

PROLONGED NARCOSIS IN MENTAL DISORDER

By

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INTRODUCTION

The subject of this thesis is entitled, "Prolonged Narcosis in Mental Disorder." By this term, I mean the artificial induction of continuous sleep lasting up to two or three weeks, by the repeated administration of sedative drugs, the desire being to obtain as constant and as steady a degree of unconsciousness as is compatible with the physical well-being of the subject. The idea of carrying out work of this nature first occurred to me two years ago, while I was a member of the Medical Staff of the Glasgow Royal Mental Hospital. I had been reading various articles on the subject by other workers, and was struck by the marked discrepancy in the results which had been obtained in different series of cases.

Thus, one writer would report a high recovery rate and a rarity of complications, whereas another would indicate the poor response he had obtained from the treatment and the dangers and serious complications which were involved. It was with the idea of discovering the exact state of affairs that in October 1934 I decided to carry out a course of narcotic therapy in a series of cases at Gartnavel. From then until December 1935, 32 patients were treated, with results which I shall describe later.

The first question which arose was the choice of a

narcotic drug. With a few exceptions most of the previous work had been carried out with derivatives of barbituric acid, and of these the one decided upon as most suitable for use was somnifaine. This preparation is manufactured by Hoffmann La Roche, Limited, Bowes Road, London. It was given by the intramuscular route as, when injected subcutaneously, sloughing of the tissues was liable to occur, and oral administration could not be relied on in an unconscious patient. For that purpose somnifaine is made up in 2 c.c. ampoules, each of which contains in an alcohol glycerol aqueous solution the diethyl amine salt of 0.2 gm. diethyl barbituric acid and 0.2 gm. of allyl isopropyl barbituric acid. The reason for choosing this drug was chiefly its convenience and ease of administration. The solution is ready sterilised, and intramuscular injections can be given to a sleeping patient without disturbing him, or causing unnecessary discomfort.

The patients were chosen arbitrarily and include examples from the manic depressive, melancholic, schizophrenic and psycho-neurotic groups. A thorough investigation was carried out in each case before, during and after the narcotic period, in order to find out the dangers involved, the response of the patient and the results which could be obtained in the various types of mental illness. The series is certainly not a large one, but it helps to give some idea of those factors.

It is intended to describe the work which has been carried

out previously, indicating the different drugs used, the complications which occurred and the results which were obtained. My own findings from these aspects will then be reported, describing in detail the exact technique used, the abnormal conditions met with and the conclusions which were drawn. A case summary of each patient is included, as I consider that mental disorder is essentially an individual affair, with consequent individual reactions.

The treatment of mental illness by subjecting the patient to a prolonged narcosis of varying duration by means of different drugs has been carried out at various times during the last fifty years. According to Hinsie and Katz⁽¹⁾ opium was used extensively in 3- to 6-grain doses, twice daily for several weeks, and ether and chloroform were favourite remedies about the middle of the nineteenth century. In 1882 Greisinger⁽²⁾ described the results which he obtained following the administration of alcohol, opium, ether and chloroform in different types of mental illness. He stated that,

"Complete and rapid recovery has occurred in several cases of recent active melancholia, but numerous observations have shown that frequently a temporary remission, sometimes a complete lucid interval, follows the awakening from the narcotic effects of chloroform. Soon afterwards the morbid symptoms return."

In 1900 MacLeod⁽³⁾ treated 9 cases by the administration of large doses of potassium bromide. He called the condition, "the bromide sleep," and by it he meant a state lasting from five to nine days in which the subject sleeps day and night and cannot be roused. To begin with, he gave the patient 120 gr. every two hours during the first day until one ounce had been

given. The full effects of the drug did not manifest themselves until twenty-four hours after the last dose, and when developed they often continued for several days. The patient was allowed to sleep, and when he showed signs of rousing, further 2-drachm doses were given, but when drowsiness was profound, administration was withheld for twenty-four hours. The patient was kept under the narcosis from five to nine days. He had 2 deaths from the treatment, one from pneumonia and one from a septic parotitis. The former mortality occurred in a morphine addict and the latter in an acute delirious mania. His remaining 7 cases showed improvement following the treatment. However, he stated that the production of artificial sleep by hypnotics left much to be desired :-

"If future experience goes to show that this bromide sleep can be induced without danger, it ought to prove a powerful and effective means of dealing with all maladies of the nervous system which require a profound and long rest to the higher centres."

In the same year Ragg⁽⁴⁾ treated a manic depressive by intensive narcosis with sulphonal and potassium bromide. The treatment was continued for ten days, following which the patient emerged rational in his talk and restful. After the treatment, he remained perfectly normal.

In 1901 Wolff⁽⁵⁾ treated 3 cases of acute confusional insanity, using intravenous trional in repeated doses for twelve days. Two of his patients recovered and one showed temporary

improvement. Later on he published the results of 3 further cases, one of which was successful.

Again in 1916 Ulrich⁽⁶⁾, at an epileptic institution in Zurich, reported that he had successfully treated 10 cases of melancholia by the use of a salt-free diet and bromide pushed to the point of marked intoxication.

Following the introduction of veronal in 1903 intensive research has been carried out to find the perfect barbituric derivative. During the last decade prolonged narcosis has been studied much more fully, and workers seem to have confined themselves mainly to the use of these barbital derivatives, the chief ones being sodium amytal (sodium iso amyl ethyl barbiturate), dial (diallyl, barbituric acid) and somnifaine. They are all closely related in their pharmacological effects, each worker having his own individual preference. Horder⁽⁷⁾ feels that barbiturates mark an advance in our available narcotics as the dosage is more exact and the effects more constant:

"The number of patients possessing tolerance is very small, and I think that the ill-effects adduced against their use have been exaggerated."

The classic experiment was that of Klasi⁽⁸⁾ in 1922. He published the results of treatment by somnifaine of 26 schizophrenics. In some of the patients two or three courses of the drug were given: 8 of his patients were so much improved that 6 were discharged and 2 were transferred to a quiet ward. Four left improved two months after the completion of their course

Eleven were unchanged and 3 died during treatment. The patients selected were all restless and excited, and the prognosis in each had been considered poor. He gave up to 8 c.c. of somnifaine daily and each course lasted seven days. He describes 3 deaths which occurred while the patient was receiving treatment: one was due to broncho-pneumonia, a second to nephritis and a third to sinus thrombosis.

In 1925 the results of 146 cases which had also been treated by somnifaine at the Provincial Hospital, Santpoort, were published by Dozy.⁽⁹⁾ Three deaths occurred during the series, 2 of them from influenza. He stated that it was important to exercise every care during the first three days, to investigate for contra-indications and to beware of times when influenza was prevalent. Müller⁽¹⁰⁾ in 1925 used somnifaine in a series of 22 cases, and two years later employed liquid dial intravenously in a further group of 33 patients, producing narcosis for ten-day periods. His most satisfactory results were with manic patients. Two of the former group died as a result of treatment. He stated that Klazi had been far too optimistic and that, while the induction of such a state as twilight sleep lasting about a week had proved of value, the use of somnifaine or its production had definite dangers. He felt that this drug should be used only as one of the many available hypnotics and that suitable combinations of these should be tried according to the requirements of each individual case.

In 1924 Dawson and Barkas⁽¹¹⁾ at the Maudsley Hospital treated 18 cases of mental illness by giving somnifaine intramuscularly and intravenously over a period of seven to ten days. Eighteen cases were treated. In 5 of these the course had to be curtailed, 4 on account of cardio-vascular weakness and one as a result of necrosis developing round the site of injection. They came to the conclusion that when treatment could be continued, a twilight sleep was maintained; that any improvement which followed was quite transitory; that considerable risks were involved, and careful observation of the heart was necessary to avoid fatal complications.

Intensive bromide therapy was revived again in 1926 by Wright⁽¹²⁾ who treated 85 patients with this drug. He did not aim at producing definite unconsciousness, and indeed he encouraged his patients to walk about during their course. When they got ataxic the drug was temporarily stopped. He felt that by this means complications were decidedly lessened. With some of his patients the best results were obtained by the administration of large doses, up to 210 gr. daily for a few days, while with others the best results were found with smaller doses of 90 gr. per day. He felt that there was no rule as to dosage and that daily observation was the best guide. Complications with these large doses differed entirely from those met with when small doses of bromide were given over a prolonged period. Apart from a transitory erythema, rashes did not occur. His

technique differed, therefore, from other workers; he arrived at a deep bromide intoxication rather than a profound sleep.

In 1927 Oberholzer⁽¹³⁾ published his results following 186 courses of treatment on 92 cases at the Zurich Clinic between 1922 and 1925. He dealt with a wide variety of mental states and treated them by somnifaine, luminal and sodium luminal. A number of his patients received several periods of narcosis. He obtained marked success with his manic cases, but other types which showed regressive changes were unaltered by the treatment. He felt that its therapeutic significance had in many cases been overlooked and its dangers overestimated, with the result that it had fallen into disrepute.

In 1928 Lutz⁽¹⁴⁾ at the Burgholzi Clinic in Zurich used a combination of dial, morphine and hyoscine to produce continuous sleep.

In a review of the treatment of schizophrenics in 1930, Bleuler⁽¹⁵⁾ recommended a narcosis of from eight to twelve days, with somnifaine or other narcotic, in order to bring them more into touch with the physician and more amenable to other treatment.

Following the experiments with this drug by Zerfas⁽¹⁶⁾ at the Indianapolis City Hospital, Bleckwenn⁽¹⁷⁾ in 1930 treated 50 psychotics with intravenous sodium amytal. In some only one injection was given, but in others repeated daily doses were administered for several days: 150 injections were given in all.

The dosage varied - according to the reaction of the patient - from 7 to 15 gr. He found that every patient fell into a profound sleep which could be maintained over a prolonged period: some of his patients were treated daily for eight to ten days. He stated that it was extremely valuable in excited mental states and with its use more rapid recoveries could be anticipated in acute manias, and lucid intervals might occur in some catatonics.

Beginning in 1929 Bohn⁽¹⁸⁾ had treated 60 cases of varying types of mental illness also by means of intravenous sodium amytal. The number of injections varied from one to 10. He states that sodium amytal will rapidly and safely produce deep narcosis in a disturbed mental state; that it is comparatively easy to administer; that it will save lives in acute exhaustion, and that its use makes the patient more tractable.

The same drug was used by Murray and Burns⁽¹⁹⁾ in 1930-31, in a series of 24 patients at the Hudson River State Hospital, and was again advocated by Palmer and Paine⁽²⁰⁾ in their paper the following year. They kept their cases in a continuous sleep for from seven to ten days, with the exception of two half hourly intervals for the purpose of nutritional needs and evacuation. Before the end of the narcosis the patients were transferred to a bright, cheery room, in the hope that the psychological effect of awakening in different surroundings would be beneficial.

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Dial was used by Magnus, Read and Nerancy at the Elgin State Hospital in 1932, to produce narcosis for eight- to ten-day periods. They treated 38 cases by giving them $4\frac{1}{2}$ gr. of dial by mouth, four-hourly until consciousness dimmed, and then continued by giving 3 gr. rectally at intervals sufficient to keep the patient deeply asleep. As a result of their treatment 14 of their cases showed marked improvement, 9 had lucid intervals and 2 died, one from broncho-pneumonia and the other from uraemia. The remainder of their 38 cases showed no change.

In 1933 Meerloo⁽²²⁾ published the results of 179 courses of treatment which had been administered to 175 patients from 1927 to 1928. Somnifaine was used with beneficial effects in 20 per cent. of his cases.

Kooy⁽²³⁾ At Cape Town treated 133 cases by means of somnifaine, and obtained a cure in 52. He endeavoured to secure sixteen to twenty hours' deep sleep per day, with a semi-conscious state for the remaining hours.

Perhaps the most intensive piece of work in this country has been done by Strom-Olsen⁽²⁴⁾ at the Cardiff City Mental Hospital. He carried out 128 courses of treatment on 107 cases of mental disorder. In 117 of these he used somnifaine, in 9 veronal, and in 2 dial. He instituted important researches into the toxic aspects of narcotic therapy, and these will be discussed later.

Hackfield⁽²⁵⁾ in 1932 subjected 10 psychotics to a com-

ination of prolonged narcosis and artificial pyrexia. He included in his group 9 depressives and acute schizophrenic reactors. To commence with, his patients were given 3-to 6-gr. phenobarbital orally each night and each morning increasing doses of typhoid vaccine, daily for five days. Following that sodium phenobarbital was administered intravenously in 3-to 4-gr. doses three or four times per day. After eight to twelve days the narcosis was discontinued, and the patient received a further course of typhoid vaccine. He found that the patient reacted gradually, and by the seventh day after the conclusion of narcosis, became co-operative. In all his cases there was a predominant affective element, and in this type he feels good results can be obtained.

Gronlund⁽²⁶⁾ in 1935 took 10 cases which had been failures previously following narcosis with sodium barbital and sodium amytal, and subjected them to an intensive sedation, using secondary butyl ethyl barbituric acid which, she considered, was less toxic than amytal and could be given in larger and more frequent doses. Three of the patients were excited, 3 depressed and 4 agitated. She came to the conclusion, however, that the effect obtained did not indicate that it was of particular value in altering the trend or behaviour of psychotic patients. The excited subject improved; one depressed case benefited, but the agitated ones remained the same.

The above paragraphs indicate something of the work which

has been done. The results and conclusions of those authors will be mentioned under the respective headings.

TECHNIQUE.

Klasi's method was to begin treatment by giving the patient gr. $\frac{1}{4}$ of morphine and gr. 1/100 of hyoscine, followed in half an hour by 4 c.c. of somnifaine injected deeply into the muscles of the leg, as he pointed out that subcutaneous injection gave rise to sloughing. He emphasised that it should be used strictly according to his method since by this means a deep sleep could be ensured from the very beginning. This method may certainly be of service in very apprehensive or agitated patients, or in those who are excited and impulsive, but on the whole there seems little advantage to be gained. Furthermore, by giving the patient an injection of somnifaine at the very commencement, one can see exactly how he reacts to the drug and whether any idiosyncrasy or tolerance is present. If the patient has already been put to sleep by another drug, this is, of course, impossible. A number of writers - among them Magnus - commence by giving $4\frac{1}{2}$ gr. of dial by mouth, four-hourly till dimming of consciousness appears, and then continuing by the rectal or intramuscular route. In this way the patient is spared a possibly painful injection until he is well-narcotised. During treatment Magnus also gave 2,400 c.c. of physiological saline, with 60 gm. dextrose, rectally in the

twenty-four hours.

In order to avoid complications, a carefully regulated technique is all-important. In the present series the patients were selected not on account of any specific mental illness, as it was desired to ascertain the results experimentally in the different reaction types. In a few cases the relatives requested that the treatment should be given. When it was decided to subject a patient to treatment, the relatives were consulted and it was pointed out to them that a possible danger existed, and their written permission was always obtained beforehand. The cases were selected in pairs as, from a nursing point of view, this was found more suitable and more economical since one nurse could conveniently look after both patients in the one room at the same time. A careful physical examination was made in each case, a note taken of the blood pressure, the condition of the heart and pulse; the evidence of any inflammatory condition in the lungs - such as bronchitis; the general nutrition of the patient, and signs of toxaemia as indicated by the condition of the skin, eyes and tongue. These findings were then carefully correlated, and any patient who showed a definite contra-indication to treatment was not included.

A detailed examination was also made of the urine. The daily output was recorded, as was also the presence of albumin, sugar, acetone or bile, in addition to any evidence of inflammation of the urinary tract. In a number of the cases a white

cell count was done. If this was high, treatment was withheld until an adequate explanation could be found for the disturbance. In a few cases also a bio-chemical estimation of the serum calcium, phosphates and blood urea was made. If the physical condition was satisfactory, the patient was commenced on preliminary treatment which was carried out during the week preceding the commencement of the narcosis proper. During this stage adequate elimination was insisted on. The patient was, if possible, made to drink large quantities of fluids daily. The bowels were opened by ordinary laxatives such as cascara, supplemented by hydrogen peroxide enemata given daily, or on alternate days according to the state of the bowels. During that week also the patient received the routine administration of glucose and insulin, in view of the findings of Strom-Olsen⁽²⁷⁾ which will be referred to later. One to $1\frac{1}{2}$ oz. of glucose in lemon water by mouth plus 10 units of insulin by hypodermic injection were given thrice daily during the period.

In co-operative patients it was pointed out that the course was being carried out in an effort to relieve their symptoms, and that a very good result could be hoped for, with the purpose that this reassurance might have a psychological effect after they emerged from the narcosis.

On the day of commencement, the patients were transferred to a small room in a quiet part of the Hospital. The nursing arrangements were in charge of a well-qualified nurse who had had

experience in both general and mental cases. The room was kept darkened, but well-ventilated and at an even temperature. The diet during the course was entirely fluid, such as milk, custard, lemon water, egg flips, etc. The reason for this was first, that feeding is easier with fluids; and second, that since dysphagia is occasionally present, the danger of choking is much less than with solid food. There were no regular times for feeding the patients as long as sufficient nourishment could be given in the twenty-four hours. Opportunity was taken during the periods when the patient was due an injection, and therefore less deeply asleep, to feed him, attend to his skin, bowels and so forth. As much fluid was given as the patient could take; in this way a diuresis was promoted and toxic products eliminated. With each feed glucose was given until at least 6 oz. were taken in the day. In addition, 10 units of insulin were injected thrice daily throughout the whole course, at feeding times. In a number of cases difficulty was met with in feeding the patient, and in 3 instances resort had to be made to tube-feeding.

As regards the dosage and the frequency of administration of the drug, this depended on two things: firstly, the reaction of the patient, and secondly, his physical state. Bleckwern⁽¹⁷⁾ found that the dosage was individual and that in the exhaustive mental state a smaller dose is effective and less hazardous. In his patients the second and subsequent doses were determined by the duration of response to the initial dose, and whether

they took sufficient nourishment during the drug's effect :-

"Repetition of the dose is necessary in order that the desired state of sleep and relaxation may be maintained over a longer period of time."

An effort was made to keep the patient more or less continuously asleep, provided sufficient nourishment was being given and the physical state remained satisfactory. For example, if, after 4 c.c., a patient was still restless and noisy, a further 2, or even 4 c.c. could be given in the twenty-four hours. On the other hand, if a patient exhibited any complication which might prove serious, the dosage was reduced and in some cases the drug was withheld for a short period, or even discontinued. There were no stated times for the injections.

At the commencement, 2 c.c. of somnifaine without preliminary sedative administration were injected deeply into the muscles of the buttock or the lateral aspect of the thigh. The reactions to this first injection were carefully noted. If the patient did not fall asleep in four hours and no idiosyncrasy was observed, a further 2 c.c. were given. As a rule after the second injection the patient fell asleep, and on his showing signs of wakening, a further dose was administered. This procedure was continued. The patient was, therefore, kept asleep with as little of the drug as possible, the injection being given whenever there was evidence of lessening of the narcosis. The dosage was an individual matter, and the responses

of the patients differed widely. In a few even with from 6 to 8 c.c. per day, a deep sleep could not be maintained. They remained restless, confused and noisy, yet at the same time, were deeply under the influence of the somnifaine. As will be seen later, a number of these showed very satisfactory results. In no case were more than 8 c.c. given in the twenty-four hours. Constipation was rigorously guarded against during treatment by means of hydrogen peroxide enemata daily, or on alternate days. The urine passed each twenty-four hours was collected, measured, and fresh specimens were examined carefully for abnormal constituents. The temperature, pulse and respirations were recorded every four hours, and note was made of the blood pressure daily, or oftener if there was any indication of cardio-vascular failure.

Certain complications were kept in mind as being indicative of temporarily terminating the course, viz. :-

- (1) A marked and progressive fall of the blood pressure
- (2) A rise of temperature to over 100°F.
- (3) Marked ketonuria or albuminuria
- (4) Persistent vomiting
- (5) Insufficient nourishment: (this could be helped by tube-feeding unless vomiting were present)
- (6) A marked diminution in the urinary output
- (7) Evidence of too deep narcosis, apparent by extreme drowsiness, dusky complexion and shallow breathing
- (8) If respiratory infection, such as influenza or pneumonia developed in the ward.

If no complications arose, the treatment was continued for fourteen days. On the other hand, if the drug had to be withheld temporarily as the result of a complication, and the

patient's condition became satisfactory again and continued so, the course was prolonged by that period.

The exact duration of treatment has varied with different workers using somnifaine. Klasi gave a course of seven days, Dawson and Barkas, four to seven days, Kooy and Strom-Olsen, fourteen days and Oberholzer and Müller also gave up to fourteen days.

Palmer and Paine advise turning the patient on to his side to prevent the tongue from falling backwards.

A nurse was in constant attendance night and day, and was instructed to report any abnormal signs immediately. She kept note of the movements of the bladder and bowels, and gave frequent attention to the mouth and back. The position of the patient in bed was changed from time to time.

