that free sweating is a sign of good prognosis. Profuse sweats have occurred constantly in cases that did not improve, while some cases that were relieved did not sweat at all freely.

The respiration varies greatly during the shock phase. It may be quiet and regular, snoring, stertorous or irregular as to rate and depth. I had one case of laryngeal spasm, but no cases of Cheyne-Stokes respiration.

Salivation is usually increased, but is usually controllable by postural treatment. When very profuse the injection of I/100 gr. of atropine sulphate is effective, but the resulting tachycardia may mask an insulin tachycardia. Where the secretion is thin, I have found a simple mucus extractor to be of benefit.

Motor phenomena. these are usually seen at some time in every case, and in some patients may monopolise the clinical picture. The movements may be generalised or localised, bilateral or unilateral, clonic or tonic, choreiform or athetotic, regular or irregular etc. The type of movement tends to remain constant for the individual, and to recur with each hypoglycaemic state. On the other hand the epileptic fit may occur once and not be repeated. Excellent descriptions of the above and other neurological phenomena are given by Sakel in his book, and by Bersot (7). The latter is reminded of the signs seen in Encephalitis Lethargica, Parkinson's syndrome, Wilson's disease, Chorea, Epilepsy, Hysteria etc.

I shall enumerate the more common movements seen in my cases. They were twitching of the face, usually unilateral, and often confined to one of the following; brow, eye-brow, orbicularis oculi, nose or mouth. The movement was usually clonic, and lasted from a few seconds to 30 minutes or longer. It was often associated with

protrusion and intrusion of the tongue, which was usually pushed to one side. Finer twitchings of the muscles of expression often preceded the clonic spasms. These movements began usually about one hour after the injection, were often seen in phase I with small doses, while they might precede the coma in phase 2. After beginning in the face the movements often spread to the limbs and trunk. Tonic spasms of one sterno-mastoid, of the masteric, arm or leg musculature were common and often sustained several minutes. They were sometimes associated with carpo-pedal spasm. Writhing or athetotic movements were common, as was nystagmus. Tonic or clonic opisthotonos was often seen.

Various grimacings occurred, e.g. tongue-rolling, abortive biting at the bed-clothes, raising the eye-brows, screwing-up the face, etc. Snout-cramp, tonic or clonic, was seen in several cases that did not normally show it. Wild head-rolling was frequent. During psychomotor excitement twisting of the whole body might occur, and necessitate a floor mattress.

It is worth stressing that the motor phenomena were often strictly unilateral.

In none of my cases was there any residual palsy.

The movements were often produced while the patient was still conscious, although often aphasic and anarthric.

The reflexes.

the swallowing and coughing reflexes were the first to go during the onset of coma. The conjunctival reflex soon follows, as does the abdominal reflex. Transitory clonus of knee and ankle may occur, and the plantar response becomes extensor. The corneal reflex remains surprisingly late, and Sakel (33) explains this by saying that, phylogenetically and ontogenetically, it is very ancient. The knee and ankle jerks become difficult to elicit, and later disappear.

According to Sakel (33) the term coma should only be applied where there is absence of the corneal reflex, or at least, where there is a positive Babinski sign.

In very deep coma there is complete areflexia, even to absence of the light reflex. This is, of course, very dangerous, and I have

not allowed the coma to proceed to this degree.

The speech mechanism is usually disordered on entering and on leaving coma, there being aphasia, anarthria or various degrees of dysarthria.

Inco-ordination of movements on entering and leaving coma is noticeable, the patient having great difficulty in holding a cup, and in bringing it to the lips without spilling the contents.

The optic fundi showed no changes other than variable alterations in the calibre of the vessels.

Echolalia, stereotyped responses and various mannerisms occurred sometimes in patients who did not ordinarily show these features. These abnormalities were especially common on coming out of coma.

Most of the above abnormal features lasted from one to thirty minutes from the first signs of returned consciousness.

Epileptic fits.

typical major epileptic fits occurred at some time in the majority of the cases, and showed the usual stages. Other convulsions were seen that showed a preponderance of tonic or clonic stages, but are still to be looked on as major fits. The fits may occur during any of the phases, or even after the hypoglycaemia has been relieved by the administration of glucose in water. This latter occurrence may be due to the hydration of an already irritable cerebrum. The fit may last any time from a few seconds to IO minutes, while the resulting coma is also variable in duration. Sakel and others formerly regarded the epileptic fit as a sign of dangerous hypoglycaemia, but it may occur very early in the morning, and at a time when the blood-sugar is not greatly lowered, hence it is more reasonable to regard the fit as the individual reaction of an epilepticogenic cerebrum and constitution. On this subject Bersot (7) says, " Regarding the epileptic fit , opinions differ. Some say that the hypoglycaemia should be interrupted at once, others that it need not be feared, while others even seek and provoke the production of fits." This last view is the one most generally accepted now, for example, see the opinions of James and his co-workers (8).

At this point the work of Ziskind (9) may be quoted. In an endeavour to provoke convulsions, he gave doses of insulin varying from 10 to 60 units to a series of 40 epileptic patients. In no case did he succeed. The addition, however, of superhydration measures produced 4 fits in the 30 patients treated. The convulsions did not coincide with the lowest blood-sugar readings, while moreover, 4 fits were produced in patients who were superhydrated alone.

Schmid (10) believes that the epileptiform seizure is the clinical expression of cerebral anoxaemia. His work on the histopathology of the insulin treatment may be commended to the student of this therapy as his laboratory experiments on animals correspond to the clinical conditions very closely.

One is tempted to speculate as to whether the value of the insulin treatment is not wholly due to irritation of the cerebral neurones, an irritation that finds its fullest expression in the major convulsion. It is of interest that Meduna (11) using first camphor, and later Cardiazol (Metrazol) by injection, has by the production of convulsions procured remissions in 19 out of 43 established schizophrenic patients. Meduna's results can claim comparison with those of Sakel, and it is the former's belief that the likelihood of cure with his treatment is proportional to the liability to convulsions. (21) and appendix A.

It remains to be said that incontinence of urine is the rule during coma and there may be incontinence of faeces also.

The pupils vary in size, and this variation is probably to be related to the amount of adrenalin in the blood, an amount that must vary greatly during the hypoglycaemic state.

Sakel's latest pronouncement regarding the epileptic fit during insulin therapy is as follows (33). He says there are two kinds of fit; the first occurs within two hours of the injection, and being only one kind of reaction to insulin, it is not dangerous and the hypoglycaemia may be ended via the nasal tube. The second kind of fit occurs after three hours and is a signal of danger, and Sakel would end the treatment at once with intravenous glucose. It appears thus that the danger of the fit is still controversial.

Types of reaction.

Day and Niver (25) describe two general types of reaction. They are vagotonic and sympatheticotonic, and depend on which side of the autonomic nervous system is most stimulated. They continue that insulin is a definite parasympathetic drug. It slows the heart, contracts the bronchioles, contracts the pupils, stimulates bowel motility, dilates the peripheral vessels, stimulates the sweat glands, contracts the bladder musculature and dulls consciousness. Hence in a pure insulin reaction one would expect to see a slow, full pulse, stertorous respiration, small pupil, hunger, warm or flushed skin, more or less profuse sweating, and voluntary urination. In addition, insulin lowers the blood-sugar, and this in turn stimulates the adrenals which usually stimulate glycogenolysis in the liver.

As adrenalin is a sympathetic drug, it accelerates the heart, dilates the bronchioles and pupils, depresses bowel motility, contracts peripheral vessels, depresses sweat glands, inhibits muscle of bladder and accentuates consciousness. Hence, in a sympathetic type of reaction one sees rapid pulse, full quiet respiration, large pupil, cessation of hunger, pallor and cold skin, diminution of sweating the bladder does not empty and the patient is wakeful. Adrenalin also produces anxiety, so in this type of reaction the patient exhibits an anxious facies, restlessness, psychic and motor excitement, and combativeness. These views of Day and Niver appear to explain the phenomena that I have seen, especially when they add that any combination of the two reactions may be seen.

These two workers state that the excitement-anxiety reaction can be relieved by a drachm of glucose, or 20 to 40 units of insulin, or 60 to 120 grains of ammonium chloride, or by rebreathing. In some cases I have been able to confirm this, and would add that the inhalation of pure carbon dioxide should have the same effect as rebreathing. Day and Niver suggest that the sympathetic reaction may be due to alkalosis, as it has been put forward that insulin is the best alkalising agent available to us.

Interruption of the hypoglycaemia.

The methods of terminating the hypoglycaemic state are as follows :-

I. The administration of glucose by the oral route.

This is the routine method during phase I. The glucose is given in tea or flavoured with orange or lemon juice. The amount of glucose needed will vary according to the dose of insulin, between two and five ounces being usually required.

II. The administration of glucose by the oesophageal tube.

This is the routine method of ending the hypoglycaemia during phase II, when the patient is comatose or unable to swallow properly. The glucose solution holds I50 grammes of glucose dissolved in ½ pint of warm water. Various medicaments may be added to the solution as desired, e.g. 5 minim doses of liquor atropine sulphate, or an alkaline mixture, in order to prevent vomiting.

The above two methods may be expected to abolish the hypoglycaemia, and procure the normal blood glucose equilibrium within 20 minutes on the average. According to Joslin (I2) in the case of dogs, dextrose is not absorbed in significant quantities from the stomach. But he suggests that where hypoglycaemia is present the absorption of glucose is hastened, and concludes that it is certain that individual variations regarding absorption are marked.This last has been my experience also, for where one patient will recover from the insulin coma within 8 minutes of receiving glucose, another may just be stirring after 30 minutes. In some patients delay in recovery after giving glucose may be avoided by previously washing out the stomach with normal saline. An alkaline wash is best avoided as there is some evidence that alkalosis occurs during the hypoglycaemic coma.(25)

It is usual, however, to find that the signs of hypoglycaemia, apart from the coma, are beginning to be relieved within from 5 to I0 minutes of giving glucose. For example, the irregularities and rapidity of the pulse usually quickly ameliorate. More rapid modes of interruption of the coma are available, and constitute the main reason for this therapy being safer than other equally

"shocking" procedures.

III. The injection of adrenaline.

This substance acts by breaking down liver glycogen into glucose, and the dose is from ½ to I c.c. intramuscularly. It is obvious that it will fail to abolish hypoglycaemia if the liver stores of glycogen are depleted, as they may be in a patient who is undernourished, or who has recently had to call on her glycogen stores. In practice, I have found that the injection often fails, and it finds its fullest use in the treatment of laryngeal spasm where it ought always to be given.
It may be said here that Sakel was first led to formulate his hypoglycaemic treatment by the observation that the symptoms of morphine-addiction resembled those due to hyperadrenalinaemia. He attempted to abolish the restlessness of drug addicts by injections of insulin, which has actions antagonistic to those of adrenalin. His success led him to use insulin in other cases of excitement, and finally in cases of schizophrenia.

IV. The intravenous injection of glucose.

I have used a sterile solution of 25% glucose in saline. Stronger solutions tend to cause clotting of blood in the syringe, while weaker strengths are not sufficiently potent. It must be realised that 25% glucose is strongly hypertonic, and almost certainly causes shrinking of the brain and a considerable and prolonged falling in the cerebro-spinal fluid pressure. only if given too fast.
For these reasons, the injection , even in an emergency, must be made very slowly. how long a time?
Recovery from the hypoglycaemia is rapid after giving glucose intravenously, a few minutes at most elapsing before signs of returning consciousness appear. It is usual to continue injecting until these signs appear, anything from 5 to 80 c.c. being a usual dose. If consciousness does not rapidly return, then the coma is no longer simply due to hypoglycaemia, and other restorative measures will be necessary, e.g. lumbar puncture.

In all cases additional glucose must be given by the oral or oesophageal routes, because intravenous glucose is very rapidly used by the tissues. Glucose may also be given intramuscularly, but absorption is uncertain.

Complications of the treatment.

(I) After-shock or secondary hypoglycaemia.

A recurrence of the hypoglycaemia may take place after the initial hypoglycaemia has been relieved by glucose. This after-shock may show any of the features of the hypoglycaemic state and especially drowsiness, sweats and motor phenomena. The nursing staff are instructed that any symptoms of physical disorder or unusual psychic symptoms are probably due to lowered sugar level in the blood, and they know the measures to take. This secondary hypoglycaemia may occur at any time during the afternoon, evening or night, hence the patients require unremitting observation throughout the whole 24 hours.

This complication is naturally only dangerous if it go unobserved, because the staff are trained to give glucose by the nasal route and they proceed with the treatment while the doctor is being summoned. The giving of sedative or hypnotic drugs is forbidden, because an after-shock might occur during sleep and go unobserved.

The question of aperients deserves some consideration. It is obvious that an aperient acting on the duodenal area may produce conditions in the bowel that may hinder or prevent the absorption of glucose. Hence, the patient may be long in recovering from the hypoglycaemia, and in addition, the chances of an after-shock are increased. For these reasons, to the ban against hypnotics is added one against aperients, which are only given on Sundays. Here, as everywhere in the treatment, the routine may require subordination to the individual.

It is probable that after-shock will be pre-disposed to by any adrenalinaemia due to rage or to exercise, hence indirect utilisation of sugar by that means is guarded against as much as is possible.

In some cases after-shock will take place, and no reason for its occurrence can be given. There are, however, so many variable factors in the metabolism of glucose, that idiopathic after-shock will probably always occur at times.

(II) Status epilepticus.

The status occurring during insulin treatment is clinically little different from idiopathic status epilepticus. In my series there was one case of this kind, which is fully described in the case-reports. In that patient remarkable mental improvement followed on the recovery from the series of fits.

The treatment for this condition 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 ¼ gr. of morphine may also be indicated. Provided the cardiac condition is good, and the proper treatment is instantly and energetically instituted, the status is not nearly so dangerous as it would appear.(I8).

(III) Laryngeal spasm.

This complication occurred twice in my series, and in the same patient. The spasm is quickly recognised by hearing the characteristic stridor. Cyanosis comes on at once, and if not quickly treated the patient will cease to breathe and will become pulseless.

The treatment is most effective if given promptly. It involves the following measures :- A. The injection of ½ c.c. of adrenalin, made intramuscularly or into the heart, according to the urgency.

B. The injection of I c.c. of Coramine.

C. The injection of 25% glucose either 30 c.c. into the arm veins, or 3 c.c. into the ventricle of the heart.

D. Artificial respiration and the inhalation of oxygen may be indicated.

E. The usual I50 grammes of glucose in water should be given per the oesophageal tube.

This complication is not common and quickly responds to the proper treatment, while it is easily and quickly recognised. If the condition occurs more than once in a patient, it will be wise to discontinue the insulin treatment as a susceptibility on the part of the larynx is undoubtedly present.(I8).

(IV) Cardiac disorders.

During the treatment there may be bradycardia or tachycardia. It is usual to terminate the coma if the pulse-rate goes below 40, or above 140. These and other disorders of the heart usually disappear when the hypoglycaemia is ended.

Extrasystoles, alternate slowing and quickening of the pulse rate may, if excessive, be looked on as complications. In all the above cases the general clinical condition will be taken into account in assessing the danger of the phenomena.

(V) Respiratory disorders.

Extreme degrees of shallow, rapid or irregular breathing may necessitate interruption of the coma.

(VI) Lessened resistance to infection.

Whether it be due to the "shocks" lowering vitality, or to the circulating insulin and glucose forming a nidus for bacteria, it is certain that patients undergoing this treatment are more susceptible to infection. In my series pyelitis has occurred in two patients, and acute dysentery in one patient. Commenting on this lessened resistance to infection, Küppers (23) concludes that this drawback should not, however, disqualify patients from receiving the treatment.

(VII) Prolonged coma.

Continuance of the coma after the usual administration of glucose has been noted by several workers, and is discussed on pages 51 and 52.

(VIII) Pulmonary oedema.

this complication did not occur in my series, but has been noted by other workers (34).

Indications for interruption.

(I) It is usual to end the hypoglycaemia not later than 5 hours after the injection, as there is some evidence that longer periods of hypoglycaemia result in irremediable changes in the cerebral neurones.

(II) Laryngeal spasm.

(III) Cardiac disorders.

(IV) Respiratory disorders.

(V) Status epilepticus.

(VI) Major epileptic fits. As has already been discussed, some workers would always interrupt the treatment on the occurrence of a major fit. It is not my practice to interrupt unless there are other indications, and in any case, the coma often lightens after the fit.

In all cases, the mode of interruption will depend on the urgency of the case.

Wortis (22) regards the motor excitement of the patients as an effort to compensate for depleted adrenalin stores, or as an effort to release carbohydrate stores without the help of adrenalin. He found that an injection of adrenalin quickly had a sedative effect on the excitement. In some cases I have had personal experience of this effect, while in others the injection had no effect. Wortis states that one-third of his patients had epileptic seizures during the treatment, thus corroborating the experience of Muller. In my series of 18 cases 9 patients had one or more fits at some time during the treatment.

When signs of cardiac irritability appear but are not severe, they may be abolished temporarily by giving a small dose of the glucose solution by the stomach or nasal tube. It is usual to give 5 or 10 c.cm. of 50 per cent glucose in water solution, and usually this dose will banish any mild signs, such as irregularity of the heart without altering the depth of coma to any material extent.

It is reported from Vienna (40) that 3 patients were kept comatose for 12 hours by giving small quantities of glucose as above; all three patients died. It will be seen that experimentation is dangerous.

Modifications in the technique.

In January, I937 Sakel reviewed his 3½ years experience of the therapy (I3), and stated that the results depend not only on the production of a hypoglycaemic state, but on the proper use and management of each hypoglycaemic shock. The results do not depend on the size of the dose of insulin, but rather on the proper termination at the proper time, of each hypoglycaemic state.

Unfortunately, Sakel gives no very clear indications of when to interrupt the hypoglycaemia. He says that in many cases clinical intuition tells him the proper time to end the treatment. There are, however, some fairly reliable laws of technique, that are mainly empirical. Sakel states that the patient tends to remain in the condition in which she is when the hypoglycaemia is interrupted. Hence, it is unwise to end the treatment during a stage of excitement. Of course, in an emergency such considerations are subordinated. In stuporous cases, however, he suggests that the hypoglycaemia be interrupted during the stage of "activated psychosis" (page 2I), and that on subsequent days of treatment, this fixated excitability be submerged by periods of fairly deep coma. In paranoid patients deep coma is said to be necessary to produce results. Otherwise one usually ends the hypoglycaemia while the patient is calm and non-psychotic.

Sakel stresses that special care is necessary in the stabilisation phase, as the patient may have become hypersensitive or relatively insensitive to insulin. This varying sensitivity to insulin has been observed by me in many cases, but it may depend on the carbohydrate stores in the body, and as my patients did not have their food weighed it is possible that these variations in reaction to the same dose of insulin were due to variations in the intake of food.

James and co-workers (8) in selected cases of a stuporous nature sometimes omit insulin for a day, and give an injection of Cardiazol which produces an epileptiform convulsion.

Guiraud and Nodet (I4) give the insulin treatment only every two days, using relatively small doses of insulin, but tea on the

previous evening contains hardly any carbohydrate, e.g. roast meat, omelette and vegetables, with a tiny piece of bread. Thus they have obtained coma with 30 units of insulin, while they find recovery more rapid, and after-shock less frequent.Their experience is limited, however, to 6 cases.

As regards the type of schizophrenia that reacts best to the therapy, there is fair agreement. Müller (3) states that paranoid types react best, and that catatonic stupor and complete mutism are less likely to improve. He continues that essentially periodic forms are resistant to treatment, especially those exhibiting alternating amelioration and aggravation in relation to the menses. In resistant cases, he advocates varying the treatment, e.g. interrupting the hypoglycaemia before coma begins.

There is general agreement that results are better in male patients. In a series of 3I cases, I7 male and I4 female, treated by Young and co-workers (34) remissions were obtained in 76.5 per cent of males, and only in 35.7 per cent of the females. The discrepancy in remissions is probably due to the stronger constitution possessed by the average male, although the differing endocrine make-up of the sexes is also likely to be concerned.

In a more recent communication (39) Müller states that where the duration is not more than I year the best results are seen in paranoid types, while over one year excited catatonic cases react best. Dussik (39) states that the period of hospitalisation in recovered cases who have been treated by insulin is 62 days, while in recovered cases not treated by insulin the stay is 202 days. However, this statement albeit impressive is discounted when one remembers that the remarkable amount of attention given to the treated cases must inevitably fit them more quickly for life outside the hospital.

Where there is an evident emotional reaction to the illness the prognosis with insulin is held to be better. Similarly, where the onset is acute, even in old cases, the results are better. The type of onset, course and duration are the most important single factors in the response to insulin.

There are now two principle modifications of the treatment. First, the standard treatment in which the management is directed to the production of daily periods of coma, regardless of the type of psychosis. Müller is the exponent of this school. Secondly, Sakel heads the school that believes each individual hypoglycaemic treatment must be managed according to the psychotic state present, e.g. stuporous cases have the hypoglycaemia interrupted while they are excited. The results of the schools are similar, and the standard treatment is preferable because comparison of results is rendered more easy.

In addition, although Sakel's views deserve consideration, many of his statements are difficult to confirm. For example, I have failed to observe that the patient remains in the state in which he is on wakening. Patients who are fed with glucose while excitable do not remain excitable, those fed while calm do not remain calm, unless the prevailing mental condition is corresponding. Parfitt (38) has similarly been unable to confirm Sakel's views.

Also, Sakel advocates giving insulin in such doses that the desired mental state be produced, e.g. the production of excitement is advised in stuporous cases, but I have found it impossible to produce mental states to order. For all these reasons the standard is the treatment of choice, and I have employed it unless otherwise stated in the case-histories.

The Rationale of the treatment.

In 1933 Sakel's view of his treatment was as follows (15). He says that in most types of excitement there has been shown to be a marked increase of sugar in the blood and cerebro-spinal fluid. He then assumes that this is associated with an increase of adrenalin in the blood and cerebro-spinal fluid. He believes that this adrenalin so excessively sensitises the neurones that normal stimuli produce pathological effects. Insulin opposes the action of the products of the adrenal system, and so the cells are left fairly quiescent. This occurs during phase I of the treatment. Insulin also revives forgotten phylogenetically ancient and infantile pathway patterns which are normally latent and subdued in healthy waking thought. In the pathological conditions under consideration here all the above primitive patterns are called into action again; they interfere with each other and produce the picture of " intra-psychic ataxia". Now, by the shock of phase 2 these pathways are again shattered, and normal pathways take precedence. In the convalescent period these pathways are still subdued as they should be, and normal paths are revived and enjoy their normal prominence. In the stabilising phase this prominence is reinforced by further insulin injections, and the normal cellular relations are said to be polarised.

In 1937 Sakel (13) summed up his views as follows:- the hypoglycaemic state weakens, inhibits and finally represses that portion of the mind which happens to be most active at the time, so that the hitherto latent, subdued and repressed portions are again brought to the surface, so that they can again prevail over the elements that are now repressed.

The primitive patterns referred to above are held responsible for the phenomena of " activated psychosis ", this latter is the name given to the psychotic phenomena that frequently burst forth during the pre-comatose period of the hypoglycaemia. Sakel believes this phenomenon to be due to an activation of the essential psychosis. It is probably more simply and correctly to be regarded as a compound of the psychosis present, and of the abnormal reactions seen in normal people as a result of excessive doses of insulin(8).

Sakel believes that there is a tendency for the patients to be non-psychotic during hypoglycaemia at the start of the treatment, and later psychotic during the hypoglycaemia and symptom-free after the termination. This phenomenon he styles the Reversal or Umkehr. I agree with Wilson that this reversal is more apparent than real(I).

The seat of action of the insulin is believed to be the vegetative centres(I5). On this head the work of Schmid(IO) is important. He says,"researches on the leucocyte count, and blood-pressure modifications show that the hypoglycaemic syndrome is composed on the one hand, of vagotonic symptoms (lowering of the temperature, bradycardia and free,cold sweating) and on the other hand, of sympathetico-tonic symptoms such as leucocytosis, increased systolic blood-pressure, tachycardia and considerable increase in the basal metabolism. The epileptiform seizures and the myoclonic fit appear to me to be the clinical expression of cerebral anoxaemia". He goes on to describe the morbid histology in rabbits, dogs and man who have died in hypoglycaemic coma. Perivascular gliosis and capillary haemorrhages were present in one human case. These severe changes led him to apply Sakel's method to rabbits in order to discover what, if any, irreversible morbid changes might be expected from the treatment. He observed the same indications for interruptions as are observed in Sakel's treatment. To his amazement, instead of discovering the grave pathological lesions he had expected, the only lesion attributable to the toxic action of insulin was a certain swelling of the cell bodies, and prolongation of the dendritic ramifications, sometimes also some tigrolysis, but no grave alteration of the cell body.

Schmid concludes that though Sakel's treatment does provoke certain histo-pathological modifications, yet these changes are not grave enough to be a contra-indication to this method of treatment.

The changes found appear to be the consequence of the circulatory modifications, which are apparently due to the compensatory secretion of adrenalin. He attributes the difference in his results from those he expected, to the fact that in his cases the hypoglycaemia was not the cause of death. The changes that he did

find occurred in the deepest layers of the cortex.

Wortis (I6) has a theory that differs from that of Sakel. He looks on schizophrenia as a symptom of nutritional disturbance in the brain. The respiratory quotient of cerebral tissue is unity, i.e. the brain normally metabolises carbohydrate. Lactic acid, glycogen and sugar are all utilisable, but the mechanism and intermediary products of brain metabolism are not fully known. But insulin or related substances must be involved. He quotes workers who say that the high lactic acid findings in schizophrenia " must be ascribed to some local factor that interferes with oxidation." He suggests that insulin therapy may promote carbohydrate utilisation, but agrees with Sakel who believes that insulin shock may simply be symptomatic treatment for a symptomatic syndrome.

Müller(3) believes that the differing susceptibilities to insulin depend probably on differences in the endocrine make-up, above all, on the pituitary and suprarenals. This susceptibility may be modified during the treatment in both directions. He asks if it is light hypoglycaemia, deep coma or epileptic convulsions that are most useful therapeutically. This question has not yet been answered satisfactorily, as there is evidence that each of these degrees of the treatment has been useful. He does not believe that the treatment is a non-specific shock, but considers that it is a question of profound changes in the endocrine system.

The views of Glueck (I7) on the psycho-pathology of insulin shock are of interest. He says the phenomena of the hypoglycaemic state are extremely varied, and from the standpoint of a genetic-dynamic psychology, reveal an amazing array of manifestations that can be best understood through an acquaintance with the phenomena of repression, regression, projection, catharsis, transference and other well-known psycho-analytic concepts. He continues, that the average patient's reaction to hypoglycaemia has much in it of the nature of a profound organismal and personality disintegration, albeit temporary in duration, as does too,the reaction to the introduction of glucose reflect, in many ways, perceptible stages of a reintegration on neurologic and psychic levels.

Another view of the rationale is that three factors are at work, namely, the quietening effect of insulin, the euphoria that is often present on wakening from the coma, and the re-appearance of normal somatic sensation.(39) These factors are probably also present in the treatment by prolonged narcosis, that has not, however, had results so good as claimed by insulin.

My own view is that in the present state of our knowledge it is best to regard insulin as a substance capable of stimulating, in a non-specific fashion, the metabolism of neurones in the central nervous and autonomic nervous systems. While the psychological effect of disrupting habitually morbid reactions by the recurrent coma may be therapeutically useful.

The treatment applied to diseases other than mental diseases.

Drug-addiction.

It has already (page I4) been described how Sakel was led to formulate his treatment. His good results have been confirmed by Piker (28) who treated IO cases of morphine or heroin addiction. The latter stresses that the addicts include a non-diabetic group, who tolerate unusually large amounts of insulin without the development of significant hypoglycaemic reactions.

Asthma.

Wegierko (29) states that insulin shock interrupts dyspnoea in bronchial asthma, and that after a series of shocks the asthmatic type is changed and the attacks become less frequent and in many cases disappear altogether. He believes that the shock increases the tonus of the parasympathetic nervous system so that it gets the upper hand over the sympathetic system. In another place he comments on the soothing effect of insulin shock on the pains of migraine and neuralgia.(4I)

Acne vulgaris.

Wortis (30) comments on the improvement effected in acne by the injection of insulin. He states that the cutaneous hyperaemia, the profuse sweats and the circulating adrenalin may be concerned in the improvement. I have also witnessed this effect; case 8 had a moderately severe acne of the face that greatly improved during her treatment.

Emaciation and Disordered circulation.

In my series of I8 cases a gain in weight during treatment was usual, and at times quite appreciable obesity was produced. Also, stuporous cases with cyanosis of the extremities showed a return of normal vaso-motor control during treatment, but where mental improvement did not finally result, the circulatory disorders returned on cessation of the treatment.

The case-reports.

here follow descriptions of the treatment of I8 female patients in the wards of West Ham Mental Hospital. The last two cases received both insulin and Cardiazol, the others were treated with insulin alone. The first patient began her treatment on the 26th January, I937 while the last finished treatment on the 4th December, I937. The longest period of treatment was I2 weeks (cases I7 and I8), while the shortest completed course was I0 days (case 3). The average period of treatment for those who finished their course was eight weeks.

Four patients failed to complete their course; cases I and 6 on account of intercurrent illness, case 4 because she exhibited circulatory weakness during the hypoglycaemia, and case I3 because she twice exhibited laryngeal spasm. There were no fatalities during the treatment, no residual physical disabilities, and no patient was made mentally worse by the treatment.

The highest dose of insulin injected was 240 units (case 7), and the lowest dose to produce coma was I6 units.(case I4). The average dose needed to procure the first coma was about 90 units, while the smallest dose that procured an initial coma was 40 units (cases 9 and I4). The highest dose required to procure the first coma was 2I6 units (case 7). The total number of treatment days for the I8 patients was 823.

The insulin used throughout was Messrs. Boots' quadruple strength brand, one cubic centimetre of which contains 80 units.

The average age on admission of the I8 patients was 25 years.

The average period of hospitalisation was I year 9 months, but it will be remembered that many patients had been psychotic for lengthy periods before admission.

It is usual to classify the patients into three groups according to the period of hospitalisation; A. less than 6 months,
B. from 6 to I8 months,
C. over I8 months.

For my series the following figures are thus obtained,

Group A.-- 5 cases (5, 9, I6, I7 and I8).
Group B.-- 3 cases (4, 6, and I5).
Group C.-- I0 cases (I, 2, 3, 7, 8, I0, II, I2, I3, and I4).

Case I.

Blanche N. aged 28 years on admission.

She was a barmaid. She was admitted on the 6th. November, I934, as a Voluntary patient, having been referred from the out-patient clinic, because of hypochondriacal delusions of a few weeks' duration Her father was a chronic alcoholic, while her great-aunt, uncle, aunt and sister had been insane. A few weeks prior to her admission she had been "jilted" in a love-affair. Her pre-psychotic personality was successful but she had always been a person of irritable temper.

On the third day after admission she became more peculiar in manner, and exhibited bizarre gestures, while at times she was disconnected in speech and faulty in habits. During her stay in hospital she has exhibited considerable fluctuations in the affective sphere, at times being capable of work in the needle-room, at others violent, abusive, noisy, obscene, shameless, dirty and degraded. On the 20th. July, I935 she had to be removed from the admission hospital to the "refractory" ward. She became more homicidal, suicidal and destructive and so was certified on the 20th. April, I936. Throughout her stay she was very much aurally hallucinated.