After the last injection had been given no alterations were made in the nursing arrangements for a further two weeks, and the routine measures which had been carried out during the narcosis were continued for that period. These included the administration of glucose, from 4 to 6 oz., with 30 units of insulin daily; the administration of abundant fluids and careful attention to the bowels. The hydrogen peroxide enemata were continued if necessary, being further supplemented by the use of laxatives. The urine was still measured and tested daily, the temperature and pulse were recorded four-hourly and daily readings were taken of the blood pressure. Each patient was

carefully observed while he was emerging from the narcosis, and a watch was kept for complications during that period. Frequent note was made of his mental state and as soon as his contact with environment was sufficient, a modified psychotherapy was commenced; and this procedure was continued daily until it was clear what the ultimate result would be. Rest in bed was insisted on for four or five days, or longer if the patient was weak or showed post-narcotic complications. At the end of that period some form of occupational therapy was commenced, first in the ward and later in the occupational centre.

Frequently, the relatives requested to be allowed to remove the patient from the Hospital, and indeed, this was encouraged, provided it was known that he would be well-looked after and not taken back to the environment in which the psychosis had developed. The friends were advised regarding these points and also the procedure with respect to therapeutic occupation and general physical attention.

Dangers and Complications resulting from
Prolonged Narcotic Therapy.

Since this form of treatment has been evolved, workers have from time to time emphasised the dangers which may result from it. A number of deaths have been described as being directly due to the action of a narcotic drug when given in

repeated doses over a prolonged period. Thus MacLeod in 1900 had 2 deaths during intensive bromide intoxication, one from pneumonia and the other from a septic parotitis. Both these patients had been in a poor physical condition before the treatment had been commenced, the former being addicted to morphine and alcohol, and the latter, a delirious mania in an extremely toxic condition.

Three deaths occurred in Klasi's series of 26 cases, one from broncho-pneumonia, a second from parenchymatous nephritis and a third from sinus thrombosis.

In Müller's first group of 22 cases, using somnifaine 2 deaths occurred. Two years later he treated 33 cases with liquid dial without any fatal complications. He warns emphatically against any attempt to produce an uninterrupted sleep, on account of the changes which occurred to the breathing and to the blood pressure. He was of the opinion that the induction of such a twilight sleep lasting about a week, had proved of sufficient value to be accepted as a useful form of treatment. The utilisation of somnifaine for its production had dangers. The death-rate recorded was 5 per cent. :-

"This drug should be used only as one of the many available hypnotics, and suitable combinations of these should be tried according to the requirements of each individual case."

He considers that death may occur from 3 causes :-

- (1) Cardiac failure with collapse
- (2) Respiratory disease
- (3) Nephritis, thrombosis and other conditions.

Dozy had 3 fatal cases out of 146 patients treated. He stated that it was important to exercise every care during the first three days, to investigate for contra-indications and to beware of times when influenza was prevalent.

In Kooy's series of 133 cases, death occurred in 5 of the subjects, 3 manic depressives and 2 confusional states. All 5 were in an acutely excited, toxic and exhausted state before treatment was instituted, and one of them suffered from pulmonary tuberculosis. He says that,

"It is difficult to estimate how far the somnifaine is responsible for these deaths, as one sometimes loses one's cases of exhaustion psychosis whatever one does."

Magnus had 2 deaths in 38 cases treated by dial, one from broncho-pneumonia and the other from uraemia.

Strom-Olsen reports 2 deaths in 128 treatments, both as the result of cardiac failure due to somnifaine intoxication. In each of these cases treatment had been carried out without the simultaneous administration of glucose and insulin. In 42 of his cases in which glucose and insulin had been administered from the beginning, no fatality occurred.

Sudden deaths may occur as described by Müller: an eighteen years old girl who had been given 4 c.c. of somnifaine collapsed and died two hours later.

Meerlo states that cases of barbital idiosyncrasy have been repeatedly recorded in the literature. The syndrome which

occurs in these cases consists of fever, anuria, nystagmus and sometimes erythema and increased excitability. He feels that, in cases where symptoms of barbital intoxication have developed, it is inadvisable to stop the drug suddenly as this may bring about serious consequences. A sudden abstention produces symptoms of its own. Of cardiac tonics he prefers those which promote diuresis, such as digitalis, caffeine and coramine: as emergency measures he recommends lumbar puncture, caffeine and coramine injections and the subcutaneous infusion of isotonic glucose solution. He states emphatically that Klasi's rule of putting the patient to sleep directly by means of a generous dose is dangerous :-

"Any patients we do not know may be expected to show unforeseen idiosyncrasies, and even in the case of a known patient a totally different reaction may be looked for in each successive course of treatment."

*The first three days should be used as a testing-period, in which the personal reactions of the patient may be discovered.

In the present series of cases one death occurred (Case 18). The patient, an agitated melancholic aged forty-six, had a history of four years' duration and had been in a very toxic state before treatment was commenced. From time to time she had suffered from septic complications, viz., cellulitis, boils and an axillary abscess. These had been adequately treated. Her general physique was poor, she took her food

intermittently and she was underweight. On account of her symptoms being so long-standing, it was considered justifiable to carry out treatment on her in the hope that at least a temporary improvement would result. For four weeks an endeavour was made to de-toxicate her by giving abundant fluids, administering yatren (Bayer) 24 gr. daily, frequent bowel lavage with hydrogen peroxide, and by glucose 2 oz. and insulin 10 units, thrice daily over that period. When no septic complications were manifest and when her general condition had improved, the first injection was given. She remained restless and resistive and ten hours later a second dose of 2 c.c. was given. Following that she passed rapidly into a deep comatose state from which she never emerged. Eighteen hours after the second injection her temperature, pulse and respirations rose rapidly, and examination revealed a commencing pneumonia at both bases. She became intensely toxæmic and died four days later. An autopsy was refused. It was difficult to say whether the somnifaine actually produced the chest complication, or whether the course was started while she was incubating the disease. The latter period varies considerably from a few hours to several days, but the marked idiosyncrasy which she showed to the drug seems to me to have been caused by the presence in her body at the time of the pneumonic toxin. This view is confirmed by Meerloo who states that patients suffering from a febrile illness react less favourably to veronal :-

"It is possible to point out certain clinical analogies as indicating a connection between influenza, for instance, and increased barbitatal susceptibility."

He quotes the case of a psychotic who had been receiving 10 c.c. of somnifaine per diem. A second course of narcosis was commenced a short time later and after 4 c.c. had been administered, severe symptoms of intoxication resulted. No signs of physical disease had been detected beforehand, but an influenza epidemic was in progress at the time.

These findings go to prove that the course must have been begun during the incubation period, and the extreme intoxication which developed after 4 c.c. had been given was due to the presence in the body of an infective toxin. As she had been in the habit of receiving veronal and other barbituric hypnotics and showed at no time abnormal reactions, the possibility of an inherent idiosyncrasy can be dismissed. Upon reflection, one feels that this patient should have been classed as a definite contra-indication to prolonged narcotic therapy, but she was one of those apparently hopeless cases in which one is anxious to try anything which holds out a prospect of improvement.

Magnus found that complications were most common on the third and seventh days, and he decreased his dosage at these times.

Apart from the comparatively rare occurrence of a fatal issue, less serious complications are met with during the course of prolonged narcosis and may involve practically any part of the body. For the purpose of discussion, it will be convenient to

divide them into various groups.

(a) Cardio-vascular changes.

The first group are those which bring about alterations in the cardio-vascular state, and which are so frequent and may cause a good deal of worry on occasions during treatment. The chief changes which occur are in the pulse and blood pressure. Gruber and Roberts⁽²⁸⁾, experimenting on dogs, found that barbiturates caused an increased coronary flow, dilatation of the cerebral blood vessels and a fall in the blood pressure of more than 40 mm.

Meerloos feels that the danger to the heart is greatest at the beginning of the narcosis because of the sudden alteration in the vegetative system on which barbitals have a specific action. In cases where the heart is slightly affected, but compensation is good, a carefully administered treatment must be undertaken.

Dawson and Barkas point out that a rapid, feeble pulse occurred in several of their cases, and 4 of their 18 treatments had to be stopped on account of this complication.

Ettleson⁽²⁹⁾ found that during sodium amytal narcosis the pulse-rate increased on an average of 15 beats per minute and its force became weaker. Magnus, Read and Nerancy also describe a rapid pulse as a frequent occurrence, and Meerloo expresses the same view.

Wagner⁽³⁰⁾ in his discussion on the pharmacological

action of barbiturates, states that in practically every case the pulse-rate is slightly increased when these drugs are given in large or frequent doses.

Probably even more important than the changes in the pulse-rate is the drop in the blood pressure which occurs. Bleckwenn found a fall ranging from 20 to 88 mm. systolic, and a diminution in the diastolic pressure to a much smaller degree, from 2 to 30 mm. After the intravenous injection of sodium amytal the systolic pressure continued to fall for more than 30 minutes. Ettleson, using the same drug, met with a fall in the systolic pressure of 30 mm. and in the diastolic of 15 mm. Magnus found a gradual reduction in the systolic blood pressure averaging about 30 mm. during the first few days, returning to normal after the conclusion of treatment. Kooy, with somnifaine, had similar results, and stated that the heart action and blood pressure required special supervision. He usually prescribed digalen in one c.c. doses. Strom-Olsen met with an average fall of 14 mm. in the systolic pressure, the drop occurring as soon as the patient was under the influence of the narcotic. He believes that the fall is due to a toxic action on the heart muscle and also to a paralysis of the vaso-motor centre in the medulla. In 2 of his schizophrenics, collapse occurred on the third and fourth days respectively and was associated in both with marked drowsiness, feeble pulse, vomiting, oliguria, ketonuria and leucocytosis. In neither had glucose and insulin been given. The symptoms cleared up in both after cessation of

the somnifaine. Since introducing routine glucose and insulin administration, no symptoms of collapse occurred in his cases. He considers that the condition is not due to any cumulative effect of the drug, but rather depends on individual sensitiveness.

An increase in the pulse of from 10 to 20 per minute was the normal occurrence during the first two to three days of narcosis in the present series of cases. A routine examination of the blood pressure was carried out daily, or more frequently if there was any indication of collapse taking place. It was found that in every case under treatment the blood pressure fell within the first twenty-four hours from the commencement of the narcosis. This reduction varied considerably from case to case and it was noted that in those patients who had exhibited a hypertension beforehand, the diminution was most marked. Thus in Case 8 where the original pressure was 165 mm. systolic, 100 mm. diastolic, a fall to 135 mm. systolic, 90 mm. diastolic took place within thirty-six hours after the first injection, and a further drop of 5 mm. in the systolic pressure occurred during the next day. On the other hand, in cases where a hypotensive state existed the fall, though still apparent, was not so marked. Thus in Case 14 where the original pressure was 100 mm. systolic, 60 mm. diastolic, a diminution occurred to 95 mm. systolic, 52 mm. diastolic on the second day. It is noteworthy that in every case the blood pressure had returned to its previous level forty-eight hours after the end of treatment. This was especially marked in

the states of hypertension: for example, in the case already mentioned, the pressure quickly rose to 155 mm. systolic, 100 mm. diastolic. Even in cases of collapse the same feature was observed: in Case 19 where it had fallen to 88 mm. systolic, 65 mm. diastolic, a rise took place to 130 mm. systolic, 90 mm. diastolic, two days after the conclusion. This practically proves that the fall in pressure is directly due to the action of the somnifaine on the vaso-motor centres. It is unlikely that a toxic myocardium could recover so rapidly. The fall in the systolic pressure during the first twenty-four hours varied from 10 to 30 mm., and in the diastolic from 5 to 16 mm., with an average for all cases of 14.5 mm. fall in the systolic, and 8.2 mm. fall in the diastolic pressure. In some of the patients a further, though less-marked lowering of the blood pressure continued during the first week. Thus, comparing the systolic pressures between the first and the eighth days, we find a fall ranging from 5 mm. to 45 mm., with an average of 28 mm.; and similarly, with the diastolic pressures, the fall varied from 5 mm. to 20 mm., with an average of 13.3 mm.

These findings rather agree with those of the other workers mentioned; the fall in the diastolic being approximately half the fall in the systolic pressure. It is interesting to note the improvement which took place in a lowered blood pressure following the administration of half a grain of ephedrine from three to six times daily. This was the routine treatment in the present cases when a reduction of more than 20 mm. systolic and

10 mm. diastolic was noted. The ephedrine was given by mouth in the above dose, and with its use the systolic pressure rose from 7 to 15 mm. (average 11 mm.) and the diastolic, 5 to 10 mm. (average 6 mm.). The drug has, therefore, a definite effect in improving the fallen blood pressure during somnifaine narcosis. Now the pharmacological action of ephedrine⁽³¹⁾ is akin to that of adrenalin. By stimulating the sympathetic nerve endings the blood pressure is raised: in other words, it appears to counteract the depressing effect of the somnifaine on the vaso-motor system.

The fall in pressure thus described may be taken as the normal result following the administration of a barbiturate such as somnifaine, and cannot really be regarded as a complication. On the other hand, if it is excessive and is associated with a feeble pulse, rise or fall of temperature and alteration in the colour of the patient, one must regard these symptoms as being in the nature of a cardio-vascular collapse and indicative of active treatment.

Symptoms of this nature occurred in 7 of the present cases, and in each of them further dosage of the drug was suspended until the condition of the patient had returned to its former state. In Case 4 collapse occurred on the ninth day, the pulse increasing in rate to 120 per minute, with a small volume and weak force. Her colour was ashy, and the respirations very shallow. She was treated by the injection of one c.c. of pituitrin and one c.c. of camphor in oil subcutaneously. In

eight hours the pulse had become much stronger and its rate had diminished to 100 per minute. In addition, her colour had improved: narcosis was then resumed.

During the second course of treatment in Case 12, collapse took place on the sixth day. The temperature rose to 100.6°F. and the pulse-rate increased to 138 per minute. The pulse was irregular and at times imperceptible. She was treated by the injection of 2 c.c. icoral (Bayer) and coramine 15 minims by mouth, four-hourly, for the next twenty-four hours. No further sedative was given for the same period, and at the end of this time her condition had improved greatly: the temperature was normal; the pulse was 100 per minute, regular and of good quality. Associated with the rise of temperature and the increase in the pulse-rate, her blood pressure fell from 120 mm. systolic, 75 mm. diastolic, to 98 mm. systolic, 65 mm. diastolic. She was given half a grain of ephedrine, four-hourly: somnifaine was recommenced on the seventh day.

In Case 17 cardio-vascular collapse occurred twice - on the fifth and sixth days - with an interval of twelve hours between. On the evening of the fifth day, while deeply under the influence of the somnifaine, her colour became pallid, the pulse rose suddenly to 120 per minute and was very feeble and irregular. Somnifaine was withheld and 2 c.c. of icoral were given. Her condition improved, but twelve hours later her pulse again became very rapid, this time markedly irregular and almost imperceptible. The respirations were very shallow. An intra-

venous saline, 500 c.c., with glucose was given and 15 minims of coramine, four-hourly. During the next twenty-four hours, her condition gradually improved: the pulse-rate returned to 90 per minute, and was quite regular and of good volume. Following the improvement the course was resumed.

Collapse took place on the tenth day of the first treatment in Case 23. The pulse became irregular and increased to 120 per minute. With 2 c.c. of icoral and the suspension of somnifaine, the pulse-rate fell to 90 per minute, and the patient's colour improved within eight hours.

In Case 28 cardiac weakness appeared on the eighth day. The pulse-rate did not increase in this patient, remaining at 74 per minute, but the volume became very small and imperceptible. He was treated by the administration of one c.c. of coramine subcutaneously which was repeated thrice daily for the next three days, with the result that the pulse quality improved considerably and by the eleventh day, had returned to normal.

In Case 29 on the fourth day, the temperature rose rapidly to 101.8°F. , and the pulse to 132 per minute; the latter became irregular and almost imperceptible. This patient was treated by ephedrine gr. $\frac{1}{2}$, four-hourly, and strychnine gr. $\frac{1}{60}$, thrice daily. No further somnifaine was given for seventy-two hours. A careful physical examination revealed no cause for the disturbance. In thirty-six hours, with the above treatment, the temperature had returned to normal, the pulse to 88 per minute, and was of good volume.

On the fourth day of treatment in Case 32, the pulse became very rapid, slightly irregular and averaged 120 per minute. His colour was poor and the blood pressure fell from 130 mm. systolic, 90 mm. diastolic, to 90 mm. systolic, 65 mm. diastolic. He was treated by the administration of 2 c.c. of icoral and of half a grain of ephedrine, thrice daily, by mouth. Further somnifaine was withheld for twenty-four hours, by the end of which time the pulse had improved considerably, was regular and at a rate of 92 per minute; and the blood pressure had risen to 110 mm. systolic, 75 mm. diastolic.

The routine treatment of collapse consisted of :-

- (1) The suspension of further somnifaine until the cardio-vascular state had returned to normal
- (2) The administration of cardiac stimulants, of which icoral and coramine were found most effective
- (3) Saline by the bowel; or, in severe cases, intravenously.

Icoral⁽³²⁾ is a synthetic preparation consisting of two bases,

- (a) M. hydroxy N- ethyl diethyl amino ethyl amino benzol

which has a stimulant action on the respiratory centres; and,

- (b) β hydroxy phenyl propanolamine

which chemically and pharmacologically resembles ephedrine, raising the blood pressure. It is issued in ampoules containing a 5 per cent. solution of both bases in proportions of 4 : 1.

It is best administered intramuscularly. Coramine⁽³³⁾ is

chemically, pyridine β carbonic acid diethyl-amide. It can be given orally or parenterally. The action is on the vital centres of the medulla. It is extremely useful in cardio-respiratory failure, especially when resulting from excessive narcotic dosage. It is non-irritating, non-cumulative and of low toxicity. The time of onset of collapse varied considerably. The earliest was on the fourth day and the latest on the tenth day. The relationship of acetonuria to cardio-vascular collapse will be mentioned later.

(b) Changes in the Respiratory System.

Respiratory complications are another common cause of anxiety during treatment. Meerloo indicates that the ventilation of the lungs is diminished and that there is a constant danger of hypostasis if the patient is too-deeply narcotised. He recommends the administration of caffeine in such cases since it neutralises the paralysing effects of barbital on the respiratory centres. Ettleson states that the respirations become increased and shallow, and that further dosage of the drug should be withheld in these cases. Murray and Burns, using sodium amytal, state that the respirations show profound alterations. Usually there is a marked reduction in rate and volume, the breathing becoming both very shallow and slow. The drug is evidently a deep respiratory depressant. Bleckwenn also found the respirations shallow, but that their rate was slightly increased. Strom-Olsen mentions bronchitis and pneumonia as being two

serious complications which were liable to occur. Two of his patients developed influenza during treatment, and one of them succumbed to broncho-pneumonia and pneumococcal septicaemia. Zerfas found that all barbiturates depress the respiratory system when large doses are given, causing the respiratory excursion to become shallow. Magnus confirms these views, and states that barbiturates decrease the frequency of respiration and affect the bronchial capillaries, predisposing the patient to bronchitis and broncho-pneumonia. He feels that the incidence of these complications can be diminished by avoiding a too-deep narcosis, by frequently changing the posture of the patient, by allowing daily rousing periods and by checking vomiting.

Wagner warns against using barbiturates in people with respiratory trouble because of their depressant effect on the respiratory centre, as well as a tendency to cause pulmonary congestion. Apart from any recognisable changes in the lungs, an irritating cough is frequently a feature during several days of the course.

In the majority of the cases, no change was found in the respiratory rate, the average recorded being 20 to 22 per minute. When the respiratory rate did rise it was associated with a corresponding alteration in the pulse and temperature. In Case 4 the respirations were very deep, but in all the others the respiratory excursion was definitely shallow. Severe paroxysms of coughing were present in 2 patients and lasted at intervals for from twenty-four to forty-eight hours. In Case 2 these occurred on the third day and in Case 26, during the sixth

day of treatment. In neither was any cause for this disturbance discovered on physical examination of the chest. One patient developed a pneumonia on the second day of treatment after only 4 c.c. of somnifaine had been administered: this case has been discussed previously. Apart from that patient, physical examination of the chest was negative at all times during the narcosis.

(c) Alterations in the Temperature.

Temperature disturbances have been recorded by most workers during the course of prolonged narcosis. Thus in Oberholzer's cases, 20 showed a rise of temperature to over 99.5°F. and in 5 of them treatment had to be curtailed on account of the pyrexia. Kraus and Meerloo⁽³⁴⁾ made a systematic study of temperature charts in 50 cases. They observed that somnifaine affected the temperature curve in various ways: very small doses have no effect on the temperature; an average dose reduces the maximum variation so that the curve is comparatively flat; but larger doses produce a very great variation, the temperature rising and falling violently. The temperature curve begins to show the influence of the somnifaine about the third day. These writers mention further that a sudden rise of temperature is very liable to occur following the conclusion of treatment, to which they give the name of "disintoxication fever." It took place in 5 out of 50 cases even after the fourteenth day. A subnormal temperature is as common a phenomenon as is fever.

especially in catatonic and confusional states. Like fever it is a toxic symptom and should be regarded as a danger signal. Kooy found that a rise of temperature occurred during the later stages of treatment - 38 times in his series of 133 cases - and he feels that in most instances it is directly due to the action of the somnifaine :-

"Nevertheless, if the pyrexia is marked, one should stop the treatment as one cannot judge of possible intercurrent diseases when the patient is deeply unconscious."