A note on the 26th. November, I936 states : " today she is coherent, relevant, logical and shows some slight insight. She admits hearing and seeing her deceased father. There is marked affective loss and evidence of intra-psychic ataxia. Today her active attention is fairly good.At times she is truculent, violent and shows impulsive excitement. She eats and sleeps satisfactorily. Occasionally she can be occupied with floor-polishing."

On the whole during her stay here she showed a mixture of catatonic excitement, hebephrenic and paranoid features. A note on the 25th. January, I937 states " she is most unstable; at times she is co-operative and fairly pleasant, at other times she is almost homicidal. She gives the impression of having no dementia, but of having a fair degree of disintegration. She is very much aurally hallucinated and has various mutable, non-systematised delusions of no depth, and of a grotesque and persecutory nature. She is generally resistive, destructive, impulsive, taciturn and

violent, while she is often doubly incontinent. One feels that physically and mentally she is eminently suitable for a "shock" therapy, as she shows considerable psychic content and at times she behaves almost in a normal fashion. Without treatment the prognosis would appear to be hopeless, and it is unlikely that she will make even a social recovery."

Physically she was in excellent condition and was a virile, muscular, athletic specimen. The blood-pressure was I40/90. There were no signs of endocrine dysplasia nor any physical stigmata of degeneracy. She had bright red hair. The urine showed no abnormalities even on microscopical examination. The blood Wassermann reaction was negative on the IOth. May, I935.

A glucose tolerance test on the I5th. January, I937 gave the following results : Fasting-- .I2%, ½ hour-- .I5%, I hour-- .I5%, I½ hours-- .I6%, 2 hours-- .I6%. There was no glycosuria during the test, which was made with capillary blood.

Hypoglycaemic treatment was begun on the 26th. January, I937 with 24 units of insulin, and was continued with daily increments of 8 units until on the 5th. February she was having 72 units. On that day pus and the Bacillus Coli were found in the urine, having been indicated by the presence of a trace of albumen found on routine examination. She was at once given a preparation of Mandelic acid four times daily. The following day she had 80 units of insulin, and the same amount on the 8th. February after a day's rest on the Sunday. However, the pyuria had increased in amount and an intra-venous pyelogram on the 8th. February showed slight dilation and distortion of the left renal pelvis, which had been tender to palpation. At no time did she complain of pain nor did she show any constitutional disturbance from the pyelitis. The insulin treatment was stopped, and on the I2th. February she was transferred to a general hospital for further investigation, which only confirmed the initial diagnosis.

Discussion.

Sweats appeared during the first day's treatment and thereafter, but they were never profuse. Even with her maximum dose of 80 units she was no more than drowsy. During the treatment she was

freer in speech, more co-operative and showed an appreciation of humourous situations. Also, she could be induced to occupy herself with knitting, and take an interest in her appearance. I am not disposed, however, to attribute these improvements to the treatment, and believe that they can all be set down to the remarkable amount of individual attention and interest she elicited. She was our first case, and as such attracted great interest among the staff, while attempts to occupy her, sometimes successful, were continually being made.

She returned from the general hospital on the I9th. March, I937 having being treated there with Mandelic acid and apparently cured. Insulin therapy was begun again on the 23rd. March, I937 with a dose of 48 units of insulin and by the 28th. March she was having II2 units, but on that day the pyuria returned and the treatment was permanently discontinued. It would appear that the attack of pyelitis was due to the stimulation of a quiescent coliform infection by the metabolic shocks produced by insulin. Since the cessation of the treatment she has returned to her original psychotic state, the improvements originally produced having disappeared.

Result.

no improvement.

Case 2.

Florence B. Aged 33 years on admission.

She was a forewoman packer in a factory. She was admitted as a Temporary patient on the I9th April, I935 with a history of mental disorder of two weeks duration. The anamnesis was accurate and detailed. She was the youngest of six children, her twin-brother having died at birth. Another brother died in adolescence from Tuberculosis. Her elder sister was a Certified patient in this hospital in I928, but within 3½ months had made a good recovery from a Schizoid attack, which was said to have followed on the death of a girl friend. Coincidently with our patient this sister had a second mental illness from I2th April, I935 until 8th May, I935. This was an attack of apparently pure Melancholia, in reaction to the death of the father, and she made a good recovery. On this occasion she was a Voluntary patient in this hospital.

In our patient the pre-psychotic personality was stable and successful., but she had always been shy and never had any male friends and few of her own sex. About three weeks before admission her father died after a long and distressing illness due to cancer of the stomach. About a week after his death she became depressed and stated that she was responsible for his death.

On admission she was in a state of resistive stupor, which persisted with periods of impulsiveness, negativism and occasional faulty habits until September, I935 when she began to talk. Her utterances were nonsensical, and have continued thus. A note on the 8th December, I936 stated, "Hebephrenic type of Schizophrenia. She shows gross verbigeration, grotesque mannerisms, and neologisms. She is grossly disintegrated and aurally hallucinated. She eats and sleeps well, but is sometimes noisy at nights. At times she says she is the " Lamb of God ", the " Holiest Virgin ", and that she has been " re-born."

An examination of the mental condition on the 9th February, I937 stated " There is apparently no dementia. She understands questions, and as far as her incoherent state allows, she is co-operative and her replies usually contain the correct phrases. However, she talks nonsense most of the time, and makes use of neologisms. In answer

to the question, "What is your name?", she said, "The Holy martyr of the World. They forged my name. Ki-nacki-ki-nooki-ki-nacka. Miracles and purification of the blessing of the pure air. They said holy, ki-nacki-ki-teeren, they said. You can understand what I'm saying. Ki-nooki-ki-nacki-ki-tooren." She is aurally hallucinated, and in response to 'voices' is obscene and abusive. She states that this is the year I927, and that she is in West Ham. The principal clinical features are the absurd incoherence, the silly smiles and grimaces, and the general religious tone of her utterances. The prognosis would appear to be very poor, although the acute onset following on adequate mental stress, and the stable pre-psychotic personality are redeeming features. Physically and mentally she appears to be suitable for a shock therapy."

Physically she was well-developed and in good condition. The blood pressure was I50/95. There were no signs of endocrine dysplasia, nor any physical stigmata of degeneracy.

The blood Wassermann reaction was negative on the I0th May, I935.

A glucose tolerance test on the 9th May, I937 gave the following results :- Fasting--.I4%, I hour--.I6%, 2 hours-.I4%.

Treatment was begun on the I0th February, I937 by the injection of 32 units of insulin, and continued with daily increments of 8 units until on the I8th February with 96 units she became comatose. On succeeding days the dose was reduced until on the 24th February she was having 72 units daily. On that day she became comatose as usual at II.I5 a.m. and was given I50 grammes of glucose per tube at I2.30 p.m. Some five minutes later, while still comatose, she had a generalised symmetrical convulsion the main features of which were clonic spasms of the limbs which latter were held in extension. This fit lasted about 8 minutes and by I2,50 p.m. she had regained consciousness and appeared none the worse. The dose of 72 units was maintained until the 4th March when it was increased to 80 units; on the 9th March the dose was further increased to 88 units; on the I7th March she had 96 units, on the I9th March I04 units, and on the 20th March II2 units. On this last day she did not go into coma at all, but instead had an outburst of psycho-motor restlessness

at II.0 a.m. which lasted some I5 minutes. The dose was increased thereafter until she had I60 units on the I9th April. The only effect of these increased doses was to produce irregularities of the pulse, i.e. the coma was not deepened. On the 20th, 2Ist, 22nd, and 23rd she received 96, 80, 64 and 56 units respectively. Thereafter the treatment was discontinued permanently.

Discussion.

She received the hypoglycaemic treatment for a period of I0 weeks, and neither during nor after the treatment did she show any mental change, for better or worse. With the majority of the patients under this treatment it is usual to find that the attention they receive causes some slight improvement, but in this case, there was absolutely no change. Towards the end of the course of injections she tended to have tachycardia and extra-systoles, which abnormalities usually responded quickly to the exhibition of digitalin. She was perhaps unusual in the comparative absence of motor phenomena, as with the exception of the one fit described, it was rare for her to show twitching in any degree. Her failure to respond with coma on one occasion may have been due to the secretion of adrenalin concomitant with her attack of psycho-motor excitement.

Result:- no improvement, during or after the treatment.

Case 3.

Jessie B. Aged 32 years on admission.

She was a Fur machinist, and was admitted as a Temporary Patient on the 28th of May I935, with a history of mental disorder of 3 weeks duration. The pre-psychotic personality was stable, sociable and successful; her own and her family history showed nothing relevant, either mental or physical.

On admission she was in a state of acute confusion - disorientated, restless, insomnic, impulsive, resistive and hallucinated. On the 28th of November I935, and on the 28th of February I936, her temporary state was extended. She remained silly and fatuous, troublesome with food, and incoherent. On the 7th of May I936, she was certified. A note on the IOth of September I936 states;- "Says she isn't discontented, but this morning was crying because of the Count of Montrose. She gives no coherent reason for this. She is alternately elated and depressed, and at times violent. Still destructive at times. Eats and sleeps well. Very much aurally hallucinated, but denies this. Considerable affective loss. She is grotesque in her ideas."

The following notes were made on the I6th of February I937:- "There is apparently no dementia. She is moderately co-operative, but her speech is somewhat disconnected. Affectively she is alternately elated and lachrymose - the affect is shallow and inco-ordinated with her expressed thoughts. She states that this is February I938, that she is in Tressillian Palace, and that the Medical Officer is a retired parson. She has other changable, non-systematised delusions of little depth. At times she is resistive, violent, impulsive and restless. There is a fatuous element in her speech and appearance. She is full of mannerisms of speech and action, and very much aurally hallucinated. The prognosis is very poor."

Physically she was healthy. The blood pressure was I20/80. There were no signs of endocrine dysplasia, nor any physical stigmata of degeneracy.

The blood Wassermann reaction was negative on the I3th of

(Case 3 continued.)

June I935. A Glucose Tolerance Test on the I2th of February I937 gave the following results:-

Fasting, .I2%; ½ hour, .I5%; I hour, .I5%; I½ hours, .I4%; 2 hours, .I2%.

The treatment will be described in detail as she showed most of the typical features.

Treatment was begun on the I3th of February I937, with 24 units Insulin. The dose was increased by 8 units daily, until on the I8th of February with 64 units she became comatose. This "shock dose" was continued until the 23rd of February, on which day she had a Status Epilepticus.

The treatment on the 23rd of February is important as it deals with a complication not fully described in the English literature on the subject.

February I3th.

24 units were injected intra-muscularly at 7.I5 a.m. while she was still fasting. This was the second day of her menstrual period. At that time the temperature was 97.8 degrees, the pulse 74, and the respirations I8. At 9.0a.m.she showed fine twitchings of the face and hands, and she was drowsy. Sweats then appeared round the mouth. At II.0 a.m. the twitchings were most marked, and at II.30 a.m. she went into a deep sleep for half an hour. At I2.0 noon she was given a cup of tea containing 3ozs of glucose to terminate the hypoglycaemia. In the afternoon she was occupied with knitting.

February I4th.

32 units Insulin. Twitchings were repeated as on the previous day. Sweating of the face was profuse, and tremors of the limbs were constant. At I0.45 a.m. she had a momentary loss of consciousness resembling a minor epileptic fit. At I2.0 noon the hypoglycaemia was ended by giving glucose tea.

February I5th.

40units Insulin. At 8.I5 a.m. she had a momentary loss of consciousness. at 8.30 a.m. sweats round the mouth and on forehead. At 8.45 a.m. She became very much aurally hallucinated, and shouted "I am a stranger." At I0.I5 a.m. she showed marked tremors of the arms

(Case 3 continued.)

and legs, along with grimacing and twitching of the facial muscles. Thereafter she lapsed into semi-consciousness, which continued until she was roused and fed with glucose tea at noon. She was occupied with knitting in the afternoon.

February I6th.

48 units Insulin. Sweats appeared on the face at 8.I5 a.m At 9.45 a.m. she showed tremor of the hands and twitching of the facial muscles. At II.Oa.m. she became semi-conscious and remained thus until she was roused and given glucose tea at noon. She was occupied in the afternoon, but in the evening became very uncertain in manner.

February I7th.

56 units Insulin. Profuse sweats on face and chest at 9.0 a.m. At 9.30 a.m. she showed marked tremor of the hands and became drowsy. She remained deeply drowsy until she was roused at I2.0 noon with glucose tea. She knitted until 4.0 p.m. when she became impulsive, broke her knitting needles, and repeatedly slapped her face.

February I8th.

64 units Insulin. At 9.0 a.m. she became drowsy and showed sweats of face and neck. At times she struck herself impulsively. At II.0 a.m. she became comatose - she was very pale, breathed quietly, and made no movement. The oesophageal tube was then passed by the nasal route. She was fed at noon with I50 gm. glucose in water. At I2.I5 a.m. she awoke with a yell and was noisy for five minutes. She answered relevantly and rationally, until about I2.45 p.m. when she lapsed into her usual silly, irrational state. She remained drowsy until 3.0 p.m. but thereafter until 7.0 p.m. she could be occupied. In the evening she was aurally hallucinated, impulsive and smacked herself repeatedly.

February I9th.

64 units Insulin. At 8.30 a.m. sweats, drowsy, twitching of face, and shivering fit. Further shivering fits at 9.30, I0.0, and I0.I5 a.m. At I0.30 a.m. her face showed apprehension, and shortly afterwards she lapsed into coma. The nasal tube was then passed. She remained pale and her pulse rate varied between 58 and 70. The coma was ended by glucose feed at I2.0 noon. At I2.I5 p.m. she be-

gan to regain consciousness, in the same manner as on the previous day. She was occupied in the afternoon, but in the evening was impulsive, screaming, slapping herself, and being resistive to attention.

February 20th. 64 units Insulin. At 8.30 a.m. sweats all over the body, and marked tremors of the hands. Between 7.0 and 8.0 a.m. she was very excited and impulsive. She was comatose and the tube was passed at 9.40 a.m. Fed with glucose at noon. All the afternoon and evening she was depressed, restless and hallucinated.

February 2Ist. This being Sunday no Insulin was given. Before the ordinary breakfast she received 2 drachms of Epsom salts. She was occupied desultorily during the day, but at times was destructive and impulsive.

February 22nd. 64 units Insulin. At 8.I5 a.m. drowsy, and sweating of face and chest. Comatose and tube passed at II.0 a.m. Fed with glucose at noon. Awake at I2.20 p.m. This afternoon she was allowed up, and made herself useful in the ward.

February 23rd. 64 units Insulin were injected at 7.25 a.m. At 9.0. a.m. she was drowsy, and at 9.I5 a.m. sweats appeared on the face. At I0.20 a.m. she became comatose, and an oesphageal tube was passed by the nasal route. Further progress in the coma was uneventful, and she was given glucose per tube at I2.I5 p.m. She regained full consciousness at I2.35 p.m. and appeared as usual. At I2.40 p.m. she had a major epileptic fit, with tonic and clonic stages. By I2.44 p.m. she had recovered consciousness fully and appeared none the worse. At I2.50 p.m. a second major convulsion occurred; she regained consciousness within four minutes, and appeared well. At I2.55 p.m. she was washed and her nightdress changed. At I.0 p.m. she took dinner, but made only a poor meal. At 3.I0 p.m. she had a different sort of fit with spasm of facial muscles at onset, staring eyes, open mouth, and head and neck were rigid. Then clonus of orbiculares oculi et oris. Throughout this there were carpal and pedal spasm.

Identical convulsions occurred at 3.25, 3.45, 4.0, 4.20, 4.40, 5.25 and 5.40 p.m. without regaining consciousness.

The following treatment was given :-

3.I5 p.m. 30 c. cm. of 25% glucose in saline given intravenously.

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

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

3.50 p.m. Adrenaline ½ c.cm. injected subcutaneously.