Wagner mentions that barbiturates in repeated doses cause an early subnormal temperature, with a slight fever after a few days. Magnus, using dial, found a rise of temperature in practically every case, chiefly on the third or seventh day. In a few of his subjects, the temperature rose to 105°F. He recommends a thorough examination to exclude infection or a chest complication; also sponging, colonic irrigation and withdrawal of the drug until the temperature subsides. He believes that the hyperpyrexias are central in origin and are the direct complicants of the drug acting on the thermogenic areas of the brain. In Strom-Olsen's series, a rise of temperature occurred in 11 cases - in 6 on, or after the sixth day - ranging from 99°F. to 101.8°F. In 2 of these symptoms of collapse were present, but in the remaining 9 no physical cause could be discovered, showing that the fever is due to the action of the narcotic on the heat-regulating centres. The stoppage of

further dosage for from twelve to twenty-four hours usually caused the temperature to fall.

A rise of temperature occurred in 22 cases during, or shortly after the completion of treatment. In 5 patients during the course, the temperature showed a daily swing from the third day onwards. The periodicity was different in each. In Case 9, the temperature rose at 10 p.m. to from 99°F. to 99.6°F., the highest readings being recorded on the ninth and the eleventh days. In Case 10, the temperature rose at 10 a.m. and reached its maximum of 99.4°F. on the thirteenth day. In Case 13, the temperature varied from 98°F. to 99.2°F. without any regular periodicity. Case 23 during the first course exhibited an evening rise of temperature, reaching from 99.4°F. to 100°F.

In 6 cases a rise occurred once during the course, viz.: Case 3, to 99°F. on the fourth day, with a fall again to normal within eight hours; Case 4, to 100°F. on the fifth day; and Case 5, to 99.2°F. on the twelfth day, both also returning to normal in a similar period. In Case 14, the temperature rose to 100.6°F. on the evening of the seventh day and fell to normal within twelve hours. In the other 2 cases where a single rise of temperature was observed, there were associated signs of collapse. Thus in Case 17 on the evening of the fifth day, the temperature rose to 99.4°F., the pulse increased to 120 per minute and the blood pressure fell to 90 mm. systolic, 64 mm. diastolic. On withholding somnifaine, the temperature fell to normal in twenty-four hours. In Case 29, a rise took place to 101.8°F. on the

fourth day, combined with a pulse-rate of 132 per minute and other symptoms of collapse. Associated with improvement in the patient's condition, the temperature dropped in twenty-four hours to 97.4°F.

In 3 patients pyrexia occurred on two occasions. Case 7 showed a rise on the eleventh and fourteenth days to 99.6°F., with a rapid fall to normal on both occasions. In the first treatment of Case 12, a sharp elevation to 99.4° occurred on the third day, and to 99°F. on the fourteenth day, with a normal temperature in the interval intervening. Case 31 registered a rise to 99.4°F. on the ninth day, and to 101°F. on the tenth day.

A rise occurred three times in Case 25 during treatment; to 100°F. on the fourth day, to 99.4°F. on the tenth day and to 100.4°F. on the eleventh day. In each instance the temperature returned to normal in twelve hours.

In 3 cases the temperature remained high for more than twenty-four hours. In Case 8, it rose to 99°F. on the fifth day and gradually increased until the eleventh day, when it reached 102.8°F. Somnifaine was discontinued and the temperature fell to normal in thirty hours. Physical examination was negative, and in view of the rapid fall following discontinuance of treatment, it seems fairly certain that the pyrexia was the direct result of the toxic action of the somnifaine on the heat-regulating centres. In Case 22, the temperature rose to 100°F. on the fourth day, but fell to normal in eight hours. On the

seventh and eighth days it was constantly above 99°F., and on the evening of the ninth day it rose to 100.2°F. From the tenth day the temperature varied from 99°F. to 100°F., and fell to normal twenty-four hours after the conclusion of treatment. No physical signs were detected in this case, and the rapid fall confirms the view already expressed. In the second treatment on Case 12, the temperature remained above normal on the fifth and sixth days, reaching 101.4°F. and 100.6°F. on each day, respectively. This pyrexia was associated with an increase in the pulse-rate to 138 per minute and signs of collapse. Following the withdrawal of somnifaine, the temperature had returned to normal in twenty-four hours.

During treatment in 2 cases pyrexia occurred, for which a definite physical cause was ascertainable. Thus, in Case 18, the rise to 104°F. was accounted for by a bilateral lobar pneumonia; and in Case 20, the temperature of 101.2°F. from the fifth to the eighth days was explained by the discovery in the urine of abundant pus cells.

Two patients developed a rise of temperature after the final injection of somnifaine had been given, and in both there were marked disturbances in the central nervous system. Thus, in Case 1, a temperature of 99°F. to 100°F. on the fifth day after treatment accompanied the onset of epileptiform attacks. In Case 2, twelve hours after the last injection the temperature rose to 103.6°F., and with it signs of meningeal irritation

developed which will be described in detail later. The temperature continued for thirty-six hours at a high level.

The temperature disturbance in the present cases was more frequently encountered than most of the previous writers have reported, and it was observed from the fourth day onwards. In only 2 of the cases was it associated with any evidence of systemic infection. In all the others it appeared to be the direct action of the somnifaine.

(d) Urinary complications.

Normally, the elimination of urine is lower in sleep than in the waking state⁽³⁵⁾, but during induced narcosis definite oliguria may occur, and in certain cases there may be an actual suppression of urine. Retention is also a frequent feature and may or may not be associated with a diminished kidney output. Meerloo⁽²²⁾ discovered that, at the beginning of treatment, the quantity of urine decreased; it then returned to normal, but as the narcosis proceeded, there was an actual increase. He considers that in cases of retention, catheterisation is distinctly dangerous and that, as a rule, after twenty-four to thirty-six hours the bladder empties itself. Anuria is most common in the early stages and should be treated by diminishing the sedative in order to promote a diuresis. He recommends caffeine in this complication on account of its stimulating effect on the kidneys.

Kooy⁽²³⁾ also met with suppression of urine in the early

stages and advises the routine use of a mild diuretic. Magnus⁽²¹⁾ found urinary retention in practically every case, accompanied in many by a slight albuminuria which disappeared after treatment. Catheterisation was found necessary by Müller⁽¹⁰⁾ in a third of his cases; and a similar finding is recorded by Bohn⁽¹⁸⁾ Wagner⁽³⁰⁾ confirms those views and says that barbiturate derivatives, when given in hypnotic doses, appreciably diminish the urinary secretion.

Strom-Olsen⁽²⁷⁾ did not encounter a complete anuria, but oliguria was noted at times. In both his cases which collapsed it was very marked. Fourteen patients had albuminuria - 2 in a large amount. The condition, he believes, is due to a toxic irritation of the kidneys. Twelve of his cases developed retention and had to be catheterised. The retention is probably due to a paralysis of the nervous centres for micturition. The albuminuria, except in one case, disappeared after treatment.

A diminished secretion of urine was found in the majority of the present cases undergoing treatment: 20 oz. was the average quantity passed in twenty-four hours. In 4 patients a definite oliguria occurred. In Case 15, the output was often as low as 12 oz. per day, and in Case 19, from the fourth to the seventh days, an average of 12 oz. was measured. In Case 21, only 10 oz. were passed on the sixth, seventh and eighth days. In order to determine the kidney function in this patient, a blood urea estimation was done. On the sixth day the results obtained were 49 mgm. of urea per cent. and 55 mgm. of non-

protein nitrogen per cent. He was treated by diminishing the dose of somnifaine to 2 c.c. per day, in order to produce only a very light narcosis, and by the administration of abundant fluids and potassium citrate 20 gr., four-hourly. By the ninth day, the urinary output had increased and the kidney function had improved, as was shown by a fall in the blood urea to 28.6 mgm. per cent., and in the non-protein nitrogen to 29.5 mgm. per cent. These bio-chemical findings indicate that the oliguria is due in part, at least, to the toxic effect of somnifaine on the kidneys. In Case 27, 18 oz were passed from the sixth to the seventh days. With this patient also, the dosage of somnifaine was reduced until the kidney secretion had improved.

In every case except 2, some disturbance occurred in micturition. Fourteen of the patients were incontinent during the course; 16 (5 females, 11 males) had retention for twenty-four hours or longer. In 2 of these the bladder emptied itself spontaneously, but in the remaining 14, catheterisation was required. It was performed once in 6 cases, twice in 6 cases, 3 times in one case and 7 times in one case. In the latter, it was found necessary to repeat the operation for two days following the conclusion of treatment. Catheterisation was not carried out unless definite distension was present, and following Meerloo's advice, time was always allowed to see whether spontaneous micturition would occur, but this, as previously mentioned, happened only in 2 patients. As regards the date of onset of retention, it was first observed in 5 cases on the

third day, in 3 cases on the fourth day, in one case on the fifth day, in 2 cases on the sixth day, in 2 cases on the seventh day and in one not until the tenth day. With the exception of this latter patient, therefore, the complication arose during the first half of treatment. In one patient cystitis developed following on the use of the catheter, but cleared up rapidly by suspending the somnifaine, by giving abundant fluids, cysto-purin by mouth and intravenous injections of amphotropin (hexamethylenetetramine camphorate (Bayer)).

Albuminuria was present at some time or other in 28 of the patients. In 2 of these it had been detected beforehand and persisted throughout the course. In no case did the quantity reach more than a trace. It was most commonly met with during the second week of the narcosis, especially about the ninth day, and it disappeared within a few days after the completion of treatment, with the exception of the 2 patients above mentioned.

In 11 cases sugar was detected. In Case 1, there was a marked reduction of Fehling's solution on the tenth day and a trace of sugar continued until a week following the last injection. In the others, no more than a trace could be detected; in 4, on one day only, in 3, on two days and in other 3, for four or five days. The most frequent time for its appearance in the urine was from the tenth to the thirteenth days.

An occasional trace of bile was noted in 5 cases. Another change which occurred in 13 patients was an increase in the acidity of the urine. In 4 of these it rose rapidly

during the first week, but in the others it was noticed only during the last few days. The most marked incidence was in Case 24 where, on the third day of treatment, the acidity of the urine was 96° . In other 3 patients it reached to over 80° . Treatment of these cases by the administration of potassium citrate and soda bicarbonate in 20-grain doses, four-hourly or thrice daily, according to the degree, was effective in producing a rapid fall in the acidity in all the cases. No definite relationship could be discovered between the increased acidity and ketonuria.

(e) Changes occurring in the Central Nervous System.

These are described in some detail by Meerloo⁽²²⁾. First, bulbar complications may occur, such as dysphagia, thickness of speech, loss of the cough reflex and hiccough; sympathetic changes, such as profuse perspiration, ptyalism and dermatographia, as well as cerebral vomiting, ataxia, nystagmus, epileptiform attacks, alteration in the reflexes, with occasionally a positive Babinski's sign and musculo-spiral paralysis. These changes, he considers, are directly referable to the effect of the drug on the brain-stem.

Difficulty in swallowing is mentioned by Strom-Olsen⁽²⁷⁾ and by Müller⁽¹⁰⁾, the latter finding it rarely absent. In the former's cases, it was more apparent when solid food was given, and in 5 instances the dysphagia was pronounced. He

confirms the complications mentioned by Meerloo and includes tremor of the hands and lips, transient oedema and hiccough. The latter proved a troublesome symptom in one of his patients, where it persisted for two days, but subsided without interruption of the narcosis. These changes in the nervous system occurred when the patient was well under the influence of the somnifaine.

Bleckwenn⁽¹⁷⁾ describes changes in the reflexes following the administration of sodium amytal. The corneal reflex disappeared in from twenty to forty minutes and this was followed by a loss of the deep tendon reflexes and dilatation of the pupils. Magnus⁽²¹⁾ found that in shallow narcosis, the knee jerk became sluggish, but the biceps jerk remained brisk. In deep narcosis, the knee jerk was lost, the biceps jerk was sluggish and the corneal reflex was absent.

Ocular symptoms are mentioned by Lindemann⁽³⁶⁾ who states that with a light narcosis, a slight, transient nystagmus may occur, associated with dilated pupils, giddiness and diplopia. In deep narcosis, the pupils become contracted and fixed; the speech is thick and slurred. Ataxia of the limbs is a conspicuous feature and difficulty in swallowing may be troublesome and may involve the danger of an aspiration pneumonia if proper care is not taken.

What is perhaps the most interesting nervous complication is the occurrence of epileptic seizures. This is described by several workers. Thus Meerloo⁽²²⁾ in a series of 500 cases at

the Provincial Hospital, Santpoort, met with 5 epileptic reactions. The fits occurred after the dosage had been stopped. In the case of one patient who had had three courses of treatment this complication was present after each. He makes an attempt to explain the occurrence of these seizures following the conclusion of narcosis. He assumes that convulsive responses arise in a hypothetical fit centre :-

"If there is a normal, though latent 'Krampfbereitschaft,' we can imagine how any sudden abstention from remedies which exercise restraint upon this hypothetical centre would allow the attack to discharge itself. Many narcotics and sedatives demonstrate this rule, that sudden abstention after habitual use brings with it motor and convulsive discharges."

Kooy⁽²³⁾ had 2 patients having epileptic fits several days after treatment,

"... showing that the effect of the drug does not finish when the last injection had been given."

He feels in this complication that there is a latent tendency to epilepsy in the individual, and he compares its occurrence to the increased number of fits which often take place when an epileptic ceases to take the bromide or luminal which he has been having for a prolonged period. In none of his cases was there a repetition of the attacks at a later date.

Fits occurred in 3 of Strom-Olsen's⁽²⁷⁾ cases, but only in those where glucose and insulin had not been administered.

Meerlo⁽²²⁾ also mentions that cataleptic states may follow the administration of somnifaine.

In my series, with one exception, the deep reflexes were found to be diminished when the subject was deeply narcotised. In this exception the patient remained tense and resistive during narcosis and with her the knee jerks were brisk throughout. No definite Babinski's sign was detected, though on stroking the sole of the foot in one case, drawing up of the legs occurred. The pupils were always sluggish to light. The size of the pupils varied; in deep narcosis they were usually, but not always, slightly contracted. Involuntary movements occasionally were evident. Thus, one patient had persistent twitching of the muscles round the mouth, and certain others exhibited purposeless motions of the arms and legs. Definite dysphagia was present in one case (No. 10) on the eighth day and lasted for twenty-four hours. In every patient, if roused, the speech was thick and, in a few cases, very slurred. This slurring persisted during the stage when the patient was emerging from the narcosis.

Hiccough was present in 5 cases and was frequently very troublesome and persistent. In 4 it commenced in the first three days and lasted from twenty-four to forty-eight hours. In Case 10, it did not begin till the fourth day and continued in spasms for seventy-two hours, and was particularly troublesome.

Perspiration was increased in every patient and in a few it was very pronounced, particularly in Case 31. Excessive

secretion of saliva was not evident in the present cases. During the narcosis and the stage of emerging, ataxia was a marked feature, and the patient had to be supported if he was allowed out of bed. Cutaneous sensibility was definitely diminished during deep narcosis, with the result that the intramuscular injections of somnifaine could be administered without giving rise to discomfort.

Profound disturbance of the central nervous system was noted in 3 patients. In Case 1, five days after the last injection an epileptiform seizure occurred. This passed off and for 3 days she remained in an extremely confused mental state. At the end of that period, general muscular twitchings developed, involving the face, arms and legs. These continued for thirty-six hours, when a further epileptic seizure occurred, followed by a third fit twenty-four hours later. The occurrence of these attacks in this patient is rather interesting when one considers Kooy's idea that in these cases, there is a latent tendency to epilepsy. On going into the patient's history, we find that in childhood she had had several attacks which might have been of an epileptiform character, and at the time of the onset of her mental illness a peculiar seizure took place, the details of which were unfortunately not obtainable. It is possible that in this case the withdrawal of somnifaine acted in the same way as the withdrawal of luminal or other anti-epileptic drug when it has been administered for a prolonged period. Somnifaine has been used in treating status epilepticus, with good results⁽³⁷⁾

and therefore falls into that category. One other point, however, arose in this patient. During the tonic stage of the fits, the limbs assumed an attitude which seemed to be tetanoid in type, the hands going into the accoucheur position. With this in mind, she was treated by the administration of calcium, both intravenously and orally. After the first injection of calcium gluconate, muscular twitchings continued, but gradually diminished and passed off in twelve hours. No further seizures took place. To confirm this viewpoint, a bio-chemical examination of the blood was done before the administration of calcium; the result obtained was 9.1 mgm. per cent. of serum calcium. Four weeks later, a further estimation showed an improvement to 10.3 mgm. per cent. of serum calcium. Even allowing for a slight experimental error, the first reading obtained does not indicate a hypocalcaemia of such a degree as to bring about symptoms of tetany; the normal serum calcium generally being recorded at 9 to 11 mgm. per cent. According to Harrison⁽³⁸⁾ seizures in tetany do not begin till the serum calcium has fallen to 6 or 7 mgm. per cent. The evidence is, therefore, in favour of the views expressed by Kooy and Meerloo as being the likely cause for the convulsions. The improvement following on the calcium therapy was probably merely a coincidence.

In Case 17, an epileptic attack occurred without warning three weeks after the last injection had been given and after she had completely emerged from the narcosis. She was treated - as was the previous case - by intravenous calcium gluconate; no

recurrence of the seizure took place. The history was carefully investigated, but no evidence of a previous epileptic diathesis was obtained. A blood calcium was not estimated in this instance, as the fit occurred suddenly and was quite unexpected. Its immediate treatment by calcium gluconate would have rendered subsequent results of little value.

Perhaps the most interesting neurological complication, and one which I have not obtained any reference to in the literature, occurred in Case 2. Twelve hours after the last injection, the temperature rose to 103.6°F.; her body became rigid, her head retracted and her back arched into an episthotonic posture. There was associated nuchal rigidity and positive Kernig's sign; the pupils were dilated and very sluggish to light. During this state, she was gradually emerging from the narcosis. She was emotional, talked constantly in a slurred voice and complained of excruciating pains in her limbs. The condition persisted for twenty-four hours and then gradually subsided, associated with a fall in the temperature. Several attempts were made at lumbar puncture, but the excessive arching of her vertebrae prevented the insertion of the needle, and it was felt that the administration of an anaesthetic, even if it did produce relaxation, would be highly dangerous. There was a leucocytosis of 10,920 per c.mm.

(f) Changes in the Metabolism.

Various investigations have been carried out to find the metabolic changes which occur during induced narcosis. Cloetta

and Thomann⁽³⁹⁾ found that during sleep produced in dogs by ether, dial and alcohol, there was a fall in the blood calcium of from 5 to 12 per cent.; the deeper the sleep, the more pronounced was the decrease. They believed that during sleep the calcium accumulated in the brain tissue. Glaser⁽⁴⁰⁾ also demonstrated that the blood calcium diminished from 15 to 20 per cent. during hypnotic sleep. Katzenelbogen⁽³⁵⁾ states that a decrease in blood calcium is characteristic of narcosis and that there is a distinct relationship between the rate of decrease of calcium and the duration of sleep. He experimented on rabbits with dial and obtained a definite decrease in the blood calcium in 86.2 per cent. of his tests. Demole⁽⁴¹⁾ believes that the calcium, while diminished in the blood during sleep, accumulates chiefly in the parainfundibular region of the brain. The changes in potassium were not constant, though in 70 per cent. of Katzenelbogen's cases a decrease was found. Inorganic phosphorous and magnesium also tended to decrease.

Alteration in the blood picture takes place from time to time during treatment. Strom-Olsen⁽²⁷⁾ investigated the leucocyte count in 22 cases. In 2 an initial leucopenia occurred on the second day; in the remainder a leucocytosis set in, either immediately, or after twenty-four to forty-eight hours. The peak of the curve was reached on the fifth or sixth day, after which there was a tendency to fall. The highest count noted was 31,000 per c.mm. He feels that the leucocytosis is an expression of the specific effect of the drug on the haemato-

poetic system and is independent of the toxic action of the drug on other organs. The blood urea was also estimated by Strom-Olsen in 2 cases: in one there was a rise of 13.3 mgm. per cent. on the sixth day from the initial figure of 20.3 mgm. per cent. This rise was coincident with the development of oliguria. In the second case estimated, the maximum deviation from the normal level was 3 mgm. per cent. In 2 cases where he carried out an estimation of the blood calcium, he found a decrease up to 18 per cent., which became specially marked after the fourth day.

Wagner⁽³⁰⁾ found that the basal metabolic rate is little affected by barbituric narcosis: there is rather a slight initial rise which then remains constant. Using sodium amytal, Dameshee⁽⁴²⁾ described results differing from those of Wagner. He states that in large doses, it produces a marked fall in the basal metabolism, averaging to 26 per cent., and that this fall is due to a depressing effect of the drug on the hypothalamus. From a practical point of view, the most important findings are those regarding glucose tolerance and the occurrence of ketosis. It has been well-known since the early days of treatment, that one of the most frequent complications was the presence of acetone and diacetic acid in the urine at different times during narcosis. Quastel and Strom-Olsen⁽⁴³⁾ found that the onset of ketonuria varied from person to person, in some cases becoming very marked forty-eight hours from the commencement of treatment. The administration of glucose and insulin brought about a decrease in the toxicity of the narcotic in this respect.

They treated 20 cases with somnifaine and, as soon as ketonuria appeared, 5 to 15 units of insulin plus 50 grams of glucose, were given at the same time as each injection. With this treatment, acetone disappeared from the urine in forty-eight hours. Thirteen out of the 20 cases developed ketonuria and subsequently received this additional measure.

In Strom-Olsen's⁽²⁴⁾ subsequent series of 128 treatments, 42 were given with routine insulin-glucose administration and 86 were carried through without this. Of the 42 cases, no deaths occurred and there was only one serious complication; but of the 86 which had not received glucose and insulin, 2 deaths took place, 3 cases had subsequent epileptic attacks and 61 suffered from complications, 24 of them being of a serious nature. Acetone appeared in the urine in 70 per cent. of the patients not receiving glucose and insulin.

Work has been done by various authors in an attempt to explain these findings. Thus Quastel and Wheatley⁽⁴⁴⁾ have demonstrated that narcotics exert a profound inhibitory effect on the oxidation by the brain of substances important in carbohydrate metabolism. They found a definite parallelism between the inhibitive power on glucose oxidation of the brain and the narcotic effect of the drug. The amount of energy available for the activity of the cells is diminished and narcosis results. Narcotics may be supposed to exert their toxic effect in the organism by interfering with the carbohydrate metabolism of the organs. These results were confirmed by the further

experiments of Davies and Quastel⁽⁴⁵⁾ who exposed fresh brain to narcotic drugs in low concentrations. This resulted in a specific inhibitory effect on the oxidation in the brain of substances important in carbohydrate metabolism, viz., glucose, lactic acid and pyruvic acid. Narcotics of the same chemical type with the greater narcotic power had the greater inhibitory action on the oxidation of glucose and lactic acid. Tod⁽⁴⁶⁾ found that veronal in clinical doses produced a marked effect on the glucose tolerance curve, resulting in a lowered maxima or shortened hyperglycemia, or both, with a markedly decreased hyperglycaemic area.

Again, Strom-Olsen⁽²⁷⁾ states that whether the fundamental disturbance is hepatic, nervous or pancreatic in origin, it is a problem requiring further elucidation: either a diminution in the secretion of insulin results from a toxic action of the drug on the Islets of Langerhans, or a greater amount of insulin is required by the tissue cells, poisoned as they are with the narcotic, in order that glucose may be oxidised. He considers that ketonuria is the outward sign only of a specific metabolic disturbance, and the readiness with which ketone bodies appear in the urine must depend on individual differences in the degrees of sensitivity to somnifaine of the mechanism concerned in carbohydrate metabolism, and also in the facility with which the kidneys excrete these substances, impaired renal function being comparatively common during narcosis. Thus, while ketonuria should be regarded as a danger signal, its absence

must not give rise to a false sense of security. Cardiac complications which are common in somnifaine narcosis are, he believes, due more to the toxic action on the myocardium as the result of altered carbohydrate metabolism than to the effect of the drug on the central nervous system, a view which has been expressed by Müller and Meerloo.

With the insufficiency of available insulin and inhibition of glucose oxidation, the nutrition of the heart may be seriously impaired and consequently the amount of energy available for contraction considerably diminished. This view is supported by the experiments of Hepburn and Latchford⁽⁴⁷⁾ who found that the average sugar consumption of the isolated rabbit's heart was increased almost four times when insulin was added to the perfusion fluid.

It is interesting to note Minnitt's⁽⁴⁸⁾ findings after ether anaesthesia. He found that when post-anaesthetic toxic symptoms and acetonuria developed, they were associated with a high blood sugar. Insulin administration reduced the blood sugar and lessened the toxic changes. He further advises its use as a preventive measure and also to increase a fallen blood pressure during ether anaesthesia.

Hardcastle⁽⁴⁹⁾ in his paper on the toxicity of medinal and other hypnotic drugs, came to the conclusion that the relation between the taking of medinal and the presence of acetonuria was not proven.

Acetonuria was present in 16 cases. In Case 28, there

was a definite quantity of ketone bodies in the urine from the third to the sixth days, and it is interesting to note that in this case collapse occurred on the eighth day. In Case 8, acetone had been present before treatment and continued during and after the course. In this patient, a rise of temperature took place to 102.8°F. on the eleventh day. A trace of acetone was present from the third day onwards in Case 17, and this patient also suffered from collapse on the fifth day. Returning to Strom-Olsen's views on the toxic effects of somnifaine, we find that in the 7 cases of cardio-vascular collapse which occurred, in one of these acetonuria was definite. In another it was present in small quantities for several days, in 2, a very faint trace was detected on isolated occasions and in 3, examination for acetone was completely negative throughout the whole course. Glucose-insulin administration, which was carried out as a routine measure, cannot be said to prevent the production of ketonuria and cardio-vascular collapse.

Blood calcium estimations were performed in 4 patients before and after treatment, and in a further case after treatment only. In 3 of the former group, a fall was observed from 10.2 mgm. per cent. to 8.7 mgm. per cent. in one case; from 10.1 mgm. per cent. to 8.6 mgm. per cent. in another; and from 9.2 mgm. per cent. to 8.4 mgm. per cent. in a third. The fourth case showed a slight increase in the calcium; before treatment it was estimated at 9.3 mgm. per cent. and after the conclusion, at 9.5 mgm. per cent. In the other case mentioned, a serum

calcium estimation was done when the patient was suffering from epileptiform convulsions. At the time of the occurrence of the fits, the result was 9.1 mgm. per cent., and four weeks later, when the patient had cleared up completely and had had no recurrence of the seizure, it measured 10.3 mgm. per cent. Following the first reading, she received 2 intravenous injections of calcium gluconate and had been given calcium by mouth daily during the intervening month. The etiology of these epileptic attacks and their relationship to hypocalcaemia are discussed elsewhere.

(g) Changes in the Skin.

Disturbances of the skin are other conditions noted during treatment. Thus Meerloo⁽²²⁾ describes the presence of erythematous eruptions, and believes that they are due to the action of somnifaine on the peripheral blood vessels. Wagner⁽³⁰⁾ mentions two skin reactions occurring during the administration of barbiturates; firstly, urticarial wheals, with intense itching, and secondly, a toxic reaction, with a morbilliform or scarlatiniform erythema. Lindemann⁽³⁶⁾ states that vaso dilatation of the peripheral circulation takes place, resulting in flushing of the skin. Strom-Olsen⁽²⁷⁾ encountered two skin eruptions. In one case, a profuse scarlatiniform rash developed on the day after the termination of narcosis and in a second case, a rash developed on the tenth day of treatment, of an erythematous, morbilliform type, confined chiefly to the trunk

and to the root of the neck. In 2 cases, Magnus⁽²¹⁾ met with a generalised scarlatinal rash, associated with a rise of temperature in the early stages.

In the present series, several skin disturbances took place. Two patients developed erythematous eruptions. In Case 1, on the fourth day, a scarlatiniform rash appeared on the chest and spread to the abdomen. It was especially pronounced along the diaphragmatic attachment and was associated with marked itching. The rash spread to the face and limbs, and after four days, gradually began to fade and this was associated with a fine desquamation. In seven days the rash had completely disappeared. There was no associated pyrexia. In Case 2, a scarlatiniform rash appeared on the third day, first on the thighs, spreading later to the abdomen and chest. After twenty-four hours, the rash gradually faded and had completely disappeared in two days' time. A third patient (Case 11) on the eleventh day of treatment complained of intense itching of her arms and legs, which persisted for twenty-four hours and then passed off. No eruption could be detected on local examination. These skin disturbances were treated by the liberal application of calamine lotion.

(h) Venous Thrombosis.

Another complication which occurred was a venous thrombosis in the thigh. In Case 15, twenty-four hours after the last injection, the left leg was found to be swollen and oedema-

tous. There was stiffness and limitation in movement and tenderness on pressure over the anterior and outer aspect of the left thigh. The condition cleared up in two weeks and was treated by the application of ichthyol and glycerin. Meerloo⁽²²⁾ mentions thrombosis as being a danger if somnifaine is given intravenously. Care was always taken during an injection, to make sure that the drug did not enter one of the large veins. It is possible, however, in the case mentioned above, that the needle pierced through one of the femoral branches, resulting in some of the drug entering the vein.

(i) Gastro-intestinal changes.

Gastro-intestinal disturbances may also occur. Vomiting is frequent and may be persistent. It has been described by Kooy⁽²³⁾, Strom-Olsen⁽²⁷⁾ and Meerloo⁽²²⁾. The last believes that the vomiting is cerebral in type and is due to the action of the drug on the brain-stem. Wagner also mentions vomiting, associated with nausea, epigastric pain and, perhaps, diarrhoea. Magnus⁽²¹⁾ makes special reference to this symptom, and says that during narcosis vomiting may have a serious result, since some of the material may be taken into the lungs, producing an aspiration pneumonia.

Constipation is also common and Kooy⁽²³⁾ recommends the use of a mild laxative every night, combined if necessary, with an enema in the morning.

Vomiting occurred in 12 patients, usually in the early stages of treatment. In 4, it took place during the first day; in one case, 4 hours after the first injection and in 2, eight hours after. In 4, it commenced on the second day; in 2, on the third day and in one, on the sixth day. In Case 1, vomiting occurred three days after the conclusion of treatment and coincided with the onset of epileptic seizures. The vomited material always consisted of undigested food. The vomiting was projectile in type, about 10 oz. being returned at each spell. With the exception of one case, no vomiting took place during the second week. In this patient, it continued right up till the eleventh day. In most of the cases where the complication occurred during the first and second days, it passed off without recurrence on the third day. Three patients, during their more wakeful moments, complained of nausea, but without actual vomiting. One patient, following repeated attacks of vomiting on the first and second days, for twenty-four hours later suffered from severe flatulence. The projectile nature of the vomiting and its occurrence, especially very soon after the commencement of treatment, suggests that it is a direct result of the somnifaine on the brain-stem.

In every case constipation was a marked feature and was treated by means of hydrogen peroxide enemata daily, or on alternate days.

In 3 cases the daily intake of nourishment was so diminished that tube-feeding was resorted to. In Case 8, during the

whole of the second course of treatment, tube-feeding was carried out thrice daily. In Case 24, it was resorted to from the fifth to the eleventh days; and in Case 30, for one day only, viz., the thirteenth day. Those 3 patients before treatment had always been difficult with their food and each of them at some time or other had required artificial feeding. No definite dysphagia was present in any of them and the complication appeared to be due to the persistence of their psychotic symptoms throughout the narcosis. It is of further interest to note that they all began to take food themselves after they had emerged fully from the effect of the somnifaine. This confirms the view expressed elsewhere, that improvement, when it takes place, occurs at the time when the effect of the drug is wearing off and not during the period of deep sleep.

In 4 cases, the course of treatment had to be stopped prematurely; in Case 8, on the eleventh day, following a gradually increasing pyrexia for 6 days, finally reaching 102.8°F; in Case 19, on the thirteenth day, following a gradual fall in the blood pressure from 130 mm. systolic, 90 mm. diastolic, to 88 mm. systolic, 65 mm. diastolic; in Case 29, on the eighth day, as the result of a progressive leucopenia, the white blood cells being reduced to 4,790; and in Case 30, on the thirteenth day, due to increasing restlessness and tolerance to somnifaine, together with difficulty in administering sufficient nourishment.

Treatment had to be interrupted on account of complica-

tions for twenty-four hours or longer in 6 patients. In Case 2, for twenty-four hours on the second day, owing to persistent vomiting. In Case 12, it was suspended on the sixth day for twenty-four hours following an elevation in the temperature to 100.6°F. and an increase in the pulse-rate to 138 per minute; in Case 18, on the fifth day for sixty hours, as the result of cardio-vascular collapse; in Case 20, on the seventh day for three days, due to the development of an acute cystitis after catheterisation. In Cases 29 and 32, treatment was terminated on the fourth day in each for seventy-two and twenty-four hours respectively, as the result of symptoms of collapse, with a rise in the temperature and a rapid, feeble pulse. In Case 21, where a definite oliguria occurred from the sixth to the eighth days, somnifaine was not completely stopped during that period, but the patient was kept in a very light narcosis.

In an endeavour to prevent complications resulting from narcotic therapy, Meerloo⁽²²⁾ recommends a combination of drugs to prevent the side effects of any one sedative. He himself used the following combination :-

100 mgm. Phenyl ethyl barbituric acid
 100 mgm. Diallyl barbituric acid
 50 mgm. Dimethyl amido pyrin
 50 mgm. Phenyl cinchonic acid
 100 mgm. Caffein sodium benzoate
 $\frac{1}{4}$ -mgm. Strophanthin.

The caffeine promotes diuresis and neutralises the paralysing effect of the barbital on the respiratory centre. The strophanthin counteracts any tendency to cardiac collapse; the phenyl

cinchonic acid has an anti-pyretic effect and the dimethyl amido pyrin, he believes, strengthens the subcortical action of the barbiturate. Since February, 1931, 44 treatments of two weeks each or longer were given in his department, using this mixture, with success in one third of the cases.

Cloetta⁽⁵⁰⁾ as well as Meerloo, sought, by combining several drugs of known sedative quality, to produce a preparation fulfilling the following requirements :-

- (1) It must have sufficient therapeutic breadth
- (2) It must be a sure means of producing sleep
- (3) It must be non-irritating to the bowel
- (4) It must be capable of rapid action, and not producing after-excitement
- (5) It must be at the disposal of the physician in a handy and durable form.

At the Burghölze Clinic during a four-year period, 160 schizophrenics were treated by prolonged narcosis of from eight to twelve days, by means of a combination of drugs to which the name of "Cloetta mixture" was given. This mixture, which contained paraldehyde, amylenhydrate, chloral hydrate, alcohol, isopropylallyl barbituric acid, digalen and ephedrine hydrochloride, was given rectally in diluted form. The author claimed that by its use, complications were considerably lessened.

Case Reports.

The following case reports illustrate in detail the types of illness dealt with, together with the individual reactions and complications observed. The cases are grouped in the order of females (Nos. 1 to 18), followed by males (Nos. 19 to 32). In both series the numbering has been arranged according to the date upon which treatment was commenced.

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CASE 1. A mixed manic reaction type of 10 weeks' duration. Treatment followed by recovery which has been maintained.

M.R.B., a book-keeper aged 24 years, was admitted to the Glasgow Royal Mental Hospital on 5/6/34. The family history was negative. From 4 years till 14 years of age, she had periodic attacks of what was diagnosed as chorea, but probably was something quite different. For nights on end, while sleeping, her muscles showed general twitching. These attacks would be present every night for several weeks and then pass off for a year or more. At the age of 5 years, she had a convulsive seizure, epileptiform in type. According to her father's description, she became cyanosed, her muscles rigid, following which she developed muscular twitchings lasting a few minutes. The spasms which occurred in childhood during the night were, therefore, probably of an epileptic, and not of a choreic nature. If she was upset for any reason as a girl, she would get "heady" and talk in a confused rambling fashion for some hours. Her general intelligence appeared to have been below the normal and she failed in her Leaving Certificate examination. After leaving school, she obtained an excellent appointment in the Shell-Mex offices. The work was exacting. She was reserved and her only friend was a girl whom she had known since childhood. Her colleagues in the office seemed to look upon her as a child and made fun at her expense.

For a few months before admission, she had been friendly with a young man who worked along with her and who championed her

against the other girls. Secretly she developed a great admiration for him. Her mother appeared to have brought her up very strictly and allowed her little freedom or liberty.

The present illness was of 10 weeks' duration. She became easily fatigued, had no inclination to go out and sat in the same chair all night. Her work began to suffer and she got mixed up in her calculations. One day in the office she collapsed suddenly on the floor. No details of the nature of this "seizure" were available. She was brought home in a very confused and emotional state. The "seizure" lasted a few minutes and was possibly a recurrence of the attacks which she had had in childhood.

She was admitted in an excited condition, constantly talking, sitting up in bed and gesticulating. Sudden changes of her mood occurred from time to time and she had spells of emotional weeping. She slept badly and took little food. She began to talk in a rapid disjointed fashion and, as a rule, gave a totally irrelevant reply to any question put to her. The following is an example of her conversation at that time :-

"Mother, father and sister dead - I knew it - am I dead too? - is my body full of air? I was outside last night and I can't tell who with. Do you know how I kept myself alive? - is this my death certificate? I've got consumption - I'm getting excited - I can see you and hear you and feel you."

It was evident that she hallucinated frequently. During a conversation, she would suddenly sit up with a start and admit that she heard a voice outside of the window shouting to her. She gave a

description of a conversation which she had had during the night with a 'Mrs. Barbour.' Constantly in her conversation she brought up sexual material; for example :-

"Jimmy Barbour, I kissed last night - thank goodness he's not full of consumption - I'll need to marry him now and I like him. Is that blood rushing through my head? - is that new life going through me?"

At other times she said that she had become blind and deaf.

The diagnosis in this case was rather doubtful. Her general behaviour was compatible with a manic reaction, but the rapid fluctuation of her mood, the marked hallucinations and bizarre remarks suggested a schizophrenia, of the catatonic variety.

For 4 months she remained in the above condition, restless, talking incoherently and mischievous. She would dress in a fantastic manner and dance up and down the ward. She said that she felt quite happy, although she frequently wept bitterly for no obvious cause.

It was in this state that treatment was commenced on 15/10/34. The dosage of somnifaine was as follows: 2 c.c. on the first, seventh and eighth days, 4 c.c. on the second, third, twelfth, thirteenth and fourteenth days and 6 c.c. from the fourth to the sixth, and from the ninth to the eleventh days. Complications were more pronounced with her than with any of the other patients.

The first day she slept very intermittently and at times between injections she became restless and complained of severe

headache and giddiness. From the second day onwards the narcosis was more satisfactory. Occasionally she would become resistive and moan for hours at a time. On the fourth day an erythematous scarlatiniform rash appeared on the chest and spread to the abdomen. It became especially pronounced along the attachment of the diaphragm. It was associated with marked itching. On the sixth day the eruption spread to the face and limbs. On the eighth day it gradually faded and a fine desquamation could be seen on the face and chest. By the eleventh day the rash had gone completely.

The temperature remained normal and there was no sore throat, circumoral pallor or other suggestion of scarlet fever. The rash was treated by the application of calamine lotion.

Cardio-vascular changes: the blood pressure at commencement was 130/90 mm.; fell on the second day to 120/85 mm. and on the seventh day to 105/70 mm. From the seventh day onwards ephedrine gr. $\frac{1}{2}$ was given thrice daily and with it the blood pressure improved to 112/75 mm. The pulse varied from 90 to 110 per minute and was of good quality.

Treatment was stopped on 29/10/34. She was very slow to emerge. She dozed for long periods of the day and when roused, was extremely confused and disorientated for time and place. She was completely out of touch with her surroundings. From time to time she had outbursts of hysterical laughter. At this period - that is, for 3 days following the cessation of treatment - hallucinations were intense. At 10 p.m. and again at 11 p.m. on 2/11/34, she was

actively sick and vomited a large quantity of undigested food. At 2 a.m. on 3/11/34, without warning, she had a typical epileptiform seizure lasting a minute, after which she again vomited. Following the seizure the temperature and pulse rose to 99°F. and 110 per minute, respectively. Eight hours later they had settled to normal. The patient was still very confused and constantly hallucinating. She remained in that state until 6/11/34 when she developed general muscular twitchings involving her face, arms and legs. These continued until 9 p.m. on 7/11/34 when another epileptic seizure occurred, followed by vomiting. At 9.30 p.m. on 8/11/34, a further fit took place.

It was decided to try the effect of intravenous calcium on her as, during the last attack, it had been noticed that her limbs assumed a tetanoid attitude in the tonic stage. Accordingly, 10 c.c. of calcium gluconate were given intravenously and calcium Sandoz 2 drams by mouth 4-hourly. For 12 hours after injection she continued to have muscular twitchings and a further 10 c.c. of calcium gluconate were given intravenously at 10 a.m. on 9/11/34. After that injection she had no recurrence of her convulsive movements.

During the next few days, a gradual improvement took place. Her confusion lessened and her hallucinations passed away. By 12/11/34 she was remarkably well. When examined at this time, she appeared happy and smiled sweetly. She realised that she had been ill. She vaguely remembered her hallucinations, but now stated

that they had completely passed off. However, she had no realisation of the serious nature of her trouble. She stated that she did not get on at the office as the rest of the girls had been very "catty" to her. Following the day when she collapsed her memory was very vague. She had no recollection of coming into Hospital, of the days which followed after, or of the time she was under treatment. Even yet her conversation tended to wander. She was childish in her talk and behaviour, though the former was quite rational and coherent.

During the next month the improvement continued, and at the time of her discharge on 14/12/34 her behaviour was much more in accordance with her age. Her orientation was good; she was looking forward to going home and felt quite fit to face the world again.

For 3 months after leaving Hospital, she remained at home happy and contented, showing little interest in current events and allowing the days to drift by. She then began to read the papers, go out to the church and to the cinema. By May, 1935, she commenced a further course of business training, following which she secured employment: she has now been working in the Inland Revenue offices for 2 months. Her father states that she is perfectly well, sleeps soundly and has an excellent appetite. She still does not remember coming into Hospital, or the events which happened between then and the completion of her treatment.

Pathological findings. The urinary output varied from 20 to

35 oz. per day. She was incontinent. There was a trace of albumin from the fourth to the sixth days and on the twelfth and thirteenth days. Sugar was present in definite quantity on the tenth day. Acetone was nil. The urinary acidity increased to 84° on the fourteenth day. A trace of albumin and sugar continued daily in the urine until 20/11/34.