4.I5 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. I c.cm. of 20 per cent luminal solution injected intramuscularly.

6.20 pm. 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 9.0 pm. the coma lightened and she became restless. At that time morphine sulphate ¼ grain was injected subcutaneously. At no time during the day did the cardiac condition give anxiety. The need for constant attention during the hypoglycaemic treatment is shown by the fact that her bedside was hardly quitted that day.

All the next day she was drowsy, but on the morning of February 25 she was found to be pleasant and coherent in conversation. As the recovery may 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, cognitive and conative 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 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 better be recorded as an incomplete remission according to the standards of Müller (3).

It should be added that 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.(I8).

Further note: on I0th December, I937 she reported again and her remission had been perfectly maintained.

Case 4.

Florence G. aged 25 years on admission.

She worked in the home. She was admitted as a Certified Patient on the I9th of November I935, with a history of mental disorder of 2½ years duration. During that period she had been in and out of observation wards. The personal and family histories were faulty, but apparently for 4 years before admission she had been mentally abnormal.

On admission she talked in a most disconnected fashion, going from one subject to another without any apparent association. She smiled foolishly in a typical Praecox manner. She was restless and mildly negativistic. From the time of her admission she steadily deteriorated, becoming depraved and faulty; she became incoherent to the point of verbigeration. It was impossible to hold any conversation with her. At times she bit herself savagely. Examination on the I6th of February I937 showed considerable disintegration and, on the surface at least, some dementia. She talked nonsense, was obscene, doubly incontinent, resistive, destructive, restless and impulsive. She was aurally hallucinated. A note on prognosis states:- the outlook is quite hopeless, she is grossly disintegrated and is a very malignant type of Dementia Praecox.

Physically she was undersized, but on examination she appeared healthy. The blood pressure was II0/70. There were no signs of endocrine dysplasia, nor any physical stigmata of degeneracy.

The blood Wassermann reaction was negative on the I3th of December I935.

A Glucose Tolerance Test on the I5th of February I937 gave the following result:-

Fasting, .I3%; ½ hour, .I5%; I hour, .I6%; I½ hours, .I4%.

Treatment was begun on the I6th of February I937 with 32 units Insulin. At 8.45 a.m. she was sweating on brow and complained mildly of hunger. The rest of the hypoglycaemia was uneventful, and it was ended at noon by giving a mug of glucose tea.

The dose was increased daily by 8 units, until on February the 20th, with 56 units Insulin, she became lightly comatose. As the nasal tube was about to be passed she had a convulsion for 5 minutes, with opis-

(Case 4 continued.)

thotonos and clonic movements of left leg only. She regained and maintained consciousness until 10.30 a.m. when tube was passed. At 10.45 she was bloodless and the pulse became weak. At 11.15 a.m. the pulse rate was 48, the heart action was weak and she was extremely pale, hence the hypoglycaemia was ended by giving a mug of glucose tea.

On February the 22nd she was given 48 units Insulin. She became comatose at 10.50 a.m. and was roused at 12.30 p.m. by glucose per tube given at 12.5 p.m. Again however she gave anxiety because of her circulatory weakness, and so her treatment was discontinued.

Result;- no improvement, during or after the treatment.

Case 5.

Amelia C. aged 20 years on admission.

She was a shorthand-typist, and was admitted as a Voluntary patient on the IOth October, I936 after having been seen at the out-patient clinic where she complained of her colleague at work having hypnotised her. The first signs of mental disorder were seen about two weeks before admission. The anamnesis was fairly good. She was the eldest of a family of six, and there had been other five children who had died in early childhood from respiratory infections. Her father has been an inmate of this hospital for the last five years; the diagnosis in his case is Paranoid Schizophrenia. She was always reserved and sometimes expressed a fear that she would inherit her father's mental trouble. Intellectually she was the 'brains' of the family and her work took her into society which was better than she had been accustomed to; apparently she was sensitive to this difference in her upbringing and that of her colleagues. She was looked on at home as a rather superior person, and as she was moody, self-willed and ambitious she tended to get her own way at home. She had no male friends and few girl friends.

On the Ist October, I937 her mother was asked to bring her home from work as she had accused her employer of attempting to hypnotise her. On that occasion she told all in the office that her father was in a mental hospital, but that she would never go there.

On admission she did not appear to realise the gravity of her mental condition. She smiled frequently as she told how her 'chief' was a spiritualist and was hypnotising her continually. She believed that her thoughts were 'touched', and that electricity was run through her. She said that there was nothing the matter mentally either with herself or with her father. She remained in this condition for the time she was here, and was often very rude and abusive. On the I3th October, I937 she gave notice of her desire to leave and she was discharged unimproved on the I6th October.

On the I9th February, I937 she was admitted for the second time , on this occasion as a certified patient. Apparently her psychosis became quiescent a few weeks after she discharged herself, and returned a few weeks before her second admission.

According to the certificate, she was " impulsive and rather aggressive in manner. She says she tried to commit suicide by jump- through a window, because 'God made a mistake'. She says that she talks to Mr. Baldwin by telepathy. She also said that Amy Johnson 'who is dumb' dropped a message to her and asked her to become Amy Johnson's secretary. While talking to me she tries to get into touch with absent persons."

On admission she was belligerent and demanded to be allowed home. She said she wasn't insane and had come here because she was involved in an accident which had given her nervous shock. She claimed to be able to talk by telepathy, and stated that she was told by telepathy to commit suicide by lying in front of a train. She said that she had become numb and died and had since been brought back to life. During the examination she frequently stopped talking to answer 'voices'. A note on the 2Ist February states " She is a classical example of Paranoid Schizophrenia. There is a certain amount of disintegration and intra- psychic ataxia. Her delusions are bizarre and poorly systematised, while her frequent aural hallucinations occur in a field of clear consciousness. The prognosis would appear to be very poor".

Physically she was well developed and in good condition. The blood pressure was I34/75. There were no signs of endocrine dysplasia nor any physical stigmata of degeneracy. The blood Wassermann reaction was negative on the I7th February, I937.

Treatment was begun on the 22nd February, I937 with an injection of 32 units of insulin, and continued with daily increments of 8 units until on the 4th March with 80 units she became comatose. This dose was continued daily until the 20th April. Her reaction to this dose was always approximately the same. She would become drowsy and begin to sweat about one hour after the injection. About 75 minutes after the injection she would begin to exhibit motor phenomena :- tremors of the limbs, various grimaces, convulsive jerkings of the body and limbs, opisthotonos, etc. During these movements she was semi-conscious but invariably aphasic. About three hours after the injection she usually became comatose.

On the 29th March with the usual dose of 80 units the usual

motor phenomena were seen from IO.O a.m., but at II.O a.m. she had an abortive fit, with severe clonus of the face and arms, associated with moderate cyanosis. This ceased spontaneously in about a minute, and she remained comatose thereafter. As she secreted a great deal of gastric mucus habitually, a stomach lavage with alkaline solution was given at I2.IO p.m., after which she was fed with glucose. At I2.50 p.m. she was still comatose, so I5c.c. of 25 per cent glucose were given intravenously without effect. She remained comatose throughout the afternoon, and at 3.45 p.m. her temperature rose to IOI degrees. At 4.45 p.m. the coma lightened, her temperature then being I03.4 degrees. During the afternoon she was sponged frequently with tepid water, and at 5.0 p.m. she was fed per tube with ½ pint milk, one egg, 5 ozs glucose, and I oz Epsom salts. Between 6.0 p.m. and 6.30 p.m. she was three times incontinent of urine and faeces. During the evening her temperature remained about I02 degrees and she was sponged frequently. By II.O p.m. the coma had lightened until she was only drowsy. She slept well that night and in the morning appeared to be her usual self. The insulin treatment was begun again the following day. It being recommended that deep coma be applied to Paranoid cases, attempts were made to increase the dose but this resulted only in the production of cardiac irregularities, which did not respond to the exhibition of digitalis. From the 2Ist of April the dose was decreased until on the 24th of April she was receiving 48 units. This dose produced the same motor phenomena, the same depth of coma and the same cardiac irregularities as had her usual dose of 80 units.

Discussion.

During the treatment her aggressive attitude changed somewhat, and she became more co-operative. It is almost certain that this improvement was related to the attention she received, and not to the insulin treatment. Her delusions and hallucinations remained as prominent as before. Usually on coming out of coma she was euphoric for a few minutes, but it was never possible to fixate this mood. So far as could be seen the treatment had no radical effect on the psychosis.

Result: No improvement, during or after the treatment.

Case 6.

Miss M.Y. aged 20 years on admission.

She was a factory hand, and was admitted on the 3rd of December I935 as a voluntary patient, with a history of mental disorder of a few weeks duration. She was the second youngest of a family of seven; a sister died at the age of 27 from tuberculosis. There was nothing else relevant in the family or personal histories. The pre-psychotic personality was sociable and bright; she had worked steadily since leaving school at the age of fourteen. For several months before admission she suffered from headaches and seemed to lack confidence. About IO days before admission she became depressed, and was afraid to be left alone. On admission she said that she had had a nervous breakdown; she complained of having "knives in her head", and of depression. She showed some insight, and gave a coherent history. A certain apathy was evident in her behaviour, she remained content to be in the hospital and did not change much until the end of January I936, when she showed praecox mannerisms. During February she had to be confined to bed because of resistive excitement, noisiness, impulsiveness, and faulty habits. She then resumed her usual dull, apathetic state, with occasional giggling spells. During January I937 she worked fairly well under supervision in the nurses' home, but she was discovered eating soap. Hallucinations have never been marked, but she appeared to be a mild hebephrenic schizophrenic. A note on the 22nd of February I937 stated that she showed marked inertia and affective loss, she giggled and wept for no apparent reason. She requires constant stimulation and supervision, she is apparently not at all demented, but the prognosis appears poor as she is drifting into apathy.

Physically she was in good condition. The blood-pressure was I25/70. Apart from overweight she showed no endocrine dysplasia, nor any physical degeneracy.

Hypoglycaemic treatment was begun on February 23rd I937 with 40 units of Insulin. The dose was increased by 8 units daily until on the 27th of March a coma-producing dose of I76 units was reach-

(Case 6 continued.)

ed. This dose was maintained on succeeding days. Throughout, the treatment was uneventful save for a Major Epileptic fit 1½ hours after injection on the 30th of March. On the 3rd of April she complained of nausea and was found to have a pyrexia. Later she vomited and had diarrhoea with blood and mucus. A diagnosis of Acute Bacillary Dysentery was made, (there had been one other case in the ward) and Insulin treatment was suspended.

From the 30th March she appeared mentally improved; from her previous dull and apathetic state she became interested in things around her, and on occasion she spoke spontaneously. This improvement was maintained for some 14 days during which she made a good recovery from the dysentery. About the middle of April she reverted to her former dull state, and so treatment was begun again on the 28th of April with 24 units; the dose was increased until on the 5th of May she had a major fit some four hours after injection. The following day she required 15 c.c. of intravenous glucose to rouse her. On the 16th of May she was discovered to have a unilateral pyelitis, hence the insulin treatment was discontinued and she was successfully treated with mandelic acid.

Discussion.

The improvement which occured during her first course of treatment followed immediately after a major epileptic fit, and was I believe due to this fit. During the second course of treatment she again improved to the same degree as before. I feel that this improvement was due to the attention, because within a few days of cessation of treatment she had become as dull as before.

Result:- no permanent improvement.

Case 7.

Mrs D.S. aged 26 years on admission.

She was a housewife, and was admitted on the 25th of September I934 as a certified patient. There was nothing relevant in the family or personal histories. The pre-psychotic personality was sociable but quiet. She had worked as a clerk until her marriage, which took place three years before admission. The husband was neurotic, but had a good position as a draughtsman. Towards the end of August I934 she was confined, this was her first pregnancy and there had been no abnormalities during the period of gestation. The labour was uneventful and she was delivered of a healthy female child. The puerperium was healthy, but on the seventh day she became depressed, and talked to herself. She was admitted in a state of stupor one month after the confinement, and appeared toxic. By the middle of October she was capable of feeding herself, and appeared much less toxic. At times she was faulty. By December I935 she had come out of her dull, semi-stuporous condition, but was then silly, childish, irresponsible and aurally hallucinated.

A note on the I5th of October I936 stated there was no change, she was disintegrated, irrelevant, verbigerative, irresponsible and disorientated. She was faulty, degraded, obscene and shameless. She was very much aurally hallucinated. On the 25th of January I937 examination showed considerable disintegration, she did not co-operate in examination. She was incoherent and conversation with her was impossible. She was usually elated in a silly fashion, and talked to herself and to "voices" all day. She was obscene, erotic, shameless and troublesome. The disintegration was too complete for delusions to be of any consequence. The prognosis appears very poor.

Physically she was in good condition. The blood-pressure was I28/28. There were no signs of endocrine dysplasia nor any stigmata of degeneracy.

Hypoglycaemic treatment was begun on the 26th of February I937 with 40 units of Insulin, and was increased by 8 units daily until on

(Case 7 continued.)

the 29th of March, with 216 units, she became comatose. On that day she was not awake one hour after feeding with 150 grammes of glucose, so 15 c.c. of 25% glucose were given intravenously, and were at once effective. A similar occurrence took place the following day, and also on the 2nd of April. Thereafter the dose was maintained at 208 units until the 13th of April when it was increased again until she was having 240 units on the 17th of April. On that day at 5.30 p.m. she had a slight after-shock which at once responded to the appropiate treatment. After the 21st of April the dose was decreased and treatment was stopped on the 24th of April.

Discussion.

During the period she was under treatment her habits improved, she was more co-operative, active attention was more sustained, and she was less troublesome. It was felt, however, that these improvements were solely due to the attention given her. An opinion which was corroborated by her having deteriorated to her former state within a few days of the cessation of treatment.

Result:- no improvement during or after treatment.

Miss B.E. aged 20 years on admission.

She was a shorthand typist, and was admitted on the 3rd March, I933 as a certified patient. She was the youngest of a family of five children; there being nine years between she and her next sister. The father was a neurotic person of uncertain temper and domineering nature. The paternal grandmother died of "senile decay", and the paternal grandfather was alcoholic. One of the patients brothers had a schizophrenic illness in adolescence for a year. She was always quiet and retiring, and never made any friends. She was above the average in scholastic work, and won a scholarship at school. In August, I932 she became even more shy, and later left her place of employment because " people were talking about her".

On admission she stated that men followed her about. She was very suspicious of everything in the ward and asked for police protection. She heard her name called out, and answered "voices". She was then noted as a case of Paranoid Schizophrenia. She soon began to show various mannerisms, and then merged into a catatonic state, with resistiveness, negativism, impulsiveness and faulty habits. On the I4th May, I934 she had to be sent to the ward reserved for " wet and dirty" patients. Since then she has appeared to deteriorate further. A note on the I7th December, I936 stated that there was no improvement, she remaining catatonic, stereotyped and secluse ive. She was aurally hallucinated. Her habits were faulty, and she required a great deal of care.

An examination on the Ist March, I937 showed that she was seclusive, resistive and did not cooperate in the examination. At times she spoke excitedly in a rambling fashion mainly about her husband and child and other phantasies. She was obviously aurally hallucinated, but it was impossible to discuss these phenomena with her. She was in a state of catatonic semi-stupor, at times showing waxen flexibility. On attempting to examine her physically she had an outburst of typical praecox excitement. Usually she stands about in bizarre stereotyped postures. The prognosis appeared very poor.

Physically she was in fairly good condition, but there were signs of circulatory stasis in the extremities, and the face showed an acnoid eruption. She had long tapering fingers, and long thin hands. The upper lip and legs were hirsute, while the

pubic hair was masculine in distribution. The blood-pressure was I30/90.

Hypoglycaemic treatment was begun on the Ist March, I937. The initial dose of 24 units was increased until on the 5th March when she had a major epileptic fit 2 hours after the injection. She was fed at once with I50 grammes of glucose, and recovered consciousness within two minutes. Two hours after this she had a second major fit, and on this occasion she was given I5 c.c. of 25 per cent glucose intravenously. She recovered consciousness almost at once. The following day she became comatose three hours after the injection of 56 units, which was the dose that had produced the fits the previous day. The following day was a rest day, and it was noticed that she showed mental improvement, being capable of participation in a simple conversation. This improvement lasted only a few hours. On the 9th March with the same dose she showed psychic excitement two hours after the injection, calling out, " I want to go in a caravan. I want to go back to Bristol. Don't copy me. I'll do as I like. I want my baby." This continued for some twenty minutes and then she began a series of movements, irregular in force and time. There were jerkings of the arms and legs, clonus of the orbiculares oculi but consciousness was not lost. After some thirty minutes of these movements they diminished and quiet coma supervened. On succeeding days the dose of 56 units was maintained, and the same motor phenomena occurred for half an hour some two to three hours after the injection. On the I9th March the dose was increased to 64 units, and she usually went into coma some three hours after the injection, however on the 27th this dose did not produce coma, and caused none of the usual marked hypoglycaemic symptoms. On the 9th April the dose was further increased to 72 units but with no obvious deepening effect on the coma. Similarly after the I5th, on which day the dose was increased to 80 units. After the 20th the dose was decreased by degrees and the treatment was discontinued on the 23rd April.

Discussion.

The only improvement shown during the three weeks of treatment was a transient improvement following on the production of two epileptic fits which may or may not have been related. Towards the close of the treatment she showed irregularity of the pulse towards the end of the

hypoglycaemia, and as this did not respond to digitalis the treatment was ended.

Result.

no improvement.

Case 9.

Miss C. B. aged 27 years on admission.

She was admitted on the 5th January, I937 on account of mental disorder of a few weeks duration. She was a Temporary patient. She was the second youngest of five children. An elder brother has been in this hospital for 7 years, while another brother died after 3 years in this hospital, the cause of death being pulmonary phthisis. The brothers had both had a malignant type of dementia praecox. A maternal uncle died in a mental hospital. the father was intemperate and of poor intelligence.

She was always rather a dull type of girl, but attended an ordinary school, and since leaving has been able to earn her living. About two years before admission she had a mild attack of mental disorder, apparently schizophrenia, but recovered at home. Again,about 6 months before admission she became strange in manner, and became worse about a week before admission, talking nonsense to imaginary voices. On admission she was acutely aurally hallucinated, her utterances were nonsensical, incoherent and accompanied by grimaces of a grotesque nature. She understood questions but her responses were silly and disconnected. By the I6th February she had improved in behaviour, but was still silly, and subject to outbursts of noisiness, violence and destructiveness. There was less incoherence, and a simple conversation was possible. She remained very much aurally hallucinated. Physically she was in good condition; the blood-pressure was I40/90.

Insulin therapy was begun on the Ist March, I937 with a dose of 32 units. On the 5th March with 40 units she became comatose. On the 9th she had the same dose but did not waken as usual when fed at noon. She was given adrenalin, intravenous glucose and another feed of I50 grammes of glucose. However, she remained semi-comatose, rolling about, groaning and writhing, She showed marked head-rolling, and rhythmical protrusion of the tongue. At 2.I5 p.m. 20 c. cm. of cerebro-spinal fluid were removed by lumbar puncture, the fluid being under increased pressure. At 2.30 p.m. a blood-sugar estimation was done in case the glucose given had produced a hyperglycaemia. The level was .I3%. Lumbar puncture was repeated at 4.35 p.m. and I5 c.cm. removed. The pressure was less

than before, but still raised. At 5 p.m. the stomach was washed-out with normal saline, and 40 grains of ammonium chloride left in the stomach, along with 5 ounces of glucose. The purpose of the chloride was to combat a hypothetical alkalosis. All afternoon she responded to painful stimuli, while the corneal reflexes were only absent for a short period. Because of restlessness ¼ grain of morphine was injected at I0.30 p.m. During the night she was quiet, but in the early morning again became restless.

She remained in this restless semi-comatose period until the afternoon of the 5th March, when she began to respond to commands that were shouted. Throughout this period she was incontinent, and showed tachycardia viz. I04, and pyrexia viz. 99.0 degrees. During the five days semi-coma she was fed with milk and eggs by the nasal tube, and given large doses of calomel. On recovery it was noted that she had lost her hallucinations and spoke sensibly and coherently. However, she was dull and never spoke unless she was addressed. Hence insulin was begun again on the I6th March with a dose of I6 units, and by the 23rd she was receiving 64 units. At this dose she sweated and became drowsy about 2 hours after the injection, and about 30 minutes later would twitch violently, and show psycho-motor excitement for some 90 minutes. Then she would become comatose until fed at noon.About the 6th April she showed irregularity of the pulse toward II.0 a.m. and so the dose was lowered to 24 units on the I3th April, and kept at this level thereafter. Treatment was ended on the 8th May, it being felt that no further improvement was occurring.

Discussion. the period of semi-coma from the 9th--I4th March produced an immediate improvement, but mental inertia and sluggishness remained. As the home conditions were poor she was not discharged, but on the 2nd June was made a voluntary patient. She maintained her incomplete remission and was finally advised to discharge herself on the 30th August, I937.

The semi-coma from which she suffered has been noted by several insulin therapists. Freudenberg (8) and (26) draws

attention to the parallel between vitamin B.I. deficiency, and insulin shock. In both conditions experiment shows a lessened intake of oxygen in the grey matter of the brain. Prolonged coma during the treatment has been held due to errors in technique, for example, too frequent "shocks", too extended duration of the coma, etc. Freudenberg claims that the administration of vitamins B.I. and B.2., and adrenal cortex hormone has been successful in interrupting coma in "non-reversible" cases of insulin shock. He believes that the exhibition of these measures is a valuable therapeutic agent in making insulin shock therapy safe.

Salm (27) who treated 80 cases, had several who did not awake from their coma after receiving glucose and adrenalin. In some cases the patients were aroused but were confused, sleepy, vomited repeatedly, and had a high temperature. He believes that in these cases the hypoglycaemia has given rise to cerebral lesions that are not relieved by the giving of glucose, and are due to a local disorder of carbohydrate metabolism in the brain neurones. Confusional states and sleepiness are due to mid-brain disorders, comparable to those in epidemic encephalitis. Similarly, the sweating and alternately rapid and slow pulse are due to extra-pyramidal disorder. In a case that came to post-mortem haemorrhages were found near the third ventricle, in the substantia nigra and in the centres regulating sleep, warmth, blood circulation and pressure, and sweating. Salm continues that these complications can not be foreseen, and are best treated by maintaining the circulation.

In my experience this prolonged coma is best treated by the administration of oxygen, lumbar puncture, purges and attempts to combat the alkalosis that may be related. Its features are prolonged coma after the giving of glucose in amounts that formerly had been adequate, restlessness, confusion, pyrexia and tachycardia.

Result. her ten weeks of treatment ended in a social recovery. Apart from this case the therapeutic effect of prolonged coma has also been noted by Parfitt(38).

Case IO.

Miss J.F. aged 2I years on admission.

She was a factory hand, she was admitted as a certified patient on the I5th July I932, because of visual hallucinations, and ideas of reference. An elder sister is tuberculous. She was the ninth child of a family of eleven. The paternal grandfather was psychotic. The pre-psychotic personality was unsociable and quiet. Since leaving school at fourteen she worked well and steadily. About two years prior to admission she is said to have been the victim of a sexual assault, and since then she believed that men were following her.

On admission she was dull and stared vacantly; she imagined that some man was trying to injure her. She was aurally hallucinated, and at times violent, impulsive and destructive. She remained thus until January I933, when she made a social recovery, and was discharged on the 6th of March I933. She was re-admitted as a certified patient on the I7th of October I933. During the time she was at home she was fairly stable, but latterly she had become hallucinated and impulsive. On re-admission she was silly, fatuous, giggly and apathetic, and has remained thus with periodic impulsiveness, obscenity, violence and destructiveness. A note on the 28th of February I937 stated that she had become mute, non-cooperative, seclusive and apathetic. She worked mechanically at scrubbing. An erotic under-current was evident e.g. exhibitionism before males. A note on the IIth of March I937 stated that there was apparently no dementia; she did not answer questions, but obeyed instructions. She was apathetic and aurally hallucinated. She is rarely free from self-inflicted injuries, she can be set to mechanical occupations, which she performs listlessly. The prognosis appears poor. Physically she was in good condition. The blood-pressure was I45/90. The pupils were large, and there was slight tachycardia, otherwise there were no signs of endocrine dysplasia, nor any stigmata of degeneracy.

(Case IO. continued.)

Hypoglycaemic treatment was begun on the I2th of March I937, with 32 units of Insulin, and continued with daily increments of 8 units until the 30th of March, on which day, with a dose of I60 units, she became comatose. This dose was maintained for a few days but the coma was light, so the dose was again increased, until on the I2th of April she was having I92 units. A few days later the dose was again increased, to 208 units. On the 30th of April she had a mild after-shock at 6.0 p.m. Thereafter the dose was gradually decreased to 64 units, at which it was maintained until the 2Ist of May, the last day of her treatment. On the I5th of May she had a short mild major epileptic fit three hours after the injection of 56 units, otherwise the course of her treatment was uneventful.

Discussion.

Neither during nor after the treatment did any improvement occur which could not be fully explained by the amount of attention she received.

Result:- no improvement.

Case II.

Miss E.R. aged 17 years on admission.

She was a factory hand, she was admitted on the 29th March I932, a certified patient, on account of aural hallucinations and delusions of persecution. She was the eldest of three children. The mother was alcoholic and in consequence of this the parents had separated. She was rather backward at school, but otherwise was normal. She had a slight accident at work on the I5th of February I932 catching her thumb in a machine, that evening she became giggly, and complained of having been branded. On admission she giggled, and cried out senselessly at times. At times she answered; at others she was mute. She was aurally hallucinated and apathetic. She gradually improved and was discharged recovered on the 4th of July I932. She went back to work for a year, but then began to be hallucinated again, and was readmitted as a certified patient on the I5th of August I933. She was dull and indifferent, did not answer questions, and was in other ways negativistic. She smiled and grimaced to herself, and said she wanted to go to school like other children. Throughout her stay she remained in the same disintegrated, regressed, hallucinated, manneristic, seclusive and apathetic state. A note on the 2Ist of March I937 states she is probably not very intelligent, she is moderately disintegrated but apparently not demented. At times she responds with a show of relevance, but more often is giggly and irrelevant when addressed. She is apathetic, and does not know nor care where she is, nor what is the date. She is very much aurally hallucinated. She is a classical case of hebephrenic schizophrenia. She shows considerable evidence of repression to a childish level and of dissociated psychic function, there is no attempt at integration, and she appears to have retreated largely into phantasy life, albeit not completely out of touch with reality. The prognosis appears poor. Physically she was healthy. The blood-pressure was I20/80. There were no signs of endocrine dysplasia, nor any stigmata of degeneracy.

Hypoglycaemic treatment was begun on the 22nd of March I937, with

(Case II. continued.)

40 units Insulin, and was increased daily by 8 units until on the 31st of March, with 56 units, she became comatose. This dose was maintained daily until the 8th of April when 64 units were given. The dose was then increased until she was getting 88 units on the 16th of April. The dose was again increased until she was getting 104 units on the 21st of April. These variations in dose did not affect the depth of the coma which was invariably moderate, hence the dose was decreased until on the 7th of May she was having 56 units. The treatment was uneventful and although she usually showed marked marked twitchings some two hours after injection this rarely lasted long, and there were no major fits. The last day of treatment was the 21st of May.

Result:- neither during nor after the treatment was there any improvement.

Case 12.

Miss M.H. aged I8 years on admission.

She was a clerk, and was admitted on the 29th April, I930.as a Certified patient. She was the second eldest of a family of four children. There was no history of nervous or mental disease in the personal or family records, but the maternal grandfather, uncle and aunt had all died of tuberculosis. She was always a shy and bookish child, and was above the average in intellect. Early in April I930 she began to show psychotic symptoms, and became almost mute and quite out of touch with her environment.

On admission she was dull and retarded, and looked around as though she could not understand where she was. Her memory was faulty, and she did not know why she was sent to hospital. She smiled fatuously and stared vacantly. A note on the 7th May I930 stated that she imagined she was a swallow. She was impulsive and was aurally hallucinated. Until August she was capable of work in the needle-room. But thereafter she became excitable, erratic, irresponsible and impulsive. Her habits became faulty. A note on the 25th February, I937 stated that she was seclusive, irritable, violent, impulsive and degraded in her habits. She continued to be aurally hallucinated. Hence it is seen that throughout her stay she has remained in the same dissociated and introverted state. On the 23rd March it was concluded that she showed typical schizophrenic apathy, appearance and mannerisms. Her thinking, as shown by her rare utterances, was composed of typical schizoid phantasies. The prognosis appeared hopeless.

Physically she was in good condition. She was of asthenic physique, having long, narrow face, chest and limbs. The hands and fingers were also long and narrow. The first and second toes of both feet were webbed. She showed slight exophthalmos and dilated pupils, but tremor and tachycardia were absent. The blood-pressure was I38/90.

The hypoglycaemic treatment was begun on the 24th March, I937 with the injection of 32 units of insulin. On the 26th with 64 units and some five hours after the injection she said spontaneously to the doctor, " I'm not going to get better. ('Of course you are.') " No, I'm not. You only say that because you know I'm balmy". On the Ist April with II2 units she had an abortive epileptic fit some four hours after the injection and was fed during the fit. The next day with the same dose she became comatose two hours after the injection

and required intravenous glucose to rouse her at noon. Thereafter she received 104 units daily and became comatose usually three hours after the injection. On being wakened she usually showed echolalia. On the 14th April the dose was increased again and from the 17th she received 120 units. After the 1st May the dose was reduced by degrees and the treatment finally ended on the 8th May.

Discussion.

During her six weeks of treatment no improvement occurred that could not be explained by the attention she received. Her habits improved and her incontinence became less marked, while she began to dress herself and take some interest in her appearance. Towards the end of the period of treatment she showed irregularity and tachycardia of the heart, which was still present even with much reduced doses.

Result.

No improvement.

Mrs. F.L. aged 27 years on admission.

She was a house-wife and was admitted as a temporary patient on the 5th March, I935, with a history of mental disorder of a few weeks duration. The anamnesis was unfortunately poor, but she was said to have suffered from "faints" in childhood, which had become less frequent but still occurred every few months in adult life.These were apparently minor epileptic fits, but none have been observed during her stay in hospital. She was always a person of uncertain temper, and would sulk for days after a minor disagreement. The maternal grandmother died at the age of 40 years from a convulsion which had followed a head injury. The maternal grandfather suffered on several occasions from delirium tremens. The patient's sister died at the age of I8 months from convulsions, while a cousin committed suicide in early adult life by "gassing" himself.

A few weeks before admission she became depressed and agitated and remained in this state until her admission, when she was seen to be in a state of semi-stupor. She did not speak but looked vacantly in front of her. For the first few months she would converse with her relatives when they visited her, but since April, I936 she has not spoken even to them. She had to be certified on theI0th March, I936. She has remained in the same semi-stuporous state throughout her stay in hospital. After a few months she began to feed herself and show comprehension of questions, even smiling when anything amusing occurred in the ward.She has never been hallucinated overtly. The facies was usually expressionless, but at times showed fleeting emotion, and occasionally an expression of perplexity was visible. She was said to have suffered much from bronchitis in childhood. Physically she appeared healthy, while there were no signs of endocrine dysplasia, nor any stigmata of physical or mental degeneracy. The blood Wassermann reaction was negative on the I0th May, I935. No glucose tolerance test was performed.