	<u>White Blood Cells.</u>	<u>Weighted Mean.</u>
15/10/34:	5,240	1.6
16/10/34:	5,550	1.8
17/10/34:	6,580	1.75
18/10/34:	4,780	1.40
19/10/34:	4,730	1.55
20/10/34:	8,150	1.46
21/10/34:	5,510	1.24
22/10/34:	9,290	1.38
23/10/34:	7,830	1.34
24/10/34:	4,520	1.5
25/10/34:	4,990	1.57
26/10/34:	5,250	1.74
27/10/34:	4,890	1.56
28/10/34:	5,740	1.44
2/11/34:	4,890	1.54
5/11/34:	8,350	1.78
8/11/34:	9,540	1.63
10/11/34:	6,080	1.86
15/11/34:	7,490	1.46
27/11/34:	5,150	1.93

<u>Differential count:</u>	<u>15/10/34.</u>	<u>28/10/34.</u>
Polymorphs:	67.5	51.
Eosinophils:	.5	2.5
Lymphocytes:	19.5	40.
Mononuclears:	12.	6.5
Basophils:	.5	Nil

The differential count shows, therefore, a fall in the polymorphs, with a marked increase in the lymphocytes.

On 8/11/34, before the administration of calcium gluconate, a bio-chemical examination was performed, with these results :-

	Total:	22.5 mgm. %
Phosphates:	Inorganic:	3.5 mgm. %
	Combined:	19.0 mgm. %
Serum Calcium:		9.1 mgm. %

On 4/12/34 after the fits had ceased and the patient's condition had improved, bio-chemical estimation was as follows :-

	Total:	22.6 mgm. %
Phosphates:	Inorganic:	3.4 mgm. %
	Combined:	18.6 mgm. %
Serum Calcium:		10.3 mgm. %

CASE 2. Paranoid schizophrenia of 7 years' duration. Treatment followed by slight temporary improvement.

L.D.H., a secretary aged 37, was admitted to the Glasgow Royal Mental Hospital on 2/3/34. The family history was negative. Her illness had begun in October 1927 when it was noticed that she was becoming depressed and was worrying over trifles. She imagined that people were talking about her and constantly watching her, and she thought that advertisements in the papers had a personal reference to her. She became very asocial, would sit for hours by herself, and at times was evidently hallucinating. For 2 years she was in Hartwood Asylum, but left there in July 1933 without improvement.

On admission she was extremely suspicious and antagonistic in her attitude. She was very deluded and hallucinated. She felt that she was being spied on and that people were slandering her. She would become emotional on the least provocation. She said that people had misjudged her, thinking that she was a bad woman and did not believe in God. She kept herself aloof from the rest of the patients and spent most of her day sitting by a window, sewing, but occasionally giving voice to her delusioned ideas. Physically, she was a well-built woman. Examination of the heart showed enlargement to the right, with accentuation and reduplication of the second pulmonic sound. There was a systolic murmur localised to the apex. No abnormality was detected in the lungs, abdomen or nervous system.

This patient was commenced on somnifaine on 18/10/34, and throughout the course proved a constant source of worry as a result of the many complications which developed. The first injection was given at 4.10 p.m. At 8 p.m. she became violently sick and vomited at intervals during the remainder of the first, and the whole of the second day. On account of this somnifaine was withheld for 24 hours. At 10 p.m. on the third day, an erythematous scarlatiniform rash appeared on the thighs and spread to the abdomen and chest. There was no associated rise of temperature. On the fourth day the rash gradually faded, and by the fifth day it had disappeared. She perspired freely throughout the treatment. On the sixth day she had a troublesome, irritating cough, but without any signs in the chest. At 10 p.m. on the fourteenth day - 12 hours after her last injection - the temperature suddenly rose to 103°F. Her body became rigid and arched into an opisthotonic posture. There were definite signs of meningeal irritation. A lumbar puncture was attempted, but was found to be impossible on account of the rigid state of her lumbar muscles. Her body and neck were fully arched backwards and the limbs were spastic. There was intense nuchal rigidity and Kernig's sign was obtained.

During the condition she was gradually emerging from the effects of the narcotic. She was very emotional, constantly sobbing and weeping. Her speech was thick and slurred. The pupils were dilated and sluggish. During the whole of the fifteenth day (1/11/34) she remained in this state, the temperature

rising at 10 p.m. to 103.6°F. On 2/11/34 the condition gradually passed off and the temperature subsided. By 2 a.m. on 3/11/34 the rigidity had completely disappeared and the temperature was normal, but she complained of severe pains in the back and limbs, and headache. In spite of these complications narcosis was very satisfactory. She slept deeply most of the time, waking up occasionally between injections, moaning and talking a little in a slurred voice. On the first day 2 c.c. of somnifaine were given; on the eighth and tenth days, 4 c.c.; and on the remaining days, 6 c.c. The blood pressure at the commencement was 125/80 mm.; it fell on the second day to 115/75 mm. and remained fairly stationary at that level throughout the course. The temperature showed considerable disturbance. During the first week there was a daily variation from 97.4°F. to 98.4°F. From the ninth to the thirteenth days the temperature varied from 97.4°F. to 99°F., being lowest in the morning and highest in the evening. The rise on the fourteenth day has already been noted.

Urinary findings. Retention of urine was another important feature in this case, and she required catheterisation daily from the third to the ninth days, from the tenth to the twelfth days and on the fourteenth day. The daily urinary output varied from 25 to 40 oz. A trace of albumin was detected in the urine on 1/11/34, i.e. when she showed signs of meningeal irritation. A trace of bile was found on the third and fourteenth days; otherwise urinary examination was negative.

This patient 4 days after cessation of treatment was definitely a little brighter and conversed more freely than she had done previously. This state of improvement lasted for 4 to 6 weeks. During that time she took more interest in her surroundings and did not speak about her delusional ideas. This improvement was only temporary and she gradually passed into a similar condition as before treatment. She is now very asocial, suspicious and antagonistic in her attitude, hallucinates frequently and occasionally accuses the staff and other patients of slandering her.

A detailed blood count was done in this case, as follows :-

	<u>Poly.</u>	<u>Eosin.</u>	<u>Lymph.</u>	<u>Mono.</u>	<u>Baso.</u>	<u>Wt. Mean.</u>
Commencement:						
18/10/34:	64.5	3.5	28.5	2.0	1.5	1.6
20/10/34:	75.5	1.0	20.0	2.5	1.0	1.64
22/10/34:	69.0	4.5	21.0	5.5	Nil	1.54
23/10/34:	75.5	3.0	17.5	4.0	Nil	1.67
24/10/34:	72.5	5.5	19.0	1.5	1.5	1.37
25/10/34:	72.0	6.5	17.0	4.5	Nil	1.67
26/10/34:	68.5	6.0	22.5	3.0	Nil	1.51
27/10/34:	62.0	4.0	28.5	3.5	2.0	1.68
28/10/34:	66.5	4.5	22.5	1.5	2.0	1.49
29/10/34:	75.0	3.5	20.0	1.5	Nil	1.61
30/10/34:	69.5	4.5	20.0	4.0	1.0	1.60
31/10/34:	81.0	0.5	14.5	3.5	0.5	1.61
1/11/34:	83.5	0.5	6.0	10.0	Nil	1.48
2/11/34:	82.5	Nil	8.0	8.0	0.5	1.64
(Fits at 11.50 p.m.):						1.75
5/11/34:	68.0	2.0	25.0	4.5	Nil	1.44
10/11/34:	69.5	5.0	23.0	1.5	1.0	1.78
15/11/34:	71.0	5.5	20.0	2.5	1.0	1.91
27/11/34:	52.5	8.5	32.0	6.0	1.0	1.90

CASE 3. Involitional melancholia. Treatment followed by remarkable improvement lasting a week.

F.M., a housekeeper aged 48, was admitted to the Glasgow Royal Mental Hospital on 12/9/35. Previous to her illness she had been an unusually clever and capable woman, though highly-strung and over-conscientious. Three months before admission, she had gradually become more and more depressed. She became restless, sleepless and agitated and spoke of little incidents in her past life as being unpardonable sins.

On admission, she was very distressed. She was filled with ideas of sin and guilt. She stated that she had buried a Bible, and because of this the Devil had taken possession of her.

"Judas has come alive again," she would say. "I am Judas - a living death - I will never die - nobody can save me. Something terrible has happened - I buried the Bible - I just thought it was another book - because of this my sister is to be twisted and turned into something else. Look at them all - they are all dead - it's all my fault - Now God has told me to say no more - This is going to be an awful death - nobody believes it, but it's quite true."

Her grasp of events and her memory were unimpaired. For over a year she remained in Hospital in the above condition: in fact, she steadily got worse. She would not lie in bed, struggled violently with the nurses, wandered about in her nightgown and attempted to get out of the ward. She kept constantly chewing her clothes, working with her hair and biting her hands. The feelings of guilt became more intense and every death which occurred in the Hospital

she believed had been brought about by her. At times she became acutely agitated, catching tightly on to members of the staff and refusing to let go. Physically, she was a thin woman of florid complexion. No organic disease was detected.

In the above condition treatment was commenced on 28/11/34. She reacted extremely well and remained in a satisfactory narcosis with from 2 to 4 c.c. per day. Occasionally she would move about in bed, but seldom spoke. She perspired freely. The blood pressure at commencement was 125/85mm; fell on the second day to 110/80 mm. and continued at that level. Twenty-four hours after completion of the course the blood pressure rose to 135/85 mm. The temperature remained normal apart from a slight rise to 99°F. on the fourth day. She was constipated and required regular enemata. During the course there was a lack of tone in all her muscles. The knee jerks were very feeble; the pupils sluggish to light. On stroking the sole of the foot marked drawing up of her legs occurred. The plantar response was indefinite.

Urinary findings. She required catheterisation on the sixth day following 48 hours' retention. There was a trace of albumin on the eighth day and a trace of bile on the twelfth and fourteenth days. Reactions for sugar and acetone were negative.

Twelve hours after the last injection on 12/12/34, she gradually awoke. She spoke in a slurred, drawling voice, saying, "I am all right - let me get away." By the afternoon of 13/12/34, she was very emotional, weeping bitterly, "I want to get home - I want Katie." She knew where she was, but could not give the day,

and had no idea how long she had been under treatment. On the morning of 14/12/34, she was very much brighter. She was correctly orientated for time and place: "I am better - I want to get home to my sister - I have been here long enough." On 15/12/34, she was extremely well. Her agitation and distress had vanished. She spoke in a soft-toned voice, and asked when she would be able to get up and go back to her work. She was questioned concerning her former ideas :-

"I feel back to what I used to be - I don't know what possessed me. I don't know why I stood behind doors and all that sort of thing. I don't know why I bit my clothes. It was a ridiculous idea about the Bible - in any case my sister lifted it after I buried it. I always wanted to hide myself here and be alone. I don't want to pull my clothes like I did."

Though a little dull, she showed no kind of emotion or agitation. For 8 days she remained well. She slept naturally at night, dressed herself in the morning and even went out for a short walk in the grounds. On 21/12/34 within 24 hours, she relapsed into her former state. On the morning of that day, she had dressed herself as usual; by mid-day she was slightly emotional and started to bite her fingers and pull at her clothes. In the evening, she was very agitated, and it was evident that her old ideas were quickly returning. Since then she has remained in Hospital, and is still restless, distressed and difficult, and feels that all the misfortune and misery in the world has been brought about through her misdeeds.

CASE 4. Catatonic schizophrenia of 6 months' duration. No improvement resulted from treatment.

A.B., a clerkess aged 19, was admitted to the Glasgow Royal Mental Hospital on 13/12/33. She had always been a very quiet, reserved girl, and below the average in intelligence. The illness was of about 6 months' duration and had been of sudden onset. One day, for no apparent reason, she had started to laugh in a foolish manner, became very rambling in her talk and restless. She remained in that state for a few weeks. She spoke of incidents which had happened in her childhood. She complained of aches and pains all over her body, and refused to remain alone at nights because she felt afraid. She gradually quietened down, and became dull and depressed.

On admission, she lay in bed with her face covered up by the pillow. Her expression was one of misery and despondency. She kept sobbing and moaning, but would not speak. When asked a question she became emotional in a way that was almost half-laughing and half-crying, bit her fingers and mumbled a few incoherent remarks. She was very impulsive. She would suddenly throw herself out of bed, and on one occasion raced to the window and put her hand through a pane of glass. Apart from these episodes, she lay in bed most of the day in a curled-up attitude. She was resistive, difficult with her food and during her impulsive outbursts, required injections of hyoscine. In April 1934, she received a course of Pyrifer, but without benefit.

Physically, she was a healthy, well-coloured young woman. She suffered from a chronic otorrhoea.

Treatment was commenced on 29/11/34. The dosage varied from 2 to 4 c.c. per day. Though deeply under the influence of the drug, she remained resistive and occasionally muttered away incoherently. The pupils were sluggish; the knee jerks were diminished; the plantar response remained flexor. During the course there were frequent twitchings of her mouth. On the second day she had a bout of vomiting. The bowels were constipated. The blood pressure at commencement was 135/80 mm.; fell on the second day to 105/70 mm., and on the fourth day to 90/65 mm. Ephedrine gr. $\frac{1}{2}$ thrice daily was given and with it the blood pressure improved to 105/70 mm. On the ninth day the pulse became very feeble and increased in rate to 120 per minute. She was given one c.c. of pituitrin and one c.c. of camphor in oil. In 8 hours the condition of her pulse improved considerably. Two days after the last injection the blood pressure rose to 148/95 mm. On the fifth day there was a rise of temperature to 100°F., but this fell to normal within the next 4 hours. The respirations in this patient became very deep and remained at 20 to 24 per minute. She perspired freely.

Urinary findings. She was incontinent throughout. The urinary output varied from 30 to 40 oz. per day. A trace of albumin was present in every specimen. There was a positive reaction to acetone on the second and third days.

For 3 days after the conclusion of treatment on 13/12/34, she remained extremely confused and disorientated. She lay on her back, rigid and stiff, with her eyes wide open.

"It's an earthquake - all over - just now - Friday, September - Gilbert knows - I do' know - I do' know."

She gradually emerged, but no improvement was noticed. She remains inaccessible, resistive, and extremely impulsive. She lies in bed covered up by the clothes, and occasionally mumbles a few incoherent remarks in a weeping tone of voice.

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CASE 5. Depression of a year's duration, characterised by marked suicidal tendencies. Treatment was followed by slight temporary improvement.

M.M.M., a shop assistant aged 39, was admitted to the Glasgow Royal Mental Hospital on 5/12/34. She had always been of a worrying disposition and of a sensitive nature. She had no hobbies or outside interests. At the age of 24, following pneumonia, she was depressed for a few weeks. The attack cleared up and she remained well until the spring of 1934, when, on being examined by a doctor, she was told that her chest was weak. She became greatly distressed over this as she always had had a dread of consumption. She was subsequently re-examined, and an attempt was made to reassure her that nothing serious was wrong, but without effect. Her depression became gradually worse and feelings of guilt became manifest. She believed that she had done something serious and had a terrible fear that a dreadful calamity was about to overtake her.

On admission, she was anxious, agitated and wept for long periods of the day. She spoke in a pleading voice :-

"I want to get well. I wonder when I'm going home. You're going to make me well, aren't you?"

On numerous occasions in the Hospital, she made attempts at suicide. At one time she put her hand through a window, and at another time, seized a bottle of iodine, intending to drink it. She continued in this depressed, emotional, suicidal state for over a year, re-

quiring a nightly dose of medinal or other sedative. She was a thin, anaemic woman, but no signs of organic disease were detected.

Treatment was commenced on 18/1/35. Two c.c. of somnifaine were given on the first, sixth and fourteenth days, 4 c.c. from the second to the fourth, seventh to the tenth, and thirteenth days, and 6 c.c. on the fifth, eleventh and twelfth days. She slept very well, though occasionally wakening up between injections and asking in a slurred voice if she would get better and be allowed home. The temperature remained normal apart from a slight rise to 99.2°F. on the twelfth day. The blood pressure had always been low - 110/80 mm. Three days before the commencement of treatment, she was put on ephedrine gr. $\frac{1}{2}$ thrice daily, and at the time of the first injection the blood pressure had risen to 120/85 mm. On the second day it fell again to 108/80 mm., and on the seventh day to 100/65 mm. She perspired freely.

Urinary findings. The urinary output was well-maintained: she was occasionally incontinent. A trace of albumin had been found previously and continued throughout the course. Sugar was present on the first and tenth days and a trace of acetone from the second to the fifth, and from the ninth to the twelfth days.

Following the last injection, she remained asleep for 24 hours and then gradually emerged. She was still emotional, though much less distressed than she had been before the course. Within a few days she was able to be up and sat reading at the fire. There was a decided, though slight change for the better in her mental state. She was more settled, took her food well and made

no attempts at suicide. She was still sleepless and required
medinal every night. She complained of extreme weakness following
the treatment.

She was taken home by her parents on 23/2/35 as it was
hoped the change would be beneficial to her. However, this was
not the case, and in a few weeks the slight improvement passed
off and she again became very distressed, emotional and suicidal.
In that state she was readmitted on 1/8/35.

CASE 6. A manic depressive. Treatment in hypomanic phase followed by gradual recovery without further attacks.

F.E., aged 21, was last admitted to the Glasgow Royal Mental Hospital on 18/1/35. She was a manic depressive, and since the age of 16 had suffered from several attacks of acute depression, during which she became stuporose. After each of these she gradually passed into an acute mania which lasted several months, and was followed by recovery. Her states of well-being were of short duration as she so rapidly passed from depression into mania, and vice versa. Physically, she was a stout, well-nourished young woman.

On her last admission, she was in a hypomanic phase which had followed on a severe depression of several months' duration. She was bright, cheery and talkative, taking an active interest in everything going on around her. She would laugh heartily and sing and dance for most of the day.

In this hypomanic phase, somnifaine was commenced on 31/1/35. She herself had asked to have the treatment. She always had an excellent insight into her illness, and hoped that the course would prevent her from passing into a future depression. Four c.c. were given on the first, from the third to the sixth, and on the ninth and fourteenth days; 6 c.c. on the second, seventh, eighth, and from the tenth to the thirteenth days. Though deeply narcotised by the drug, she exhibited throughout the course purposeless movements; e.g., she would

throw her arms up, toss about in bed so much that on one occasion she actually fell on to the floor. Occasionally, when due an injection, she became emotional, moaning and weeping. The temperature remained normal from 97°F. to 98.4°F.; pulse from 76 to 92 per minute. The blood pressure at commencement was 130/86 mm., fell on the second day to 120/70 mm. The pressure remained at 110/70 mm. and 125/75 mm. during the course. Constipation required treatment by enemata.

Urinary findings. The urinary output varied from 16 oz. on the fourth day to 38 oz. on the eleventh day. There was a trace of albumin on the second, sixth and eighth days; a trace of sugar on the eleventh day and a trace of acetone on the eleventh day. Acidity increased to 72° on the eighth day with the administration of potassium citrate gr. 20, 4-hourly; it fell gradually to 22.5° on the fourteenth day.

No complications occurred in this patient. She emerged very quickly, and for a week showed little improvement. She was still hypomanic, constantly talking, singing and laughing. She then gradually settled down, and on 24/4/35 she left the Hospital and has remained well since. This period of a year is the longest spell which she has had free from a mental breakdown since the age of 16.

CASE 7. Depression of 3 months' duration. No improvement followed treatment.

Mrs. A.H.B., a married lady aged 38, was admitted to the Glasgow Royal Mental Hospital on 19/1/35. Her early life had been quite uneventful. She had been married for 9 years, but had no family. Her present symptoms had begun 3 months previous to her admission when she went off her food and complained of a lump in her throat, believing that she had cancer. This idea passed off after she had received medical advice, but she became increasingly depressed. She kept constantly worrying over expense and money. She suffered from severe insomnia for which ordinary sedatives brought little relief.

On admission, she was very distressed. She sat up in bed wringing her hands and weeping bitterly. She described a terrible sadness which had come over her and which she could not get rid of. Everything she used to enjoy now made her miserable. She was constantly tormented in her mind by something quite indescribable.

"I can't be at peace," she would say. "I have no worries - just utter sadness which I can't get rid of. It isn't easy to describe - a sort of despair - an acute sadness."

Following on admission, she gradually became more agitated and depressed, and on account of this somnifaine was commenced on 26/2/35. She was very agreeable to have the treatment performed

and kept asking whether it would be beneficial to her. Six c.c. of somnifaine were given per diem for a fortnight, but even with this dose she would at times waken, sob and moan for short periods, and ask in a slurred voice whether she would get better. At 10 a.m. on the fourth day she was actively sick, vomiting a large quantity of yellowish fluid. Throughout the same day she complained of nausea associated with the regurgitation of mouthfuls of fluid.

During the course she perspired freely. On the fourth and ninth days she was incontinent. The bowels were constipated and required enemata. The pupils reacted sluggishly and the knee jerks were diminished. There was slight rise of temperature on the eleventh and fourteenth days to 99.6°F. The pulse ranged from 84 to 108, quality variable and at times the pulse volume was small. The blood pressure at the commencement was 125/80 mm.; on the second day, 110/72 mm.; on the third day, 108/92 mm. On the ninth day it had fallen to 100/65 mm., but rose on the tenth day to 110/70 mm., at which level it remained until the end of treatment.