The diagnosis in this case is not easy, and the psychotic features fit in best with a diagnosis of benign stupor, according

to Hoch's description(I9). It will be remembered that Hoch described about a score of cases of stupor, studied over a period of years. He found that they made apparently complete and permanent recoveries. On a basis of these and other factors he believed that they were cases related to the manic-depressive insanity, and that the outcome was benign. He laid down a number of diagnostic and prognostic criteria, that are not, however, either definite or satisfactorily demarcate his cases from malignant or praecox stupors. Recently, Rachlin has followed up Hoch's cases (20), and has shown that of the score or so "benign" stupors, 7 are now clear-cut cases of schizophrenia, 2 are tentatively so grouped, only I is grouped with the manic-depressive group, and another in the group of psychoses with other somatic disease. Rachlin was unable to classify 2 cases as no diagnosis could definitely be reached.

Notwithstanding these facts I propose to include this case in the group of benign stupors, as it shows most of the features described by Hoch, and otherwise cannot be easily classified.

The hypoglycaemic treatment was begun on the 7th April, I937 with a dose of 24 units of insulin. On the 23rd April she was receiving I04 units. On the previous I4 days of her treatment the hypoglycaemia had usually been interrupted before she became at all deeply comatose, and interruption was always carried out if she showed any signs of awakened affectivity. On this occasion she became drowsy as usual about one hour after the injection and showed the usual sweats. At I0.30 a.m., three hours after the injection she suddenly showed inspiratory stridor, and at once became cyanosed and unconscious. The pulse was 40 beats per minute and was intermittent. She was at once given I c.c. of adrenalin intramuscularly, I c.c. of coramine intramuscularly , and 5c.c. of 25% glucose in saline intravenously. By this time, I0.32 a.m. she had stopped breathing, was pulseless and deeply cyanosed. Along with the other measures artificial respiration had been begun, and she was simultaneously fed with I50 grammes of glucose in water per the oesophageal tube. By I0.33 a.m. she had recovered, was breathing normally, her colour was good, and the pulse was regular although accelerated, I00 beats

per minute. Within another five minutes she had regained consciousness. She gave no further anxiety that day.

After two day's rest the treatment was begun again with a dose of 32 units of insulin, and on May 5th she was receiving 64 units. On that day she again showed laryngeal spasm 3¾ hours after the injection, and, as on the former occasion, while still awake. Almost at once she became cyanosed deeply, pulseless and unconscious. She was given the same treatment as before and quickly recovered. The treatment was permanently discontinued after this, as it was felt unwise to risk a further occurrence of the complication. Her laryngeal susceptibility was perhaps to be associated with the bronchitis from which she suffered in childhood.

Her 24 days of the treatment had resulted in no change in her mental condition. Even the very "shocking" experiences she had suffered had failed to alter her psychosis. (18).

Result :- no improvement.

Case I4.

Miss Violet T. aged 2I years on admission.

She was admitted as a Voluntary patient on the 28th June, I935, with a history of mental disorder of at least one year's duration. She was the younger of two sisters. There was no history of mental disorder in the family, but the paternal grand-parents were alcoholic. She was always delicate and 'highly-strung', and suffered from night-terrors as a child. She was always shy, and disliked meeting strangers. When she left school at I4 years, she said she didn't want to go to work, and so she was kept at home, where she occupied herself with needle-work. She was never sociable, and preferred home to any other place. In June of I934 she became nervous and depressed, and imagined that she was the subject of others' conversation. After a few weeks she recovered, but continued to be treated for 'nervous debility' by the family doctor. In January of I935 she began to have strange ideas, waking up at night fearing that she was about to die, or to become seriously ill, or crippled. Shortly after this she heard 'voices' and imagined that an elderly neighbour was in love with her. She continued like this until her admission to the mental hospital on the 28th June.

On admission she complained that she heard her neighbours talking about her and making unpleasant remarks about her. She said that she was in love with a doctor, and he with her, but the neighbours had kept them apart. She said she was not sure of the doctor's name, and that he had not spoken to her. She stated that it was all a drama. She added " We have both lost our memories. I mean to marry him, but my nerves are bad." In September, she believed that her mouth and bowels were stopped up, and she retained her urine unduly long. Thereafter she was faulty at times in her habits. Since then she has not changed much although the delusions have become less obvious while the aural and visual hallucinations have become more patent.

An examination on the 2Ist April, I937 showed unimpaired intellect. She was fairly co-operative and spoke freely about the 'people' who keep distracting her by their talk to her. She said that she didn't know why she was in the hospital. The aural and visual hallucinations

are the [illegible]

were the predominant features. Her occasional outbursts of violence and talkativeness are in response to 'voices'. On other subjects she is apathetic, and shows no desire to leave here, being content to stand in a corner and answer 'voices.' She shows more Paranoid traits than any others, and her whole pre-psychotic life has shown a sensitive paranoid personality. The prognosis appears quite hopeless. Physically she was a poor under-developed and under-nourished specimen. Her breasts were infantile in development. There was slight squint due to weakness of the left external rectus muscle. She was myopic and wore glasses. The blood-pressure was I32/90. She was anaemic, and there was a haemic bruit audible suring systole at the apex of the heart.

Hypoglycaemic treatment was begun on the 22nd April, with the intramuscular injection of I6 units of insulin. By the 25th she was having 40 units, and on that day she became lightly comatose about noon. From the 3rd May to the I9th May she received 32 units and this dose daily produced drowsiness and sweating I½ hours after the injection, and light coma some threehours after the injection. It was unusual for any motor phenomena to occur save a few twitches during early coma. She was habitually collapsed during late coma, showing weak, soft pulse with moderate bradycardia, and extreme pallor and coldness. On several occasions she required injections of digitalis to abolish these signs, and frequently the coma was ended early because of her circulatory weakness. On the 20th May the dose was reduced to 24 units, and on the Ist June to I6 units. With these smaller doses the same effects were produced. The treatment was ended on the I6th June.

Discussion. her eight weeks of treatment had produced no change at all in her mental condition. Deep coma is recommended for paranoid cases, and although at times she did have short periods of deep coma, on the whole her circulatory weakness forbade any prolonged deepening of the coma.

Result. no improvement occurred during or after the treatment.

Case 15.

Miss A.E. Aged 15 years on admission.

She was a factory hand, and was admitted on the 12th September, 1936 as a Voluntary patient. She was the second child in a family of seven. As a child she suffered from pneumonia on one occasion and had three fits during the illness. An uncle was said to suffer from occasional epileptic fits. Otherwise there was no history of nervous or mental disease in the family, or in the patient's own case. She was rather backward as a child, and her personality was introverted and unsociable always. She was always under-sized and myopic, and these inferiorities may have caused her some mental distress.

In March, 1936 her family noticed that she was nervous, and she had moods of laughing and crying alternately. She would laugh and talk to herself. Her mother stated that she would run about and play " just like a young child". She thought that the neighbours were going to take her on a holiday. She became s spiteful, and once attempted to injure her young sister with a knife, for no vouchsafed reason. Her conduct became worse, and she was admitted to the mental hospital as a voluntary patient.

On admission she showed well-marked affective loss. She said that she didn't at all mind being in the hospital. She described how her sister had been horrid to her in little ways, and had turned people against her. These allegations were without foundation. She said that things had always been made difficult for her at home and at work, because of her childish size and appearance. She admitted hearing "voices", and said that when at home the "voices" had ordered her to attack her sister. It will be seen that she showed affective loss, paranoid tendencies, and a flight into phantasy. One may look on the psychosis as the response of the organism to an unsympathetic environment and an "organ inferiority".

She settled down well to hospital life, and never once asked to go home. She worked well in the needle-room. Gradually she became more seclusive and reticent, while the auditory hallucinations came to occupy a large part of her waking life.

On the 20th April, 1937 a mental examination showed the intellect to be unimpaired. She amswered questions correctly, but

gave the impression that she was thinking of other things, while at times she would reply " I don't know" to simple questions. She was grossly aurally hallucinated, and even while working she continually answered "voices". She denied hearing them, however, and could not be got to discuss the nature of the "voices." She appeared to be largely withdrawn from reality, but retained enough contact to preserve personality. There is evidence of regression in her childish behaviour. She would appear to be a case of hebephrenic schizophrenia, and the prognosis would appear to be very poor.

Physically she was undersized, and had a slight degree of dorsal kyphosis. She was myopic. The menses had not been seen ever. Since admission she had put on over one stone in weight, and was now plump and well-nourished. Organically she was sound. The blood-pressure was I20/78.

Hypoglycaemic treatment was begun on the 22nd April, I937 with the injection of I6 units of insulin. On the 26th she menstruated for the first time. On the Ist May with 80 units she showed clonic twitching of eyes, face and all four limbs at noon i.e. some 4¾ hours after the injection. On that day she required to be fed by the tube although she was only lightly comatose. The above movements were observed thereafter with every injection, and as the dose increased the motor phenomena appeared earlier. On the 5th May with 96 units the clonic twitchings appeared at I0.45 a.m. and increased in intensity until at II.I5 they merged into a short major fit with clonic spasms only. She recovered from this without any assistance, and was wide awake, whereas before the fit she was drowsy. She was more communicative for about an hour, and admitted hearing voices that were nasty. On the IIth May with I20 units the usual clonic spasms appeared at II,0 a.m. and becoming more severe, at II.I0 they merged into a typical major convulsion. On this occasion she was again freer in her responses for about an hour. On the I8th she had another major fit with a dose of I04 units. Another fit occurred on the 22nd with a dose of II2 units, also on the 25th with I20 units. About this period she showed some mental improvement, in the direction of a lessening of her apathy. She once asked if she might go home soon. This improvement did not endure. Again on the 27th May she had a fit with I20 units. Thereafter the dose was increased until on the IIth June

with 208 units she had another fit some three hours after the injection. On the I6th the dose was reduced to I04 units, and even with the reduced dose she had a fit three hours after the injection. That was the last day of her insulin treatment.

Discussion.

She was remarkable for the fact that during the treatment she had almost every day marked motor phenomena, which on eight occasions merged into a major convulsion. After these fits a mental improve- was often noticeable but never lasted more than a few hours. Towards the end of her treatment the dose was increased in order to deepen the coma which was always very light. The only affect, however, was to produce irregularities of the pulse. The eight weeks of treatment had produced no significant improvement, and temporary improvement that did occur appeared to follow the fits.

Result.

No improvement.

Case I6.

Miss D.H. aged I9 years on admission.

She was a clothing machinist, and was admitted on the I2th February, I937 as a Temporary patient, with a history of mental disorder of two weeks duration. The anamnesis was fairly reliable. She was an only child, and there was no history of nervous or mental disease in the family. The patient's mother died from Phthisis on the I9th September, I936, and this is said to have worried the patient. In January, I937 she suffered from Influenza. On the 30th January she wept when she came home from work, and gave no explanation for this. She remained lachrymose that night, and the next day went into a stupor. She was admitted to the mental hospital on I2th February after some days in the observation hospital. She was always a quiet, home-loving girl, who did not make friends easily. She had been employed steadily since leaving school.

On admission she was stuporous. She spoke only once during the first few days and said that she had done wrong. However, she did not appear depressed and was apparently apathetic. After some ten days she began to talk and her responses were accurate. She had not previously given evidence of hallucinations, but now she said that she could hear her father speaking to her. She remained dull and apathetic. On the I5th April she was sent to work in the Nurses' Home, but was found about to take a bath in a private room. She said her only reason was that she liked to be clean. On another occasion she was found resting on a Nurse's bed, " because she felt tired." At this time she said that she had been sent to hospital in order to see the nice girls. It will be seen that although the stupor had quickly disappeared, yet the outlook was still uncertain. She might make a good recovery, or might drift into apathy. Hence, it was decided to apply the insulin treatment, realising that if she recovered, the recovery could by no means attributed to the treatment.

Physically she was healthy. The blood-pressure was I28/82. There were no signs of endocrine dysplasia, nor any stigmata of degeneracy, save that the skin was of the seborrhoeic type.

Treatment was begun on the 27th April, 1937 with 24 units of insulin. On the 4th May with 72 units she became excited about 1½ hours after the injection, and then was alternately excited and depressed for almost an hour. In response to questions she said, " I came here to see the nice girls. No, that's not right, is it? I never liked sweet tea, but I'ld like some now. I seem to have been here for years, I think I must have lost my memory." She then became manic in behaviour, and tried to kiss the doctor. Thereafter she was drowsy.

The next day with 80 units she became lightly comatose at 11.0 a.m. This dose was maintained and on the 7th May on coming out of coma, she said, " Why do you do this to me? It's terrible. My toes bend, and my tongue hurts. It's like torture. Just leave me a minute, I feel paralysed." The last day of her treatment was the 22nd May.

Discussion.

She was treated for some four weeks, and imperceptibly during the treatment she improved mentally, becoming more lively and exhibiting at least the beginnings of insight. She said that she had had a nervous breakdown, but was now well, and would like to go home. She said that she must have imagined hearing her father speak to her. Volition having returned after a few days treatment, she was made a Voluntary patient on the 25th May, and discharged herself on my advice on the 1st July, 1937.

It is quite possible that she would have recovered without any treatment, and in any case, she was on the road to recovery before treatment was begun.

Result :-

She showed complete disappearance of schizophrenic symptoms, with normal affective relationship, and ability to return to the normal sphere of work. However, she did not show full insight, and so will be classed as an Incomplete Remission.

Case I7.

Mrs. A.F. aged on first admission 28 years.

She was admitted as a voluntary patient on the IIth August, I936. Her paternal grandfather died in a mental hospital. She is the eldest of four children, the others being alive and well. She left school at I4 years having only attained the IVth standard, it will thus be seen that she was backward, this probably being due to congenital defect. She kept in fairly constant employment until she fell pregnant and " had to get married " in February I935. The child died of pneumonia at the age of seven months.

As a child she was quiet and seclusive, but quick-tempered and made few friends. Her married life was said to be unhappy. Three weeks before admission she became more difficult than usual and would not talk. She fancied people were calling her, and said she was going mad.

On admission she was melancholic in a shallow manner, and spoke in a peculiar clipped fashion. She was content to sit about all day, and showed no great desire to leave the hospital. Soon she began to hear voices that said " Poor dear, poor dear." She remained in this state until the 22nd October, I936, when her husband persuaded her to send in her discharge.

She was re-admitted as a certified patient on the I6th July, I937. In the interval she had steadily become worse. On re-admission she was silly and rambling in speech. She showed no appreciation of her position, and was apathetic and vaguely orientated. She thus showed typical schizoid fatuity and emotional blunting. She was aurally hallucinated and faulty in her habits.

Physically she was in good condition. The blood-pressure was I20/75.

Hypoglycaemic treatment was begun on the I0th September I937 with I6 units of insulin. The dose was increased by 8 units daily. On the I5th September she was given 5 c.cm. of Cardiazol intra-venously and responded with a convulsion. No insulin was

given that day. The insulin treatment was continued as usual the next day. Some improvement was observed on the I7th September, and she attended to her own dressing, while she began to occupy herself in reading. This improvement was maintained and consolidated during the rest of her treatment. On the 26th September with 96 units she became comatose. On the 4th October instead of insulin she was given an intra-venous injection of 5 c.cm. of Cardiazol, and responded with a fit at once. Thereafter the dose of insulin was increased to I28 units daily. On the I3th October she was given another convulsive dose of Cardiazol, to which she responded with a fit. Due to extraneous causes no treatment of any kind was given between the I5th and 20th October. Insulin was begun again on the 2Ist with I20 units, and after two days a dose of I28 units daily was given until the 4th November, when phase 3, the stabilising phase of her treatment was begun by reducing the dose to 64 units, then 32 units,then I6 units, until her treatment was ended on the 4th December, I937.

Discussion.