Urinary findings. The urinary output measured from 15 oz. on the sixth day to 46 oz. on the thirteenth day. A trace of albumin was seen on the first, third, seventh and ninth days. A trace of acetone was detected on the third day.

On this patient a blood calcium estimation was done before and after treatment. Before treatment the blood calcium was 10.2 mgm. per cent.: after treatment, 8.7 mgm. per cent.

This patient emerged slowly from the narcosis, but as she did so no definite improvement could be detected in her condition. She remained distressed and felt that she could not settle down because of the sadness which kept coming over her. After the conclusion of the treatment other sedatives had to be given at night in order to ensure sleep. She felt very disappointed because the treatment had not helped her as she had hoped it would have done. She left the hospital on 23/3/35 in order to have a trial under home conditions, but without success, and she was readmitted in July 1935 in an extremely distressed and agitated state.

This patient received a good deal of psycho-therapy following her course of treatment. Attempts at reassurance and discussion of her symptoms and their likely cause were without avail. She complained of terrible pains in her head and her back, and choking in her throat. She did routine jobs about the ward, but systematic occupational therapy was useless. She could not concentrate; something went on in her head like "sand-paper" rubbing her brain. She had a hazy recollection of the treatment and remembered getting some of the injections, but was very confused and even, during her wakeful moments, quite disorientated. As soon as she emerged from the narcosis, she stated that the depression was still there, but that she had tried to combat it as much as possible. She could not say that the treatment had produced any real beneficial effect.

CASE 8. Involuntional melancholia of some months' duration.

Two courses of treatment were given, both followed by remarkable improvement.

Mrs. J.C.B., a married lady aged 49, was admitted to the Glasgow Royal Mental Hospital on 13/6/34. The illness had been of several months' duration. Following an operation for uterine prolapse, she had become nervous, sleepless and easily upset.

Her condition gradually progressed, and on admission she looked physically exhausted. She sat up in bed, tugged at the clothes, and conducted a disjointed monologue, each group of words being apparently unconnected, and separated by long periods of whimpering and sobbing. She seldom spoke and took very little food. She had the appearance of agitation and acute depression. She refused to lie in bed and wandered about the ward muttering away to herself in an incoherent fashion. She was extremely tense and resistive, and it was with the greatest difficulty that she was fed and had her daily needs attended to.

She would pick her skin and was constantly wringing her hands. Occasionally she got into a state of panic, would rush about the room and attempt to get out of the door whenever it was opened. It was extremely difficult to get into touch with her. A few remarks such as :-

"I didn't do as I should, - Forces are against me - I don't know - My power's left - I am really in two halves - I can't hold anything - My right hand's paralysed - What am I to do? I can't explain,"

were about all that could be obtained. She would make a statement of that nature and then struggle to get away without continuing any further. Physically, she was in a very toxic state. Her tongue was coated and her complexion muddy. There was a marked degree of pyorrhoea associated with foetor oris.

For a year she continued in the above state and somnifaine was commenced on 26/2/35. Throughout the whole course a really satisfactory narcosis was not obtained. The injections served to render her unconscious, but there remained the tense resistiveness which had been a characteristic feature in her case previously. Feeding her with sufficient fluids was always difficult.

Six c.c. of somnifaine were given per diem until the eleventh day when treatment had to be stopped on account of a marked pyrexia. At the beginning her temperature was 97.2°F. and remained normal till the fifth day, when it rose to 99°F. It continued above normal: on the sixth day, 99.4°F., seventh day, 100.2°F., eighth day, 99.6°F. and on the ninth and tenth days, 100.2°F. At 10 a.m. on the eleventh day the temperature shot up to 102.8°F. Somnifaine was withheld and she was given rectal salines, 10 oz., with glucose every 4 hours. By 2 p.m. on the twelfth day the temperature had fallen to 97.8°F. No further rise was noted. The pulse and respiration rate rose along with the temperature to 120 and 24 per minute respectively. Nothing abnormal was detected in the lungs to account for the pyrexia. No further injections were given.

At the commencement the blood pressure was 165/100 mm.; on the third day, 135/90 mm.; by the ninth day it had fallen to 125/90 mm. After cessation of treatment it rose within 48 hours to 155/100 mm. During the course the knee jerks were increased and there was some ill-sustained ankle clonus. The pupils reacted sluggishly to light. The plantar reflex was flexor. She perspired freely during the course. There was constipation throughout.

Urinary findings. The output varied from 14 to 37 oz. per day. From the seventh day onwards she was persistently incontinent. A trace of albumin was present from the second day onwards. Acetone was detected in the urine before treatment was commenced and continued during and for a prolonged period afterwards. The urinary acidity rose to 42°.

Treatment was concluded on 8/3/35. Following treatment, a serum calcium estimation was carried out. The result obtained was 8.6 mgm. Ca. per cent. On account of this low figure she was given calcium sandoz by mouth for several weeks.

For a week following the last injection, she remained extremely restless and resistive. She struggled violently when an attempt was made to do anything for her; she kept on muttering incoherently and appeared confused and disorientated. During that period paraldehyde and chloral were given every night, and with them she would sleep for a few hours. At the end of the above period, she quickly showed an extraordinary recovery. Within 24 hours she changed completely from a state of resistive

depression to one of comparative well-being. She got up, dressed herself, talked perfectly clearly and sat down at table to have her meals. She spoke of going home and had every confidence that she would remain well. At times she was quite bright and smiled and laughed pleasantly. Physically, she was looking much better and her skin was clearer and less toxic. She did not talk much about her illness and appeared to have very little insight into it. She had a very hazy recollection of the events which took place after her admission to hospital, and had a complete amnesia for the period during which she was undergoing the treatment. It was really remarkable how this lady within a day showed a complete resolution of her symptoms. She left on 9/4/35 and went home with her husband.

For 6 weeks she maintained her improvement, though she was occasionally a little excitable when she talked incessantly. She met her friends, entertained them, and went out regularly in her car. At the end of that period she gradually began to relapse. She became dull, did not want to meet anyone and would pace about the floor muttering to herself. She gradually became worse, refused to dress herself or take sufficient food.

She was readmitted on 25/6/35 in a condition similar to that in which she had been before treatment. She was very agitated and depressed, constantly asking to get home and pleading with us to send for her husband. She showed a curious indecision: when approached she walked away and yet if one was leaving her, she would follow one.

She continued in that state until February 1936 when a further course of somnifaine of 14 days' duration was given. During this latter course, she required tube-feeding daily. On its conclusion, a result identical with that following the previous course was obtained. For a week she was confused and resistive; then within 24 hours, she cleared up and is now (31/3/36) perfectly well. Whether this second improvement will continue or not is difficult to say.

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CASE 9. Chronic depressive state of many years' duration.

Treatment followed by recovery lasting 4 months.

Mrs. A.A.V., a married lady aged 42, was admitted to the Glasgow Royal Mental Hospital on 19/3/35. Since the age of 19 years she had been mentally unstable, though the symptoms had never become really severe until 5 years ago when she had a severe attack of depression. She was quite a capable woman. She married 15 years ago, but has had no children.

For hours she sat in the house in a distressed agitated state, bemoaning her condition, saying that she would never get better, and could do nothing to help herself. She had suffered from menstrual irregularity which had improved after the administration of menformon.

On admission, she complained, as she had done for many years, of feeling weak, easily tired and exhausted. If she worked too hard she got dizzy and had to lie down. She felt her back weak so that at times she could hardly sit up. She was constantly worrying over her health, being afraid that something was wrong with her stomach or her bowels. She was slightly depressed, but she could smile and look quite pleasant. She herself asked to receive a course of somnifaine as she had heard of the treatment and wished it to be carried out in the hope that she might obtain some relief from her depressive ideas.

The treatment was started on 20/3/35. The physical examination before treatment was quite negative. The blood

pressure was 120/75 mm.; temperature 97°F., pulse 80 per minute, and respirations 20 per minute. Two c.c. of somnifaine were given at 11.30 a.m. and by 12.30 p.m. she was sound asleep. Six c.c. per diem were required to keep her in a state of narcosis, but this was not attained until the fourth day. At 6 p.m. and at 9 p.m. on the first day, she became violently sick and vomited curdled milk. On the second day at 6 a.m. she had a further bout of vomiting, and complained of severe giddiness. On the third day she had troublesome flatulence. On the fifth and sixth days there was occasional nausea with regurgitation of mouthfuls of fluid. From the seventh to the fourteenth days, narcosis was very satisfactory and free from the minor complications of the early stages. The temperature showed a daily swing, highest at 10 p.m., lowest at 10 a.m. The highest temperature was 99.6°F. on the ninth and eleventh days. The pulse varied from 76 to 104 per minute. The blood pressure fell on the second day to 105/70 mm.; on the seventh day it was 100/70 mm. and it remained at that level until the end of the treatment. To combat the nausea in the early stages, fluid magnesia was given freely. The treatment was concluded on 2/4/35. Throughout she perspired freely.

On the third, ninth and fourteenth days she was incontinent. The urine passed measured from 14 oz. on the fourth day to 46 oz. on the fifth day. During the narcosis her pupils reacted sluggishly and her knee jerks were difficult to elicit.

Urinary findings. A trace of albumin was detected on the

first and second days, and from the fifth day until the end of treatment. Sugar and acetone were absent during the course. Urinary acidity remained from 25° to 32°.

The narcosis gradually passed off in from 24 to 48 hours after the last injection. At first she talked in a confused, rambling fashion, disorientated as to time and place. By 6/4/35 she was remarkably bright and cheery, and thanked us all for our kind attention. Her symptoms, she stated, had all disappeared. She had ceased to worry about her bowels and she was now looking forward with hope to the future. She remained very well until August 1935 when she nursed her mother through a 4 weeks' illness. The mother died and gradually since then her neurotic symptoms have returned. She has now the same feelings of exhaustion, dizziness and inability to concentrate.

CASE 10. Paraphrenia of several months' duration. Treatment followed by recovery lasting for 4 weeks.

Mrs. M.F.S., a married lady aged 46, was admitted to the Glasgow Royal Mental Hospital on 3/7/34. Her husband gave a history of the gradual development of delusions of persecution and hallucinations over a period of several months. The family history was negative. Her early life had been quite uneventful. She had been a clever capable woman, highly vivacious, sociable and a good mixer. She tended to be headstrong and when she had formed an opinion, adhered to it. She had married at the age of 26 and had three children, the youngest being 12 years old. After the birth of the last child, she had suffered from uterine haemorrhage.

The first symptoms had begun 6 months before her admission. She would mention the names of her neighbours, saying that they were talking about her and accusing her of certain things. She believed that they followed her about and were going to blackmail her.

Examination on admission showed that she was intensely hallucinated and suffered from strong ideas of persecution. The neighbours, she said, believed that she was a bad woman and a special newspaper had been published broadcasting her misdeeds. Men had been flashing lights, and the neighbours and her husband had a secret code which they used to communicate with each other. She had heard hints for years that her husband had been keeping

company with other women. She believed that she was being spied on wherever she went.

Physically, she was a healthy woman, of good physique. Heart and lungs were normal. She complained of some pain in the left iliac fossa which was later diagnosed as being due to an inflammatory mass in the left parametrium. From the time of her admission up to the commencement of the treatment, she remained in the above state. She had no insight whatever into her condition.

As no improvement had occurred, somnifaine treatment was commenced on 20/3/35. For a week previous to the first injection she had been receiving the usual preliminary treatment with enemata, glucose and insulin. Physical examination on 20/3/35 was negative apart from the slight tenderness in her left iliac fossa. Blood pressure was 130/80mm.; temperature 97°F., pulse 76 per minute and respirations 20 per minute. Urinary examination was negative. She was transferred to a private room at 2 p.m. and 2 c.c. of somnifaine were given intramuscularly at 6 p.m. By 6.15 p.m. she was dosing, and by 6.45 p.m., was in a deep sleep.

From the beginning she reacted very well to the drug, and from the first to the tenth day remained narcotised with 4 c.c. per diem. From the eleventh to the fourteenth days, 6 c.c. per diem were given. Treatment was concluded on 3/4/35.

On the second day of the course, the blood pressure fell to 118/65 mm.; on the sixth day it was 112/65 mm., and on the

ninth day, 105/62 mm., at which level it remained until the end of the treatment. The pulse ranged from 72 to 92 per minute; respirations were constant at 20 per minute. The temperature showed a varying daily swing, raised at 10 a.m., lowered at 10 p.m. The maximum temperature was 99.4°F. on the thirteenth day; the minimum temperature was 96.8°F. on the first day.

Urinary findings. The daily output of urine varied from 18 oz. on the thirteenth day to 58 oz. on the fourth day. On the third, fourth, eleventh and thirteenth days, a trace of albumin was present, as was a trace of sugar on the thirteenth day and a trace of bile on the tenth day. No acetone was detected during the course. She perspired freely throughout.

On the fourth, fifth and sixth days, she had a troublesome hiccough which did not seem to be affected by the dosage of the drug. On the eighth day she had difficulty in swallowing, but by the next morning this had passed off. From the eighth to the fourteenth days, she had occasional incontinence of urine.

For 48 hours after the last injection on 3/4/35, she remained in a deep sleep and then gradually emerged. At first she muttered incoherently and then began to ask questions as to where she was and how long she had been there. This state of mild confusion lasted for 48 hours, and by 8/4/35, a remarkable change had come over her. She showed an amazing recovery. She stated that she felt weak as a result of the treatment, but now denied the presence of hallucinations and spoke no longer of her persecutory ideas. She talked sensibly on general subjects and

also about her husband and family. When asked about her previous ideas, she admitted that she had heard voices and had thought that influences had been brought to bear on her, but now felt that it was all a matter of imagination and could not understand why she had believed these things.

On 19/5/35 she was allowed home as up till that time she had maintained her improvement. After a fortnight at home, however, she gradually reverted to her former state, believing that people were talking about her and sending messages in code, that her husband was not faithful and that she was being slowly poisoned. Hallucinations again became prominent, and she was readmitted on 26/7/35 in a state very similar to that on her first admission.

CASE 11. An obsessional depressive state of many years' duration. Treatment had no effect on the course of the illness.

Mrs. A.T.K., a married lady aged 34, was admitted to the Glasgow Royal Mental Hospital on 19/6/34. In her early years she had been an extremely capable and conscientious woman, but sensitive and reserved. Her illness had dated since 1925 when she developed a febrile attack which was diagnosed as influenza. Since then she had been constantly under medical attention, suffering from a long list of complaints. She complained of a bearing-down feeling of her lower abdomen; she felt that her heart was weak and the least exertion brought on marked exhaustion. She had frequent attacks of vomiting, and the presence of a gastric ulcer was suspected, but not confirmed.

The present acute symptoms commenced 3 years ago when one night a dreadful fear came over her. She felt that she wanted to harm her child and throw herself over the window. Since then terrifying thoughts constantly entered her mind. She remained in a state of extreme terror lest she should harm herself or her child.

On admission she was very emotional, weeping and sobbing bitterly. The tears seemed to flow to her eyes at any time and for no apparent reason; sometimes because of her "thoughts," at other times through sheer "weakness of will."

"Oh, those dreadful thoughts - I hate to talk about them - it makes me worse. Thoughts come into my

"mind that are terrible. I feel I simply cannot be left alone in the house with my daughter without wanting to do her some harm."

Her orientation and memory were unaffected. She would lie in bed for most of the day and make no effort to do anything for herself. She kept complaining of extreme "exhaustion," and said that the least noise put her into a panic. Physically, she was a thinly-built woman without evidence of organic disease.

She remained in this state, and somnifaine was commenced on 28/4/35. She herself had requested that the therapy should be given to her and hoped that it would have some beneficial effect. Four c.c. were given on the first day and 6 c.c. daily from the second day onwards. For the first week she slept very well, but during the second week she appeared to become more tolerant to the drug and in spite of the 6 c.c. per day, was at times wakeful, distressed and complaining of headache and giddiness. She vomited once on the first day, once on the second day and twice on the third day. On the eleventh day she complained of intense itching of her limbs, but nothing could be made out on local examination. The temperature varied from 97°F. to 98.8°F. and the pulse from 72 to 84 per minute. The blood pressure at commencement was 130/80 mm., fell to 120/75 mm. on the second day and remained at that level.

Urinary findings. She was incontinent during the whole course. The urinary output measured from 16 to 34 oz. per day. There was a trace of albumin on the third day and from the ninth

to the fourteenth days. There was a trace of acetone on the tenth day. The urinary acidity rose to 60° on the eleventh day, but fell rapidly after administration of potassium citrate. A complete blood examination was carried out on this patient before and after treatment :-

	<u>White blood cells.</u>	<u>Weighted Mean.</u>
29/4/35:	7,480	1.86
21/5/35:	8,400	1.93
29/4/35:	Total:	24.7 mgm.%
	Phosphates. Inorganic:	2.4 mgm.%
	Combined:	22.3 mgm.%
	Serum Calcium.	9.3 mgm.%
21/5/35:	Total:	24.0 mgm.%
	Phosphates. Inorganic:	2.7 mgm.%
	Combined:	21.3 mgm.%
	Serum Calcium.	9.5 mgm.%

Twelve hours after the last injection, she began to emerge and no marked improvement was noticed in her condition. She remained distressed and required continuance of sedatives every night. For a fortnight after treatment, she complained of extreme weakness and for that time scarcely moved. She lay in bed in a distressed, agitated and weepy state; she talked of being terribly "strung-up," of a nervous feeling being inside her and "churning her up." She had tried, she said, to take an interest in her surroundings, but found that the least thing "knocked her up." Every morning she would complain about the awful night that she had been through. She imagined that something was clouding over her brain and that she felt miles away from everything. She left the Hospital on 27/7/35 in much the same condition as that in which she had been admitted.

CASE 12. A mixed manic state of 3 years' duration. Received 2 courses of treatment, but without improvement.

P.M.W., aged 26, was admitted to the Glasgow Royal Mental Hospital on 14/4/35. She had always been of a bright, cheery disposition, with plenty of friends and wide interests. The illness had been of 3 years' duration. Following an attack of influenza, she became restless, excited and talkative and refused her food. For a time she improved, but 10 months ago, became as bad as before.

On admission, she was very excited. She was incoherent in her speech, restless and destructive. Her mood showed a rapid variation; one minute she would be singing, shouting and laughing and then she would commence without warning to weep bitterly. Occasionally, for short periods of about an hour she was remarkably clear, and would talk in an understanding fashion, but would immediately change from this into violent excitement. Most of the time she spent laughing, giggling and behaving boisterously. Frequently she hallucinated and admitted that she heard her father's and her mother's voices during the night. Feeding was always difficult with her. She would throw her food on the floor, break her plates and so forth. Her talk was foolish and disconnected. Physically, she was a well-developed young woman; no signs of organic disease were made out on examination. In this excited state somnifaine was commenced on 29/4/35.

For the first 3 days narcosis was unsatisfactory: in spite

of 6 c.c. per day she did not sleep well, became noisy, restless, and impulsive. From the fourth day onwards she slept much better, though still at times throwing her arms about in a purposeless fashion and trying to jump out of bed. On the first and second days she had persistent troublesome hiccough. On the morning of the third day she had a spell of vomiting. There was a rise of temperature to 99.4°F. on the third day and to 99°F. on the fourteenth day; apart from that the temperature remained normal. The blood pressure at commencement was 110/65 mm., fell on the second day to 95/55 mm., but rose again on the eighth day to 102/60 mm. The pulse rate varied from 84 to 106 per minute and was of good quality.

Urinary findings. She was incontinent throughout the course. Apart from an occasional trace of albumin, urinary examination was negative. Twelve hours after the final injection on 13/5/35, she awoke and became very noisy, struggled with the nurses and resisted violently any attempt to deal with her. She shouted and screamed in an incoherent fashion; her mood changed rapidly and between spells of excitement, she would weep bitterly. The above state lasted for 48 hours when she gradually calmed down and for about a month showed slight, but definite improvement. She slept better, was less destructive and much quieter. She took some interest in her surroundings, knew us all by name, and at times spoke intelligently about her past life and about her parents. She would spend hours writing letters to her friends in a large, sprawling script. After this period she

gradually deteriorated and became increasingly more difficult.

A further course of treatment was commenced, lasting 14 days from 13/9/35. The dosage varied from 2 to 8 c.c. per day. It was very difficult to obtain a satisfactory narcosis in spite of pushing the dose. On the fifth day she had a rise of temperature to 101.4°F. and again on the sixth day to 100.6°F. Associated with the last rise of temperature on the sixth day, the pulse rate increased to 138 per minute and its quality became poor. Two c.c. of icoral were given and coramine 15 minims, 4-hourly for the next 24 hours. Somnifaine was withheld for one day. By the seventh day the temperature had settled to normal and the pulse to 100 per minute and much stronger. The blood pressure was 120/75 mm. at the commencement; fell to 105/72 mm. on the second day and 98/65 mm. on the sixth day. Ephedrine gr. $\frac{1}{2}$ was given 4-hourly from the sixth day.

Urinary findings. She was incontinent during the course. A trace of albumin was present in the majority of specimens as had occurred during the first treatment. Other examination of the urine was negative.

Following this second course, no improvement whatever occurred. After emerging, she was very restless, noisy, destructive and impulsive, and has remained in that state up till the present.

Between the two courses of somnifaine, this patient had a good deal of supplementary treatment in order to put her into as perfect a physical state as possible before the second series

of injections were commenced. Earlier in life, she had suffered from attacks of colitis and lest any toxic focus still existed in the bowel, she was given a prolonged course of yatren (Bayer) and bowel lavage, supplemented by injections of 2 c.c. antibacsyn (Antibody products) on alternate days. Similarly, as menstruation had for some years been irregular, she received a course of menformon (1 c.c. twice weekly) and ovarion tablets (1 thrice daily). (Both ovarian extracts prepared by Organon, Limited).

The above intensive preparation did not improve the result from the second course of somnifaine as had been hoped.

CASE 13. Recurrent attacks of depression over a period of 10 years. Treatment of present attack of 6 months' duration followed by cure.

A.B.W., a secretary aged 35, was admitted on 25/5/35. The family history was negative. Ten years ago she had had an attack of depression following on the death of her mother, and after a few months she had made a good recovery. From then until the onset of the present attack there had been several short spells of depression lasting from 4 to 10 weeks. The present attack had begun in January 1935: she became sleepless and felt extremely exhausted in the mornings. She had difficulty in concentrating, was apprehensive and nervous lest something was going to happen. Occasionally, she would have fits of weeping, during which she kept constantly asking if there was any hope of her recovery. Between her illnesses, she was a clever, energetic, but reserved woman; over anxious and too conscientious.

On admission, she was slightly depressed, but had a very good insight into her illness and could talk at length concerning her symptoms. She herself had requested somnifaine therapy, and hoped that it would cure her. Her main symptom was sleeplessness, and after a sleepless night, she would wake up the following day extremely exhausted and suffering from severe headache. At times her mind felt more or less a blank. A "dullness" came over her head which prevented her from thinking properly. She would become apprehensive and feel that some

disaster was going to overtake her. She was always entertaining hope of her recovery, but each day seemed no better than the previous one. Her memory and powers of orientation were perfect. Physically, she was a well-nourished woman. Apart from a functional systolic murmur at the apex, nothing was detected on examination.

Treatment was commenced on 28/5/35. A satisfactory narcosis was obtained throughout. From the first to the seventh days, 6 c.c. of somnifaine were given daily; on the eighth day, 8 c.c. and from the ninth to the fourteenth days, 6 c.c. Occasionally, between injections she would rouse herself, weep softly and ask in a slurred, drawling voice if everything was going on satisfactorily. The temperature showed a small daily swing from 98°F. to 99.2°F. without definite periodicity. The pulse varied from 88 to 102 per minute. The blood pressure at the commencement was 120/70 mm.; it fell on the second day to 100/65 mm. and on the third day, to 95/58 mm. On the third day there was some sickness; from the fourth day onwards, a tendency to incontinence of the urine. The bowels were constipated and required regular enemata.

Urinary findings. The urine passed measured from 10 to 40 oz. daily. From the third to the seventh days and on the ninth day there was a trace of albumin. Urinary acidity rose from 10° on the first day to 64° on the ninth day. Under potassium citrate and sodium bicarbonate, the acidity rapidly fell to 16° on the eleventh day and 12° on the fourteenth day. The urine

was negative for sugar, acetone and bile.

Following treatment, this patient was very much better. She felt more composed, less exhausted and apprehensive and slept better at night. She admitted that the course of narcosis had produced a distinctly beneficial effect on her, and she was now for the first time in years looking forward with hope to the future. She left on 22/6/35 and has since returned to a secretarial post.

CASE 14. Involutional melancholia of several years' duration.
Treatment followed by temporary improvement of her symptoms.

A.M.A., a single woman aged 60, was admitted to the Glasgow Royal Mental Hospital on 20/4/34. She was very depressed. She lay in bed with her head flat back on the pillows and for long periods refused to speak. At other times she gave voice to her depressive ideas.

"I am so miserable - I've done such wrong - I've sinned - Is all this quite lawful? Where is my sister - is she all right?"

She would keep on talking disjointedly about her supposed sins. She had lived a bad life and had made serious mistakes for which other people might suffer. She admitted that she frequently heard the Voice of God speaking to her, and reproaching her for her misdeeds. She did nothing, no matter how trivial, without thinking that she had broken the law in some way. For example, she spoke of leaving the water running, and God would send drought to the land because of this sin. She was correctly orientated as to time, place and person.

For a year she continued in this state. She became extremely difficult with her food, so much so that tube-feeding had to be resorted to. For days on end she lay with her head under the bedclothes, refusing to speak to anyone. Physically, she was a thin, anaemic woman and generally in poor condition, though no signs of organic disease were detected.

Treatment was started on 29/5/35. Dosage varied from 2 to 6 c.c. per day. The narcosis was satisfactory; she slept well most of the time, but occasionally would moan for short intervals. At 6 p.m. on the seventh day, the temperature rose to 100.6°F., but fell to normal in 12 hours. The blood pressure was always very low and was in accordance with the asthenic state of the patient. At the commencement it measured 100/60 mm. and fell on the second day to 95/52 mm., at which level it remained until the end of the course. Ephedrine gr. $\frac{1}{2}$ thrice daily was given throughout the treatment. On the second day she developed a mild conjunctivitis which yielded rapidly to frequent bathing.

Urinary findings. On the fifth and sixth days there was retention which was relieved without catheterisation. From the seventh day onwards she was persistently incontinent. The urinary output averaged 30 oz. per day. An occasional trace of albumin and acetone was detected during the last few days of treatment.

This patient left the Hospital on 16/6/35, as it was thought that if she woke up in a different atmosphere the psychological effect would be beneficial to her. She gradually emerged and for a few weeks was definitely improved. She was taking her food well, and her depressive ideas were less marked. After that period she relapsed badly. She became excited and emotional, and her old feelings of sin and guilt returned.

A further 10-day course of somnifaine was given in a private nursing home with excellent results. She improved and is now much stronger, able to go about and look after herself. She

is still rather emotional and distressed, but when one considers that for several years she had been a chronic invalid, the improvement is quite striking.

CASE 15. Depression with paranoid trends of several months' duration. Treatment followed by slight temporary improvement.

J.C.N., a school teacher aged 24 years, was admitted to the Glasgow Royal Mental Hospital on 22/4/35. She had always been a bright, cheery girl, fond of fun and company. She qualified as a school teacher, but remained unemployed for 2 years. Shortly after securing a post, she developed a severe attack of influenza. Following it, she felt her work a great strain, and began to think that she was a poor disciplinarian and might lose her job. She became depressed, took very little food and could not sleep.

On admission, she was very depressed and for the first few days she would scarcely speak, stating that there was no use talking over old subjects and making herself more worried than ever. She took her food badly and slept very little at nights. Associated with her depression there existed marked paranoid trends. She felt that she had worried far too much over public opinion and now people thought very little of her. She thought that others had been getting along in front of her and that she had not been receiving a proper chance. At other times she would blame herself, saying that she was not fit for the work which she had been entrusted to carry out. She was a well-built young woman, but in a very toxic state, with muddy complexion and coated tongue.

At the request of her parents, somnifaine treatment was

commenced on this lady on 27/6/35. Two c.c. of somnifaine were given intramuscularly at 12.15 p.m. She fell asleep at 1 p.m., but awoke at 3 p.m. in an extremely distressed, tense and agitated state. Two c.c. were repeated at 4 p.m. and again at 7 p.m. with little effect. She remained restless and distressed most of the night. She was actively sick at 8.20 p.m. and continued to vomit all throughout the second day. On the third day she slept better and required only 4 c.c. in the 24 hours. From then until the end of the course the narcosis was fairly satisfactory, but for short periods when she would wake up, become very tense and distressed and talk in a slurred voice. The temperature remained normal from 97°F. to 98.4°F., with no regular swing. The pulse varied from 80 per minute to 104 per minute. The blood pressure at the commencement was 125/80 mm; on the second day, 110/70 mm. and on the seventh day the blood pressure fell suddenly to 85/50 mm., and the pulse volume became extremely small. Ephedrine gr. $\frac{1}{2}$ was given thrice daily from the seventh day till the end of the course. This resulted in an improvement in the blood pressure, rising to 95/60 mm.

The urinary output was definitely diminished throughout the whole course, and in addition, she suffered from retention of urine. On the fifth day she required to be catheterised. The daily output of urine varied from 12 to 26 oz. She perspired freely throughout the course. During the third night there was a troublesome hiccough. The bowels did not move without enemata.

Urinary findings. A trace of albumin was detected during the last few days. From the eighth to the fourteenth days acetone was present in the urine, associated with a marked increase of urinary acidity, the latter rising to 70° on the fourteenth day. Acetone persisted in the urine for a week after cessation of treatment. The treatment was concluded on 10/7/35.

Twenty-four hours after her last injection, her left leg was found to be swollen and she complained of pain and stiffness on movement. There was definite oedema from the knee downwards without systemic disturbance. This was due to a venous thrombosis in one of the femoral branches, and was treated by the application of ichthyol and glycerin, with which it gradually resolved and cleared up in 2 weeks.

Following the treatment, she continued depressed and anxious for 7 days and then gradually brightened up, her agitation becoming less intense and her persecutory ideas less marked. She was still depressed, very antagonistic to those attending her and had a constant appearance of suspicion and distrust. She left the Hospital on 24/7/35. Her improvement did not last long, and in a few weeks she gradually relapsed into her former state. She has since been readmitted in a very depressed condition, with hallucinations and pronounced ideas of reference.

CASE 16. A catatonic schizophrenia of 2 months' duration.

Treatment lasted 14 days and was without beneficial effect.

J.P., a single woman aged 21, was admitted to the Glasgow Royal Mental Hospital on 2/9/34. Up till July 1934 she had been apparently perfectly well, but suddenly one morning she awoke and commenced to sing and shout in a loud voice, saying that members of the family were tormenting her. These fits of screaming and shouting occurred at frequent intervals, and between them she would have dull periods when she would speak to no one. She would attempt to get out of the house in her night attire and wander down to the sea. She heard people talking outside her room, and felt that her brothers were laughing at, and talking about her.

On admission, she lay quietly in bed. When spoken to, she would not answer, but turned round and giggled foolishly, covering up her face with her hands and hiding herself under the bedclothes. She remained in this peculiar state; at times quiet, at other times talking in a rambling, incoherent fashion, or singing away to herself. She was violently impulsive; would spring out of bed and throw herself on the floor, or attempt to smash a window without provocation. From her mannerisms she was evidently hallucinating constantly, although she could not be made to explain what voices she heard. She was completely detached from her surroundings. Her habits were faulty and on one occasion she smeared herself with tooth paste.

Treatment was commenced on 27/6/35. Physically, she was a well-built, well-nourished young woman. Nothing abnormal was detected on physical examination. The first injection was given at 12.15 p.m. Following that, she quietened down, but did not sleep and at 2 p.m., was again extremely restless and resistive. A further injection was given at 4 p.m. and again at 7 p.m. By 7.45 p.m. she was deeply asleep and remained so until 4 a.m. on the second day, when she awoke and became violently sick. Up to the fourth day it was difficult even with 6 c.c. per diem to keep her well under, and from time to time she would struggle violently, attempt to get out of bed and make for the windows. From the fifth till the fourteenth days narcosis was much more satisfactory, and she remained in a deep sleep with from 4 to 6 c.c. per diem. She perspired freely throughout. The temperature remained from 97°F. to 98.4°F. The pulse ranged from 62 to 96 per minute. The blood pressure at commencement was 125/75 mm.; on the second day, 105/65 mm.; on the eighth day the pressure fell to 95/60 mm. Ephedrine gr. $\frac{1}{2}$ was given thrice daily and the blood pressure improved to 110/65 mm.

Urinary findings. For 48 hours on the second and third days she did not pass urine. On the third day she was catheterised and 36 oz. of urine were withdrawn. From the fourth to the fourteenth days she was incontinent. Urinary examination was negative for albumin, sugar, acetone and bile throughout the whole course. Treatment was concluded on 10/7/34. The bowels did not move except with enemata.

She remained deeply asleep till the evening of the 11/7/34, when she became very restless and resistive, so much so that chloral had to be administered. In this case the treatment brought about no improvement: in fact for a week afterwards she was so impulsive and violent that hyoscine had to be injected on several occasions. She still remains in Hospital.

...and sobbing bitterly. She imagined that she was ...
 ...that she had done terrible things which ...
 ...forgiveness. Physically, she was a thin, pale ...
 ...signs of organic disease were detected ...
 ...depression, and was extremely distressed. She ...
 ...singing and sobbing and talking incoherently ...
 ...little food and required large doses of ...
 ...was difficult to get any information from her ...
 ...was quite unobtainable. ...
 ...the same thing again ...
 ...this time, and agitated ...

CASE 17. An agitated melancholia of 9 months' duration. Treatment followed by temporary improvement.

C.R., a secretary aged 30, was admitted to the Glasgow Royal Mental Hospital on 2/9/35. The family history was negative. She had always been a clever, conscientious girl. She would worry over trifles, was reserved and never seemed able to settle down to a job for any length of time.

The present illness began 9 months ago when it was noticed that in her office she wept for long periods of the day. She did not sleep at nights and roamed about the house, wringing her hands and sobbing bitterly. She imagined that she had deceived everybody, that she had done terrible things which would never be forgiven. Physically, she was a thinly-built young woman; no signs of organic disease were detected.

On admission, she was extremely distressed. She kept tossing about, sighing and sobbing and biting her fingers. She took very little food and required large doses of sedative every night. It was difficult to get any information from her. When approached she became emotional, saying that it was no use going over the "whole thing" again.

In this depressed, agitated state, somnifaine was commenced on 13/9/35. She reacted well to the drug and slept deeply. The dosage varied from 2 to 6 c.c. per diem. From the first to the fifth days the blood pressure fell gradually from 125/80 mm. to 90/64 mm. On the evening of the fifth day the pulse rose

suddenly to 120 per minute and became feeble and irregular. Somnifaine was withheld and subcutaneous salines and 2 c.c. of icoral were given. She rallied a little, but 12 hours later, collapsed a second time. Her colour was extremely poor and her pulse imperceptible. An intravenous saline (500 c.c.) with glucose was given and 15 minims of coramine, 4-hourly. Under this treatment she quickly recovered, and by 21/9/35 the pulse had returned to 90 per minute and was of good volume. Further injections of somnifaine were commenced on that day and continued till 28/9/35. She continued to sleep well, and no further cardiovascular complications were encountered. Associated with the collapse there was a rise in temperature to 99.4°F.

Urinary findings. The output averaged 20 oz. per diem. There was a trace of albumin on the sixth, seventh and thirteenth days and a trace of acetone on the third, fourth, eleventh and twelfth days. No sugar was present in the urine at any time. The acidity remained low.

This patient gradually emerged 24 hours after the last injection. There was not a great deal of change in her condition, though she was rather less distressed and did not become so emotional as she had been before treatment. She showed more inclination to talk. Her depressive ideas were still present. She felt she would never get better in the Hospital and kept constantly asking when she could get up and go home.

On 17/10/35 - fully 3 weeks after the last injection had been given, she had a sudden epileptiform seizure, from which

she recovered quickly and which left no subsequent defects. The attack was typical with tonic, followed by clonic movements, cyanosis and biting of the tongue. In view of the tendency to a hypocalcaemia following narcosis, she received 10 c.c. of calcium gluconate intravenously and 20 gr. calcium chloride by mouth thrice daily. There was no recurrence of the epilepsy.

Since then she has, if anything, gradually become worse. She is now in a constant state of agitation; she keeps on pacing up and down the ward, wringing her hands and biting her nails. When an attempt is made to speak to her, she will reply with some such remark as, "Oh, dear," and immediately wander off out of the way. She requires medinal regularly at night.

CASE 18. An agitated melancholia of 4 years' duration. Treatment resulted in a fatal issue.

Mrs. M.D.K.M., a widow aged 46, was admitted to the Glasgow Royal Mental Hospital on 3/7/31. She was very agitated, confused and indecisive. She wandered about the ward day and night, talking in broken sentences and unable to maintain a stream of talk for more than 15 seconds at a stretch. For 4 years she remained in that state. Physically, she was an under-developed woman and in a toxic condition.

Treatment was commenced on 20/12/35. Two c.c. were given at 10 a.m. and a further 2 c.c. at 8 p.m. Between the first and second injections she was very restless and resistive, and would not lie in bed. After the second injection she passed into a deep sleep. On 21/12/35 she remained comatose all day and it was impossible to rouse her by external stimuli. In the afternoon the temperature rose to 101°F., pulse 120 per minute, respirations 30 per minute. She became cyanosed and a diagnosis of pneumonia was very suggestive. On 22/12/35 examination revealed a pneumonic process involving both sides, but especially the left base. The temperature continued to increase to 104°F., pulse 130, respirations 40. She did not regain consciousness, and died at 8 a.m. on 25/12/35.

Urinary findings. The urine gave a definite reaction for albumin.

CASE 19. An acute depression of 6 months' duration. Treatment lasted 12 days and was associated with a marked fall in blood pressure. Following treatment, he passed into an acute mania which cleared up spontaneously in 3 months.

J.F.M., a lawyer aged 31, was first admitted to the Glasgow Royal Mental Hospital on 19/10/34. As a child he had been very nervous, and gave considerable trouble up to the age of 3 or 4 years. When at school he had been confined to bed with an attack of "nerves." He was an intelligent man, and always very interested in sport. Three years previous to his admission he had become engaged, and at that time suffered from sleeplessness and loss of appetite. This mental state persisted until his marriage after which he remained well till a few months ago. He would sit for hours doing nothing, simply staring in front of him. He slept badly, and woke up during the night perspiring freely, and in a state of intense anxiety. Six weeks before admission, he attempted suicide by trying to strangle himself with his tie.

On admission, he was depressed and anxious. He felt that he was incapable of making a decision for himself, and at times a fear of something quite indescribable would come over him. He looked upon himself as an individual doomed to insanity. Physically, he was a well-built man showing a tendency to sympathetic over-activity, with dilated pupils, brisk reflexes, rapid heart and frequent sweating. He showed no improvement after admission. He became more and more depressed, ate little food,

and required sedatives at night. He masturbated constantly.

"I do not want to get better, I should be dead," he kept on saying. He stated that he was in Hell, and that he heard his parents' and his wife's voice in the room upstairs.

Treatment was started with this patient on 6/12/34. A first injection of 2 c.c. was given at mid-night. He feel asleep half an hour later and did not waken till 5 a.m. At 6 a.m. he started to struggle violently in an attempt to get out of the room, following which a further 2 c.c. were administered. The narcosis was light throughout, and from time to time he would wake up, and talk in a depressed tone about his ideas of guilt. Two c.c. were given on the fourth, eighth and thirteenth days; 4 c.c. on the third, fifth, seventh, ninth, eleventh and twelfth; and 6 c.c. on the first, second, sixth and tenth days. On the second and third days he vomited on several occasions. It was difficult to give him sufficient food, but this was due to his mental state and not to any dysphagia. The temperature remained normal. A marked change occurred in the cardio-vascular state preventing pushing the dose and obtaining a more satisfactory narcosis. The blood pressure to commence with was 130/90 mm.; on the second day, 120/85 mm. From the seventh day onwards there was a gradual fall in the pressure to 88/65 mm., notwithstanding the 4-hourly administration of gr. $\frac{1}{2}$. ephedrine. On account of this lowered blood pressure, it was decided to stop treatment on the thirteenth day. The pulse-rate varied considerably and at times rose to over 100.

There was retention of urine for 48 hours on the fourth

and fifth days, and similarly for 24 hours on the sixth and seventh days. In addition to the retention, urinary output was diminished, at times as low as 12 oz. per day. A trace of albumin was found in all specimens from the second day onwards. The urine was negative for acetone throughout. A white cell count was done following treatment on 6/12/34: leucocytes numbered 8,770 per c.mm.: weighted mean 2.06. The blood pressure returned to normal 48 hours after the completion of the course.

Twenty-four hours after the last injection on 18/12/34, he began to talk, and it was evident that a definite change had come over him. He was more easily accessible and answered questions about himself quite lucidly. He was much less distressed, his habits had improved and he no longer masturbated. He still displayed a strong sense of guilt, but this did not cause him the same anxiety as it had done formerly.

On 31/12/34 a sudden change came over him within the space of 12 hours. He became elated, laughed merrily and said that he never had felt so well in his life. He became very aggressive and difficult. Physically, he was very much better. This manic state continued for 3 months. He insisted on leaving the Hospital and went home, where he became violent, threatening to strike his mother and kill his wife. He was accordingly certified and re-admitted in an acutely excited state. After 3 months he gradually settled down, left the Hospital on 28/10/35 and has remained very well since.

CASE 20. Catatonic schizophrenia. Treatment was complicated by a severe cystitis following catheterisation. More accessible and co-operative for a short period.

R.G.A., a student aged 26, was admitted to the Glasgow Royal Mental Hospital for the second time on 4/1/34. There was a definite family predisposition to mental disorder, and an aunt was also a patient in the same Institution, suffering from an involuntional melancholia. He was a definite catatonic schizophrenic type. He was negativistic and at times restless and impulsive. He refused his food and had to be tube-fed on numerous occasions. His habits were faulty.