After the first Cardiazol convulsion she showed improvement which was maintained until, at the end of her treatment she was exhibiting a good social remission. She was rational, relevant and coherent, while she no longer showed hallucinations. Affectively she was normal, and showed a keen desire to go to her home. She was anxious to be kept occupied. Insight was present but was not complete. The prognosis in this case had appeared very bad, and her social remission would appear to be the result of her 44 days of actual treatment with Insulin and Cardiazol.

Her improvement was maintained and she was finally discharged on the 6th December I937.

From the psychic point of view she was poor material, and I shall not be surprised if her remission is of short duration.

Result.

social remission.

Case I8.

Miss M. S. aged 24 years on admission.

She was a shorthand-typist and was admitted on the 8th June, I937 as a certified patient. She was an only child, and had exhibited the classical schizoid personality all her life. In adolescence she still used to enjoy weaving phantasies of the Cinderella type, and for years before her certification was given to talking to herself. There was no history of nervous or mental disease in the family. Intellectually she was always a little above the average. A year before her admission she left her home in Wales to seek a better post in London, and shortly after this her letters to her widowed mother began to show signs of her commencing psychosis. She stayed a few months in several jobs, and was reduced to performing house-work.

Her conduct became abnormal and she was certified. On admission she was grossly aurally hallucinated, and had various grandiose delusions of a bizarre nature, e.g. she wrote letters to her mother that were addressed to the Grand Duchess Charlotte. She stated that she had appointed herself " Queen of England." She remained in the same silly condition, becoming more engrossed in her hallucinations and phantasies.

Physically she was in good condition. The blood pressure was II0/75.

On the 3Ist August I937 treatment with Cardiazol was begun with the injection of 5 c.cm. intravenously, this resulted in a fit. Similarly on the 3rd August. The following day 5 c.cm. caused momentary twitching but no fit. The next day some improvement was observable; she was less hallucinated and appeared more in touch with her environment. On the 6th 5 c.cm. caused momentary clonic spasms but no fit. The improvement was consolidated and she wrote home for the first time, and spoke intelligibly about her work as a typist. On the 7th 5¼ c.cm. caused momentary pallor and a cry of "OH!" That day she conversed rationally and normally, and expressed a desire to go home. The following day 5¾ c.cm. caused blanching and a cry only. About this time diff-

iculty began to be experienced in finding suitable veins for the injection. Her veins were naturally of poor calibre, the arms were obese while the previous injections had thrombosed the best veins. On the 9th 6 c.cm. did not cause a fit. The next day 6¼ c.cm. caused a strong fit. Similarly on the IIth. On the I4th 6½ c.cm. caused a fit. On the I6th September 6¾ c.cm. produced the sixth convulsion. On the 2Ist the same dose caused blanching and a cry only. On the 23rd she had deteriorated a little way; this probably to be associated with the fact that she had had no fits for a week, because of the difficulty in finding a vein. She was hallucinated that day. The following day 6½ c.cm. caused the 7th fit. The deterioration continued. On the 27th 6 c.cm. caused the 8th fit, and the following day she was improved. She had her 9th fit on the 29th with 6½ c.cm. of Cardiazol. The following day she was very well mentally. However, by this time all her veins had thrombosed and it was impossible to continue the treatment with Cardiazol. It will be seen that she had I5 injections that produced nine convulsions. Following the second fit she showed considerable improvement which was augmented with further fits. But after the interval when she had no fits she became worse. After the 8th fit she again improved, but this improvement was lost when the injections had to be discontinued. It is justifiable to conclude that the Cardiazol convulsions in this case exerted a specific curative effect of a temporary nature. As I believe that the Cardiazol and insulin treatments can influence the same types of case, I decided to treat her with insulin.

The insulin treatment was begun on the 2nd October with 24 units. At this period she was markedly giggly and aurally hallucinated but would respond relevantly to questions. By the 25th October she was having I04 units and on that day she became comatose. This dose was continued daily thereafter and she showed gradual improvement, slowly losing her hallucinations and mannerisms. During the hypoglycaemia she showed marked clonic spasms for about an hour each morning. These spasms began usually I½ hours after the injection. By the 20th November she appeared well mentally, being free from hallucinations and showing a normal aff-

ective response. On the 29th November the dose was reduced to 32 units and this was given daily until the 4th December, when the treatment was finally stopped. Her improvement was maintained and she was discharged on the 6th December, 1937. Because of her morbid personality a recurrence of her psychosis is likely. On discharge she was classed as an incomplete remission, but as a rather poor example of this class.

Result.

incomplete remission.

Results in the present series.

Group A. where the period of hospitalisation was less than 6 months. There were 5 cases in this group, and 4 of them made recoveries sufficient to permit of their discharge from hospital. Case 9 was a social remission probably to be attributed to the treatment. Case I6 was an incomplete remission not attributed to the treatment. Cases I7 and I8 were respectively a social and an incomplete remission probably to be attributed to the treatment. Case 5 failed to respond to the treatment.

Group B. where the period of hospitalisation was from 6 to I8 months. There were three cases in this group, but two of them, cases 4 and 6, did not complete their treatment due to intercurrent illness, or failure to tolerate shocks. The remaining case I5 did not respond to treatment.

Group C. where the period of hospitalisation was more than I8 months. There were I0 cases in this group, and of 8 who completed their course, only I remitted. This was case 3 who had an incomplete remission.

Hence my results broadly are to be considered as confirming those of other workers, but my interpretation of these results is less enthusiastic than that of most workers.(see page 81)

Those patients who remitted were of the following types:-

Case 9--- Hebephrenic type.

Case I6-- Benign stupor.

Case I7-- Hebephrenic type.

Case I8-- Paranoid-hebephrenic type.

Case 3--- Paranoid schizophrenia occurring in a cyclothymic.

General discussion.

The dementia praecox of Kraepelin was a fairly well-defined disease entity, whereas the schizophrenia of Bleuler is only vaguely defined. Hence, it will be difficult to lay down exact criteria for diagnosis and prognosis. The former question has been discussed on page 2. Regarding prognosis, the opinions of Faurbye (3I) are most important. He draws attention to the need for accurate information as to the frequency with which spontaneous recoveries occur. In his own hospital he found that the proportion of remissions was 42%, these being cases who had been hospitalised at least one year, and who had more or less recovered on discharge. The highest proportion of remissions and the best recoveries were seen in the katatonic types. He considers that his figures are an under-estimate, as the remaining patients might possibly include some who would recover later. Faurbye commends his observations as a sobering corrective to enthusiastic advocates of new methods of treatment.

Quite the best study of prognosis in schizophrenia is that of Strecker and Willey (32). These workers made a painstaking study of the life-histories of I86 schizophrenic patients. Of these, 38 recovered, and the authors studied these recoveries from various view-points. Of those 38 cases there were I8 catatonic, 8 hebephrenic, I2 paranoid and no simple types. Of those who did not recover there were 45 catatonic, 49 hebephrenic, 85 paranoid and 7 simple types. The average symptom-free period in the recovered cases was 5 years, while their average age of onset was catatonic -- 28 years, hebephrenic -- 24 years, and paranoid --35 years.

Strecker and Willey conclude that,

(I) Racial traits do not determine to any significant extent the presence of symptoms that bear a malignant aspect.

(2) Heredity occasionally exerts an indirect effect, and the previous existence of chronic mental disease in a parent may apparently create an environment from which a truly benign psychosis in the offspring may take some of its superficially unfavourable symptomatological aspects.

(3) A close study of the personality is often fruitful, and

furnishes helpful prognostic guides. It is important to differentiate between a basic and constitutionally seclusive make-up, and one in which withdrawal from socialisation constitutes a logical defence against inimical surroundings.

They add that catatonic symptoms may be due only to ingrained stubbornness, and that abnormality of personality in itself is not pure evidence of chronicity.

(4) Rarely, sensory deprivation due to organic disease may influence the behaviour during the psychosis, so that it seems bizarre and malignant, and unrelated to the affective condition.

(5) The precipitating situation must be considered in regard to its intrinsic seriousness, its somatic and psychogenic elements, its acuteness or chronicity, and the possibility of its correction. If the precipitating situation is innately significant, and the psychotic content reflects its component factors, then the psychosis may be benign, even though the symptoms in themselves have a somewhat sinister aspect.

(6) At the onset of a psychosis extraneous accidental happenings may be deeply impressed, and later elaborated into apparently malignant symptoms. Other things being equal, an acute stormy onset is a favourable prognostic sign.

(7) Ordinarily, marked inco-ordination of affect and ideation is a criterion of chronicity. But not an infallible criterion as, for example, a childhood habit of evasion may determine a distortion of the affective display.

(8) Toxicity or exhaustion may give a deteriorative aspect to a benign psychosis, for example, confusion may blunt the affective responses.

(9) Catatonia is widespread in its incidence and not peculiar to dementia praecox. When it is due to toxicity the outlook is hopeful.

(IO) The influence of the somatic factor in the production of stupor has not been fully and properly estimated.

(II) When the psychosis as a total reaction constitutes an escape, and a correction of serious circumstances in life that have brought the patient to an impasse, then the prog-

nosis may be favourable, even though the clinical aspects are not promising.

The above criteria are valid, but many cases will be found in which they do not help. The main reason for quoting these opinions is to stress that we know very little about the syndrome named schizophrenia. The fact that new treatments have always improved some cases and left others uninfluenced should teach us that in the words of Bleuler (35) " -- schizophrenia does not appear to us as a disease in the narrower sense but as a disease group, about analogous with the group of the organic dementias, which are divided into paresis, senile forms, etc."

If it does nothing else it is probable that the new treatment for schizophrenia, insulin shock, cardiazol, somnifaine narcosis, etc. will enable us to formulate a more accurate prognosis, and perhaps lead to a more satisfactory nosology.

In evaluating insulin therapy we must remember that there have been other treatments that were claimed to produce equally good results. By eliminating focal sepsis Cotton (36) claimed 86 per cent of remissions in the total psychoses.

Massive thyroid therapy, artificial pyrexia, hormone treatment, and many other treatments have claimed good results, which have not been substantiated. It would appear to me that the conclusion to be taken from these unconfirmed claims is not that the various therapies are devoid of use, but rather that schizophrenia is so mixed a syndrome that no one treatment will be a panacea. Conversely, most of these treatments will be capable of influencing some cases of schizophrenia.

Insulin therapy differs from the other therapies that have been put forward in that it has aroused wide interest and wide application. The results that have been produced by followers of Sakel on the whole are poorer than his, but are nevertheless good enough to command interest. Sakel's experience now comprises 300 cases, He divides the material into three groups: recent cases of less than six months duration, cases of less than one and one-half years duration, and chronic cases of over one and one-half years. He states " In the successfully treated cases the concept of a

full remission is very strictly defined. We have only included these patients in this group who were not only symptom-free, with full insight into their illness, and with full capacity for return to their former work,but also where one had no intuitive feeling that there might have been some change in personality!

He continues " We called those patients good remissions who were completely symptom-free and who had insight and were able to go back to their work, but where one had the intuitive feeling that there was some personality change. Under social remissions we understand the third group of patients with more or less marked improvement, but who are not however included in the group of successfully treated cases."

Sakel's results are as follows, "In recent cases the treatment has given us over 80 per cent of good remissions with capacity for work, of which about 70 per cent are full remissions. In chronic cases the results are all poorer in direct relation to the duration of the illness. In our group of cases we have had 40 per cent of remissions with capacity for work. The statistics for spontaneous remissions vary with different authors from approximately 5 to 25 per cent."(33).

Let us examine these results. In the first place, we will remember that Faurbye (page 75) states that not less than 42 per cent of cases hospitalised at least one year make a good recovery spontaneously. When it is remembered that Faurbye's patients probably received no other treatment than routine occupation therapy, it will be seen that his results compare favourably with Sakel's cases of the same duration who received the insulin treatment. It is reasonable, therefore, to conclude that in chronic cases Sakel's treatment does not achieve results that are incomparably better than those achieved by ordinary methods.

To consider now the recent cases. Very many of these cases were of very short duration. So soon as a diagnosis of schizophrenia was made these cases were treated with insulin. It is obvious that a large number of these cases would have recovered without any treatment. Those who have conducted a psychiatric

clinic for out-patients will know that there are many cases of schizophrenia who make good recoveries without any energetic treatment. Again, the insulin treatment is the first that has been applied on a large scale to recent cases, and the first treatment that has been applied for four or five hours every day, six days in the week, for two or three months. Also it is a dramatic treatment. The paraphernalia of nasal tubes, syringes, oxygen cylinders etc. must have some effect by suggestion.

Now, it is unfortunate that no control series has ever been treated concurrently with an insulin-treated series. Only then would we be able to evaluate the insulin shock therapy.

Sakel claims that the quality of the remissions obtained by insulin is far superior to that of spontaneous remissions, and indeed it would appear true that the insulin-treated patient has better insight. Here again, however, the various adjuncts of the treatment might well be responsible for this improved realisation of the illness.

It does however occur that patients do improve immediately following on the insulin treatment, and we must admit that in some cases the improvement is because of the treatment. It is my belief, however, that the efficacy of the insulin shock treatment is not definitely proven, and when we remember that the cardiazol and somnifaine treatments can produce almost an equal number of remissions with much less labour, time and expense, then it is wiser to regard insulin shock as only one of several valuable therapeutic weapons in the attack on schizophrenia.

It will be seen from case I8 in my series that a patient who had given a good therapeutic response to Cardiazol, was finally discharged after she had been treated with insulin. It is reasonable to conclude from this that the points of attack of insulin and Cardiazol are probably similar. The combined use of the two treatments appears to me to offer the best chance of a successful result. A patient who has failed to respond to insulin may begin to do so after an injection of Cardiazol.

At present there is a general tendency to believe that insulin does not cure schizophrenia, but stimulates the natural tendency to to remission. It has been suggested that there are two large classes of schizophrenic insanity (40), first, Schizophrenia proper which is an endogenous disease, and secondly, atypical Schizophreniforme conditions and psychopathic reaction types. According to Langfeldt endogenically conditioned schizophrenia has a bad prognosis. He studied I00 cases of "schizophrenia" ten years after they had been admitted to the Psychiatric Clinic. He found that 66 cases were uncured and worse, I3 were improved, 4 were cured with defects, and I7 were completely cured. However, on exhaustively reviewing the histories of all the cases he found that I4 of the I7 cured cases could not be classified as of endogenic origin, because they showed demonstrable psychogenic or somatogenic precipitating factors, plus a symptomatology differing from that in the endogenous group. Of the I7 cured cases II showed an atypical schizophreniforme symptomatology marked by strong admixtures of manic-depressive, psychogenic and symptomatic (incoherence and cloudiness) trends. Contrasted were the endogenous symptoms such as massive primary persecution ideas, sensations of influence, depersonalisation and derealisation, and massive catatonic stuporous symptoms. Langfeldt concludes that unless there is knowledge of the natural remissions and the final prognosis of the different forms, then statements of such and such a percentage of cured " schizophrenias " have no real value.

Langfeldt's work is of great importance, and appears to have been conducted with every care. Should his conclusions be confirmed it is obvious that we must view with redoubled care the claims made for new therapies. In my own series only one case made a really good recovery from an established psychosis. This was case 3, and as there had never been any sign of a remission during her one and three-quarter years stay in hospital, and as her recovery followed at once on a status epilepticus it is reasonable to consider her as an undoubted triumph for the treatment. However, there are objections to including her in the class of undoubted schizophrenics. For instance, the pre-psychotic

personality was not schizoid, indeed if anything, she was of a cyclothymic type. Also when admitted she was in a state of confusion, and during her stay she showed moods of elation alternating with shallow depression. After recovery she was euphoric. Indeed her psychosis would appear to correspond to an anomalous manic-depressive insanity having a schizoid colouring.

Hence in my series, no good recovery occurred in an established case of undoubted schizophrenia. Case I8 appears to be a constitutional schizophrenic, as her whole personality showed a retreat from the realities of life into a phantasy. But her recovery was not perfect by any means. I look on case I7 as a schizoid attack in a defective. The other remissions procured, cases 9 and I6, were respectively a poor remission, and a remission not attributable to the insulin treatment.

It is, therefore, my conclusion that undoubted endogenous schizophrenia has not been proven curable by insulin therapy.

These considerations do not deny that atypical schizophreniforme insanities may be stimulated to remission by insulin therapy. It is to be suggested, however, that the published figures for remissions are unsatisfactory inasmuch as they include cases that might well have recovered without treatment, and also cases that might well have recovered after intensive psycho-therapy alone. I believe, therefore, that the true recovery rate for insulin therapy of schizophrenic states is much below that now claimed. It is undoubted, however, that the use of insulin has given a great impetus to psychiatry, and has resulted in the production of many remissions that otherwise would not have occurred. I do not believe that it can yet be said that this treatment should be available for every schizophrenic, but as a higher percentage of remissions follows this treatment than any other treatment I do believe that some modification of insulin therapy is the best available ameliorative for schizophrenic psychoses.

It is as yet too early to state how long " insulin remissions " will last, but from Switzerland Muller reports 6.4 per cent of relapses in cases that had remitted(40)

Conclusions.

(I) Insulin therapy is not unduly dangerous.

(2) The results of treatment are not conclusive that an undoubted remissive effect due to the insulin is procurable in true endogenous schizophrenia.

(3) The results suggest that a remissive effect due to the insulin may occur in atypical schizophreniforme states, but it is still possible that in many cases the good effect might be attained by simpler means.

(4) In established cases the results are poor, and are probably little better than those due to spontaneous remission.

(5) The treatment should only be given to robust patients and unremitting observation is essential.

(6) The major epileptic fit, whether due to insulin or to Cardiazol appears in many cases to have a therapeutic effect on schizophrenic insanities.

(7) A combination of insulin and Cardiazol treatments appears more useful therapeutically than either alone.

(8) To evaluate this therapy properly, control series of treated and untreated cases should be taken, and regard should be paid to the elimination of atypical cases.

(9) One useful result of this new treatment will probably be a revision of nomenclature in the schizophrenic insanities.

Convulsive therapy in schizophrenia.

Since I934 von Meduna of Budapesth has been treating schizophrenia by the injection of convulsants. He believes that there is a biological antagonism between epilepsy and schizophrenia, and that the production of convulsions in schizoid patients is responsible for remissions. In early cases he procures remission in 80 per cent of cases. For his total cases whose duration varied from one week to IO years he was able to procure remission in 50 per cent of the cases. It will be seen that his results can stand comparison with those of Sakel. While his method requires almost no learning, and the complications are negligible. The technique:

super-therapeutic doses of Cardiazol are injected intra-venously. In small doses e.g. O.I gramme, this proprietary drug is known as an analeptic, its chemical name being pentamethylentetrazol. In the United States it is sold under the name of Metrazol. Meduna (II) advises the injection of a solution of IO or 20 per cent Cardiazol by the intravenous route. I have used the IO per cent solution which is prepared according to the following formula:

Cardiazol powder I.O gramme.
Di-sodium phosphate O.OI grammes.
Distilled water ad IO.O grammes.

The solution may be sterilised by heating for 30 minutes in a water-bath at IOO degrees centigrade. For the best results the solution should be prepared daily.

The patient should be in bed, and should be fasting. The initial dose is 5 c.cm. of the IO per cent solution, i.e. 0.5 grammes of Cardiazol. The injection is made into the veins of the elbow, and I usually use a needle of 0.90 mm. diameter. It is essential that the injection be made rapidly, and Meduna advises a rate of I c.cm. per second. In the same patient I have injected 9 c.cm. slowly and failed to produce a fit, while the following day the rapid injection of 5 c.cm. was at once successful. If the initial dose of 5 c.cm. does not cause a fit, then the following day the dose is increased by 1 c.cm. and so on. However, with increased skill it is usual to find that 5 c.cm suffice

with most patients. The epileptic fit comes on almost instantly often with a premonitory cough. Usually the fit is a typical major convulsion, but I have seen fits composed of tonic spasm only, and also equivalents in the form of furor or momentary confusion. The only attention needed during the fit is to restrain violence, and to insert a soft tampon between the jaws to prevent injury to the tongue. After the fit the patient may or not have a short period of coma, but in any case rest in bed for some five hours is advisable. Meduna advises that fits be produced twice weekly, but I am of the opinion that to stabilise any therapeutic effect, it is often necessary to give fits 4 or 5 times weekly (see case I8).

Mental improvement may occur after only a few fits, or may be delayed until I5 or more fits have occurred. It is wise to continue until at least 20 fits have been produced, even if improvement has occurred early in the course. It is Meduna's belief that the prognosis with Cardiazol is best where the patient responds with strong fits to small doses of the drug. As a generality I can confirm this statement.

As regards complications and dangers in a series of I000 fits Meduna has seen no serious complications. He quotes the results of electrocardiographic and renal investigations as follows:-

" -- the Cardiazol convulsions exert no deleterious and certainly no permanent influence on a healthy system, particularly not on the circulatory organs." In my own experience of some 200 fits, produced alone or in combination with insulin the only ill-effects seen have been transient attacks of vomiting, transient attacks of mild tachycardia, and the occasional thrombosis of the injected vein, This last complication seems to disappear as increased skill is attained.

The restraint with which Meduna has advanced his claims must receive respect, and my own experience of Cardiazol therapy leads me to believe that it has a therapeutic effect on <u>early</u> cases of <u>schizophreniforme</u> insanities probably equal to that of insulin. Its extreme simplicity of application, and its comparative safety commend it for extensive trial.

THE INSULIN SHOCK TREATMENT OF SCHIZOPHRENIA.

INSTRUCTIONS TO THE NURSING STAFF.

This treatment is to be given daily to the patients suffering from Dementia Praecox.

It has been known for many years that there is a special type of insanity which attacks young people and rapidly causes dementia, i.e. loss of the intellectual functions. Hence the name Dementia Praecox was given to this type of insanity - literally, the name means, "loss of intellect occurring in young people and occurring early in the course of the mental illness."

However, in recent years, it has been recognised that the above type of insanity may occur in people who are not young, and that the condition may continue for years, sometimes for a life-time, without causing loss of intellect. Hence the name Dementia Praecox is not accurate - and so a new name has been given to this type of insanity - it is Schizophrenia.

Schizophrenia means literally, a breaking apart of the mind into fragments, and the name is a description of the psychological process which we assume to be taking place. Normally there is a close connection between our thoughts and our emotions - if we think of something sad, then we feel sad. But the patient suffering from Schizophrenia may think of something sad, and instead of appearing sad, she may laugh. Another example of this breaking up of the mind is seen in the incoherent conversation of these Schizophrenic patients- the ideas to which they give speech seem to have no apparent connection with each other. If we tried to imitate their incoherent talk, we should soon fail - our minds are working as a whole, not as a number of disconnected parts.

Now, the above psychological explanation of Schizophrenia is no more than theory, but it will help us to understand the patient, and the treatment. And we shall further assume that the mind is split up into disconnected fragments, because the cells of the brain are disconnected from each other. We shall also assume that our treatment by Insulin if it does good, does so because the shock to the brain abolishes the disconnection between the brain

2.

cells, and allows them to resume their normal functional relationship.

THE TREATMENT IN DETAIL.

The Pancreas is a gland which manufactures:-

I. A digestive juice,

2. A substance called insulin.

Dissolved in the blood is a sugar called Glucose. The amount of Glucose present in the blood may be increased if there is not enough Insulin present in the body, and the amount of Glucose may be lessened if there is too much Insulin present in the body. Too much Glucose in the blood is called HYPERGLYCAEMIA or DIABETES. Too little Glucose in the blood is called HYPOGLYCAEMIA, and is the state of affairs which we are going to produce by injecting Insulin. The signs and symptoms of Hypoglycaemia are varied - they include coma (or unconsciousness), epileptic fits and finally death.

SIGNS AND SYMPTOMS.

Hunger, malaise, nausea, vomiting, sweating, drowsiness, twitchings, excitement, epileptic fits, coma, and finally complete collapse and death.

THE INTERRUPTION OF THE HYPOGLYCAEMIC STATE.

Fortunately, there are ways of quickly abolishing Hypoglycaemia.

I. ADRENALIN INJECTION. Normally the liver contains a substance called Glycogen. When there is adrenalin in the body, this adrenalin changes the liver glycogen into glucose, and this glucose is sent into the blood. Hence the injection of adrenalin may indirectly abolish the hypoglycaemia by raising the amount of glucose in the blood.

2. INTRAVENOUS INJECTION OF GLUCOSE. Naturally this will raise the amount of glucose in the blood, and abolish the state of hypoglycaemia.

3. ADMINISTRATION OF GLUCOSE BY MOUTH. If the patient is still conscious enough to swallow glucose, then this is fairly quickly absorbed from the alimentary tract, and reaches the blood and increases the amount of glucose in the blood.

3.

If the patient be unconscious, the glucose may still be given by means of a stomach tube.

Methods I and 2 are rapid. Method 3 is slower, but in all cases it will ALWAYS be used in addition to a rapid method.

THE PRODUCTION OF THE HYPOGLYCAEMIC STATE.

Treatment is begun by injecting 24 units of Insulin intramuscularly at 7.0.a.m. while the patient is still fasting, having had no food since the previous evening. She gets no food until dinner time. The injection is repeated at 7.0.a.m. each morning, except Sundays, increasing the dose by 8 units daily until a"shock dose"is reached. A "shock dose" is one which causes unconsciousness or coma. This coma will come on usually from one to four hours after the injection of the "shock dose". This "shock dose" varies enormously from patient to patient; one patient may become comatose from a dose of 24 units, another may require 300 units. The Insulin which will be used is of strength 80 units to Ic.c. Provided she shows no "danger signs" she will be left in coma for a variable period, on the average one and a half hours. After this period, or at any time should she show "danger signs", the hypoglycaemic coma will be interrupted and ended by one or more of the methods which have been outlined.

TO THE NURSE IN CHARGE OF THE PATIENT.

Before injecting, take the patient's pulse, respiration rate, and temperature --- if there is any abnormality, inform the medical officer, and do not inject.

Before injecting, inspect the Interruption Tray, and verify from list that every thing is there, especially stomach tube and connections, prepared glucose solution, intravenous glucose solution, sterile syringes and needles, adrenalin, etc: --- if there is any thing missing,do not inject until the omission is rectified. The glucose solution consists of I50 gm. of glucose dissolved in ½pint of warm water.

At 7.0.a.m. you will inject a dose of insulin into the muscles of the buttock. The dose you will inject will have been noted in the

4.

patient"s special report book, and signed by the Medical Officer. Use alternate buttocks on alternate days. The patient is to be between blankets, and is to have a hot water bottle.

After the injection, take and note the patient"s pulse every quarter of an hour. When the patient appears to be going into coma, inform the Medical Officer at once. He will introduce the stomach tube by the nose, and secure it to the face by adhesive tape. The mouth of the tube is to be kept closed by a wooden cork, because otherwise the acid stomach juice might fall on and irritate the skin of the face. To verify that the tube is actually in the stomach and not coiled up in the throat, or even in the lungs, the Medical Officer will remove some stomach juice by the special syringe, and test it with a piece of blue litmus paper - if the fluid removed is stomach juice it will be acid, and therefore the blue litmus will turn red in colour. Should the patient struggle at any time it is possible that the tube may become dislodged from the stomach, hence you will yourself remove a little juice and test it - if it is not acid, inform the Medical Officer, who will replace the tube in stomach. Keep the patient"s head to one side so that she may not inhale her saliva which is often profuse.

During the coma, note the patient"s pulse, respirations, and temperature every quarter of an hour. These and other observations are to be noted in the patient"s special report book, as well as charted. From the explanation given, of the nature of Schizophrenia, you will realise that the patient"s utterances may be of value in informing us of the state of her mind. Hence, especially as she goes into and comes out of the coma, you should note in the report book what she says. During the coma, you are to watch the patient ununceasingly. Especially during jerkings as the tongue may be bitten- always look out for this, and have a wooden wedge or mouth gag ready. The sweat, which is often profuse, is to be continually wiped off. NO APERIENTS, ENEMATA, DRAUGHTS, OR OTHER MEDICINES ARE EVER TO BE GIVEN EXCEPT BY INSTRUCTION FROM THE MEDICAL OFFICER IN CHARGE.

5.

DANGER SIGNALS.

These are numerous, are all due to the hypoglycaemia, and can all be removed at once by interrupting the hypoglycaemia by means of the methods outlined.

I. The Pulse. Should this go below 40 or above 140, or should the pulse become irregular, then INTERRUPT THE HYPOGLYCAEMIA.

2. Epileptic Fits. twitchings are common, as are spasms of rigidity, but a complete epileptic fit may occur, in which case, then INTERRUPT THE HYPOGLYCAEMIA.

3. Respiratory Disorders. Extreme degrees of shallow, rapid or irregular breathing may occur. In addition, Laryngeal Spasm, which causes noisy, whistling, breathing and may cause extreme cyanosis of the face sometimes occurs. In all the above cases, INTERRUPT THE HYPOGLYCAEMIA.

If any of the above danger signals appear, at once inject ½c.c. of Adrenalin intra-muscularly, administer glucose, and inform the Doctor.

If you are in doubt, inject ½c.c. of Adrenalin, administer glucose, and inform the Doctor.

AFTER SHOCK.

Now suppose the patient has been brought out of the hypoglycaemia by one of the measures described, we know that her blood sugar is normal in amount, and if she takes her dinner, she will obtain more glucose from her food, and there will be little danger of hypoglycaemia.

Unfortunately, for various reasons, later in the day the blood sugar may fall in amount again, and the hypoglycaemic state may recur. This is called after-shock, and must be watched for; the patient must be under observation every minute of the 24 hours. If she should complain of feeling ill, should twitch, have a fit, become drowsy or unconscious, then give ½c.c. of adrenalin, administer glucose, and inform the Doctor.

PSYCHO THERAPY.

As the patients come out of coma, they are usually co-operative and often informative, at these times especially, it behoves the nurse to comfort and converse with the patient.

6.

TO THE NIGHT NURSE.

The patient must be watched throughout the night, because after-shock may occur during sleep. If the breathing changes in character, becoming louder, or shallower, or rapid, or slow, if she twitches, or sweats profusely, or if she appears to be comatose, then inject ½c.c. Adrenalin, administer glucose, and inform the Doctor. If you are in the least doubt as to whether the patient is sleeping normally, or is in a coma, then attempt to waken her. If she is in coma she will not waken, and you will treat her for after-shock.

For your benefit, a list is provided for you describing the appearances of each patient during hypoglycaemia.

When you come on duty inquire from the day staff as to the behaviour and condition of the Insulin patients.

If you require the Medical Officer --- between 7.0.a.m. and 10.30.p.m. telephone the Hall Porter -- 42; between 10.30.p.m. and 7.0.a.m. telephone Male Ward I -- 01, and ask that the Medical Officer be informed.

LIST OF DRUGS AND INSTRUMENTS.

Atropine Solution.

Adrenalin Solution.

Insulin 80 units per c.c.

Glucose for intra-venous use.

Glucose powder for oral use.

Coramine ampoules.

Glass syringe for removing gastric juice.

20 c.c. Syringe.

IO c.c. Syringe.

2 c.c. Syringe.

Needles - various.

Oesophageal tubes - sizes IO and 8.

Glass connecting tubes.

Blue litmus paper.

Glass funnels and clip.

Enamel bowls.

Jug to hold prepared glucose solution.

Mug " " " " " .

Elastoplast.

Mouth Gag.

Methylated Spirit.

Olive Oil.

Cotton Wool.

Gauze.

Hand towel to be used as tourniquet.

Lumbar Puncture Needle.

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