Somnifaine was commenced on 6/12/34. The narcosis was fairly deep, but occasionally he would have outbursts of incoherent shouting and try to get out of bed. He required catheterisation on the sixth day following 48 hours' retention, and one pint of urine was withdrawn. Following that he was incontinent. He perspired freely throughout. Hiccough was troublesome. Constipation was severe and required regular enemata. This patient showed considerable temperature disturbance. At 2 p.m. on the fifth day the temperature rose to 100.6°F., but by 10 p.m. on the same day it had returned to normal. At 2 p.m. on the seventh day the temperature rose again to 100°F., and at 9 a.m. on the eighth day it reached 101.2°F. Examination of the urine revealed bacteria in large numbers and pus cells. This second rise of temperature, therefore, was due to a cystitis which was treated by the exhibition of cystopurin and daily injections of amphotropin. Treatment was

suspended for 3 days during which the urinary condition improved and the temperature returned to normal.

Treatment was resumed on 17/12/34 and was continued with from 6 to 8 c.c. per day for 9 days. The blood pressure was well-maintained. He emerged 24 hours after the last injection and showed himself more co-operative than he had been since his admission. He would make an attempt to answer questions, although many of his replies were irrelevant. For 10 days he continued in this improved state. He took his food himself, his habits were improved and he had no impulsive outbursts. At the end of that period he gradually relapsed into his former state of negativism. He refused food and became incontinent.

For the following year he remained in the last-mentioned state, but during the past month he has gradually shown improvement, is now taking his food himself and is able to be up daily and out walking in the grounds. During the course of treatment he suffered a loss of 10 lbs. in weight.

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CASE 21. An acute depression of obsessional type of a few weeks' duration. Treatment lasted 17 days and was associated with marked oliguria. Following treatment, he cleared up completely.

J.A.G., a book-keeper aged 37, was first admitted to the Glasgow Royal Mental Hospital on 28/7/34, with a history of having been depressed for 2 months. This attack lasted 6 weeks and he was discharged on 24/8/34. He was readmitted on 30/12/34, with a similar type of illness. Two weeks previously, following recovery from an acute influenza, he began to feel apprehensive and awoke one night in a state of panic with a feeling of impending suffocation. A similar attack occurred a few nights later when he jumped out of bed and rushed into the street. He spoke of a lump constantly in his throat, and complained of intense palpitation.

On admission he was very depressed, thought that he was going to die and that because of this he did not require any food. He felt extremely miserable. At intervals he was liable to severe emotional outbursts during which his eyes became staring, his limbs rigid and his respirations deep. There was no disturbance of memory or orientation. He believed that he had a serious heart condition, and that a clot of blood had formed on his brain. No abnormality was detected on physical examination.

Treatment was commenced on 21/1/35 and lasted 17 days.

He was resistive to the drug, and at intervals would waken up, sit up in bed, become very distressed and weep bitterly. Dosage varied from 2 to 8 c.c. per diem. The temperature remained normal.

The pulse varied from 64 to 80 per minute and at times was poor in quality. Perspiration was profuse. He vomited on the second, third, sixth, ninth and eleventh days.

This patient gave rise to anxiety on account of a marked diminution in his urinary output. Only 10 oz. of urine were passed on the sixth, seventh and eighth days. With the administration of potassium citrate and abundant fluids, the urinary output gradually increased, but did not return to normal. Following on this oliguria there was retention for 48 hours on the ninth and tenth days and again for 24 hours on the fourteenth day. He was catheterised on the tenth and fourteenth days when 18 oz. and 38 oz. were withdrawn, respectively. Forty-eight hours after the last injection on 7/2/35, he began to urinate normally. Constipation required relief with hydrogen peroxide enemata. A trace of albumin was present on the fourth and fourteenth days, acetone on the fourth day and a trace of bile on the fifth, sixth, seventh and twelfth days. Acidity rose to 62° on the fifth day, but after administration of potassium citrate 20 gr. 4-hourly, the acidity fell to 15° by the end of the sixth day. On the sixth day, when the urinary output diminished, blood urea had increased to 49 mgm. per cent., non-protein nitrogen to 55 mgm. per cent. On the ninth day the result was 28.6 mgm. of urea per cent. and 29.5 mgm. non-protein nitrogen per cent. This improvement coincided with an increase in the urinary output.

Up till the last injection this patient during his wakeful moments remained very distressed, but during his period of emerging

from the influence of the drug he showed a remarkable change. Twenty-four hours after the last injection he looked distinctly brighter and forty-eight hours after, he was wide awake, stated that he felt very much better and showed no evidence of emotional disturbance. He maintained his improvement and left the Hospital on 6/3/35. Before his discharge he was on parole in the grounds, took his food well and slept naturally every night. Since his discharge he has remained very well and has returned to work.

Treatment was prolonged in this case to 17 days as the neurosis was kept very light during the days when the urinary output was diminished.

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CASE 22. A reactive depression of 12 months' duration. Treatment of 14 days, after which he had a hypomanic phase lasting a week, followed by complete recovery.

W.D.O., a dentist aged 51, was admitted to the Glasgow Royal Mental Hospital on 21/1/35. He had been a patient 3 years previously suffering from depression which had diminished in severity, but had never cleared up satisfactorily. The present attack was similar to the first.

On admission he was dull, very depressed and refused to answer questions about himself. He took his food badly and required sedatives at night. His whole appearance was one of intense misery. Physically, he was a thinly-built man who looked much older than his years. No evidence of organic disease was detected.

Treatment was started on 22/1/35. He reacted very well and remained in a good narcosis most of the time, though occasionally when due an injection, he would mutter away to himself, and ask why he was not allowed to die. Dosage varied from 2 to 6 c.c. per diem. Blood pressure at commencement 140/95 mm., fell on the second day to 120/80 mm., and continued to fall gradually during the first week. On the sixth day the blood pressure was 95/65 mm., at which level it remained till the end of the course. At times his colour was poor. On the evening of the fourth day the temperature rose suddenly to 100°F., but fell to normal within the next 8 hours. On the seventh and eighth days the temperature was constantly above 99°F. and in the evening of the ninth day, rose to

100.2°F. The temperature continued from 99°F. to 100°F. until 24 hours after the last injection on 5/2/35. He perspired profusely throughout.

On the first and second days he was incontinent. From the third day onwards there was retention of urine and, as definite distension was present, he was catheterised on the third, seventh, eleventh, twelfth and fourteenth days. The same procedure had to be resorted to for the 2 days following the completion of the course.

Urinary findings. There was a trace of albumin present in every specimen. Sugar was present on the twelfth day and a trace of acetone on the third and fourth days. From the sixth day onwards bacilli were present in large numbers in the urine, but only a few pus cells were detected.

The patient gradually began to emerge 24 hours after the last injection, and a remarkable change had come over him. He showed a definite degree of elation, was no longer depressed and, without provocation, began to talk about the symptoms of his illness, saying that for the last 2 years he had been obsessed with thoughts of his own misfortune and had entertained the idea of taking his own life. Now he could not understand why he had brooded in that fashion, and felt that he must have lost his sense of proportion. He wondered why he had taken such a gloomy view of things and spoke of getting away as soon as possible and starting work. A week later the hypomanic phase disappeared and he now felt as he had done before his depressions had commenced. He looked

forward to the future with every confidence.

He was discharged on 20/2/35 and for a few months remained very well, but when he became faced with the responsibility of his practice, he again broke down. He was readmitted in January, 1936 in a further attack of severe depression.

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CASE 23. Manic depressive. Six courses of somnifaine were given in 6 separate maniacal attacks, with excellent results.

A.L.P., a bank-teller aged 40, was first admitted to the Glasgow Royal Mental Hospital on 20/6/34. This was the patient's third attack of acute mania and had been of 4 days' duration on admission. He was a typical, recurrent manic. His previous attacks had lasted a few months and he had settled down without any permanent mental change after each of them. With this patient the experiment was carried out to find whether or not a course of somnifaine could cut short a manic attack of this nature.

The first course of somnifaine was commenced on 14/2/35 and was of 14 days' duration. At the time of the first injection he was acutely excited and restless, unable to lie in bed, talking incessantly and at times shouting at the pitch of his voice. A large dose was required to give a satisfactory narcosis. He received 8 c.c. the first two days and 6 c.c. per diem thereafter. He slept well, but from time to time would become talkative, but not noisy or restless. From the fourth to the ninth days he suffered from retention of urine necessitating catheterisation. On the tenth day the pulse-rate increased to 120 per minute and was irregular. Two c.c. of icoral were given and with this the pulse improved and its rate fell to 90 per minute after 8 hours. On several occasions the temperature rose to 101°F., but returned to normal during the next 4 hours. The first course of treatment was concluded on 28/2/35.

For 2 days following he was dull and mildly depressed and scarcely spoke, but on the third day he brightened up considerably, and for 2 months remained very well, when he again suddenly relapsed into an acutely excited maniacal state.

Following on a further 14-day course of somnifaine he emerged, remained slightly depressed for 48 hours and then returned completely to normal. Within the next 7 months he suffered from 4 further attacks of acute mania which were treated from their very commencement with a short course of somnifaine lasting 7 days. This was found sufficient to arrest each attack, and on every occasion he awoke slightly depressed, and became perfectly normal 48 hours after the last injection.

Several complications occurred at various times during the different courses. On the second and third days of each treatment he was sick and vomited, and from the fourth day onwards had retention of urine which necessitated catheterisation. On each occasion also, as in the first course described, the temperature showed an evening rise from 99.4°F. to 100°F.

Urinary findings. There was occasionally a trace of albumin, and acetone was present at sometime during all the courses, but only in minute quantities.

CASE 24. Manic depressive. Treatment was given during the depressive phase, and was followed by gradual recovery.

H.G.S., a torpedo-fitter aged 29, was admitted to the Glasgow Royal Mental Hospital on 1/2/35. This was the patient's third mental illness. Ten years ago he had a manic attack following on influenza. The condition cleared up in from 2 to 3 months. Three years ago he had a second attack of mania which resolved in a similar period. From this last attack he remained well until 5 months ago, when his wife had informed him that she was going to have another child. This appeared to upset him. He became very quiet and reserved in his manner, and for 3 weeks was very depressed. At the end of that period the depression gave way to a state of restlessness and excitability which increased up till the time of his admission.

On admission he talked constantly, though quite coherently. He showed definite flight of ideas and distractability. He stated that he never felt better in his life. He refused to stay in bed and spent the day walking about the ward, talking to the other patients. Physically, he was a thin, slightly anaemic man. No evidence of organic disease was detected on examination. Two months after admission this patient gradually changed from a condition of mania into one of depression. He had outbursts of weeping during which he would accuse himself of ingratitude to his wife and of other crimes too awful to be mentioned. This depression gradually increased. He refused food saying that he was not

worthy of it and spent the greater part of the day sitting in a corner of the room in complete silence.

It was in this depressive state that somnifaine was commenced on 14/3/35. Under its influence he slept well, but occasionally when being attended to, he would become restless and resistive. Great difficulty was encountered in giving him sufficient nourishment and he was tube-fed thrice daily from the fifth to the eleventh days. Four c.c. of somnifaine were given on the second, third, sixth and eleventh days, and 6 c.c. per diem for the remainder of the course. There was retention for 48 hours on the third and fourth days necessitating catheterisation and withdrawal of 20 oz. of urine. From the sixth to the fourteenth days he was incontinent. The temperature and pulse remained normal. The blood pressure to commence was 130/82 mm., fell on the second day to 120/75 mm., and remained at that level until the completion of the course.

Urinary findings. A trace of albumin was present on the third, and from the ninth to the twelfth days; a trace of sugar on the twelfth day and a trace of acetone on the second and third days. Urinary acidity rose to 96° (Ph 5) on the third day, but following intensive treatment with potassium citrate (gr.20, 4-hourly) this fell gradually to 27° on the ninth day and 16° on the twelfth day. Treatment was concluded on 30/3/35.

Forty-eight hours after the last injection he had completely emerged and was decidedly brighter and more communicative, but remained emotional and kept on mumbling his gratitude, and excusing

himself for all the trouble he had given. During the week following the conclusion of the treatment, he gradually improved. He became much more stable emotionally and had none of the attacks of acute depression and excitement which preceded the treatment. He was still, however, far from well and at times would sit in a chair staring in front of him for hours on end.

During the next 4 months, this patient gradually cleared up. By October he was sleeping 6 to 7 hours every night without sedatives, though he was difficult to get into touch with and refused to give his confidence. He was mildly content, said that his surroundings were admirable, that everyone had been most kind, and that he would be sorry to leave.

He was discharged on 22/11/35, and has since resumed his work.

CASE 25. Depression of involuntional type of 2 months' duration. Treatment followed by temporary improvement which was not maintained

R.G., a joiner aged 42 years, was admitted to the Glasgow Royal Mental Hospital on 11/2/35. He had always been a very quiet and reserved man, with few friends. He had been married for 24 years and has 3 children. The illness commenced 2 months before admission. He complained that his sight was failing and because of this, had difficulty in performing his work. He slept badly, would get up during the night and walk about the room muttering away to himself. He refused to go to his work and would lie in bed weeping bitterly, saying that he would be better dead. On one occasion he asked his wife to go and get him a razor so that he could cut his throat.

On admission he was very restless and agitated, being subject to frequent outbursts of weeping. He said that he was the worst man in the world and that it would have been much better if he had died many years ago as he had brought disgrace to his family. He felt that the other patients in the ward had been put there for the purpose of reproaching him for his misdeeds. Physically, he was a well-built, middle-aged man. Apart from a functional systolic murmur at the apex, no organic disease was detected.

Treatment was commenced on 15/3/35 and lasted for 14 days. Six c.c. of somnifaine were given on the first, third, fifth and seventh to the tenth days; 4 c.c. on the second, fourth, sixth,

thirteenth and fourteenth days, and 2 c.c. on the eleventh and twelfth days. The narcosis was satisfactory, though occasionally he would rouse himself, mutter incoherently and show signs of distress. He perspired profusely. At 6 p.m. on the fourth day the temperature rose to 100°F., but fell to normal at 10 a.m. on the fifth day. Another rise of temperature to 99.4°F. occurred at 10 p.m. on the tenth day, but fell to normal within 8 hours. A third rise of temperature occurred to 100.4°F. at 10 p.m. on the eleventh day. Associated with this last rise of temperature there was an increase in the pulse-rate to 92 per minute and in the respiration-rate to 32 per minute. During the twelfth day the temperature, pulse and respiration-rate gradually fell to normal. The blood pressure to commence was 150/95 mm., fell on the second day to 120/85 mm. and remained fairly stationary at that level.

There was incontinence of urine from the fifth day onwards. The urinary output averaged 20 oz. per day. There was a trace of albumin from the eighth to the twelfth days, a trace of sugar on the second and thirteenth days, and a trace of acetone on the second day. Urinary acidity rose gradually during treatment from 16° on the first day to 64° on the thirteenth day. Treatment was concluded on 29/3/35.

After emerging from the narcosis he felt pleased, quite hopeful and no longer depressed. Three days later, however, depressive ideas again became apparent. He began to worry over the condition of his bowels and said that he had had no motion for

several days. For the succeeding 8 months he remained in this depressed condition. He felt that he had a tumour of his bowels which would prove fatal, and also that other people in the ward were discussing him and hindering his recovery.

He was allowed home on 11/12/35, since when he has gradually cleared up. His depressive ideas have gone; he is now taking his food well and sleeping at nights without sedatives.

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CASE 26. A paranoid schizophrenic of 12 months' duration.

Treatment lasted 14 days and was followed by a temporary change in his condition.

W.M.M., an engineer aged 42, was admitted to the Glasgow Royal Mental Hospital on 25/3/35. His illness had been of about 12 months' duration. At that time he began to feel that his actions were being controlled by external influences and he was constantly being disturbed by voices.

On admission, he was distant and difficult to approach. He stated that he felt a hissing noise in his ears, and that this noise was frequently transformed into a voice. He felt that some wonderful machine must have been employed by his persecutors. During a conversation the voices were always intruding and upsetting him. At times he was conscious of a strange smell, and believed that this was some new form of torture inflicted by his persecutors. He answered questions clearly and coherently and there was no disturbance of memory or orientation. He had no insight into his condition. Physically, he was a tall, well-built man, in good condition. Blood pressure was 115/75 mm.

Treatment was commenced on 14/4/35. The doses given ranged from 4 c.c. on the first, third and eighth days, to 6 c.c. per day during the rest of the course. The narcosis was light and when due an injection, he would become restless, speak in a slurred voice, and attempt to come out of bed. On the second day he complained of nausea, but no vomiting occurred. On the third

day he had severe paroxysms of coughing. The temperature remained normal. The pulse on the second day rose from 88 to 120 per minute and its quality was poor. He was put on ephedrine gr. $\frac{1}{2}$ thrice daily. The pulse-volume improved. The pulse-rate continued from 90 to 102 per minute till the end of the course. Blood pressure remained at 110/70 mm. Constipation was marked and his bowels did not move without enemata.

He required catheterisation on the seventh day following 36 hours' retention: 34 oz. were withdrawn. From the 8th till the 12th days, he was incontinent.

Urinary findings. A trace of albumin was present on the ninth day. A trace of sugar was noted on the fifth and seventh days. Reaction to acetone was negative throughout. There was a marked increase in the urinary acidity, rising to 85° (Ph 5) on the sixth day. With intensive alkali administration, acidity fell rapidly to 32° on the eighth, and 15° on the ninth day.

During the last few days of the treatment his mental condition changed completely. In his more wakeful moments he was excited and happy. The hallucinations ceased entirely. He emerged from the narcosis 24 hours after the last injection on 28/4/35 and was in a hypomanic state. This passed off within the next few days and he became dull and apathetic, but his hallucinations had completely passed away. He said that he remembered very little about the treatment except that he had received a number of injections, and had been very confused. He did not know how long

day he had severe paroxysms of coughing. The temperature remained normal. The pulse on the second day rose from 88 to 120 per minute and its quality was poor. He was put on ephedrine gr. $\frac{1}{2}$ thrice daily. The pulse-volume improved. The pulse-rate continued from 90 to 102 per minute till the end of the course. Blood pressure remained at 110/70 mm. Constipation was marked and his bowels did not move without enemata.

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the treatment had gone on. He remembered perfectly his mental state before the course had been started, but he exhibited no insight whatever into his previous symptoms. He merely stated that his persecutors had taken a holiday and would probably return to annoy him.

This improvement was of short duration and a week later hallucinations began to trouble him again, and increased in their intensity. He remained, however, more communicative and not so suspicious as he had been. Since then his condition has remained much the same, constantly hallucinating, extremely irritable and suspicious. He sleeps badly and is constantly disturbed by the voices.

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CASE 27. An anxiety state of 3 to 4 years' duration. Treatment lasted 14 days and was followed by no improvement.

A.M., a bank clerk aged 27, was admitted to the Glasgow Royal Mental Hospital on 1/5/35. His illness had begun 4 years previously. He complained of difficulty in concentrating, and felt unable to perform his work in a satisfactory fashion. He became asocial, ceased to occupy himself and was slovenly in his dress. He suffered from severe attacks of anxiety during which he would wander away from home.

On admission, he was nervous, apprehensive and restless, and complained of a tight feeling in his stomach when he ate. He was unable to carry on a conversation for any length of time, constantly worrying about himself and his symptoms. He would get up, pace about the room and make curious movements with his hands. Frequently a feeling came over him of impending catastrophe. Physically, he was in a toxic condition, with muddy complexion and coated tongue. Blood pressure was 110/75 mm. His mood was one of mild depression.

Treatment was commenced on 3/5/35. The narcosis was light and between injections he would say that a terrible fear had come over him and complain of profuse sweating. Dosage varied from 4 to 8 c.c. per diem. The temperature remained normal. Blood pressure fell on the third day to 85/65 mm. On the eighth day, the pulse became poor in quality and averaged 100 to 104 per minute. Ephedrine gr. $\frac{1}{2}$ thrice daily was given from the eighth day onwards

and with it the pulse improved in quality and the rate settled down to from 70 to 80 per minute. In addition, the blood pressure rose to 95/70 mm. Sweating was very pronounced, especially on the twelfth day. Constipation was treated by hydrogen peroxide enemata.

There was retention of urine for 24 hours on the fifth day, 36 hours on the sixth and seventh days, and 48 hours on the ninth and tenth days. He was catheterised on the seventh and tenth days, 18 and 30 oz. respectively being withdrawn. The urinary output varied from 12 to 41 oz. per diem. There was a trace of albumin from the twelfth to the fourteenth days; sugar from the sixth to the ninth days; and a trace of acetone from the third to the sixth, and from the eighth to the twelfth days. Acidity rose to 85°(Ph 5) on the eighth day, but with alkaline treatment it diminished steadily to 48° on the fourteenth day.

This patient showed no definite improvement following the treatment. He continued to be apprehensive, nervous, indecisive and mildly depressed. He slept well, took his food well, but complained of vague gastric symptoms. He was unable to settle down to any useful work.

He left the Hospital on 30/5/35 in much the same condition as he had been on his admission.

CASE 28. Acute mania of 2 to 3 weeks' duration. After treatment he remained well for 2 weeks, but this was followed by a further manic attack.

M.M., a medical student aged 19 years, was first admitted to the Glasgow Royal Mental Hospital on 4/6/35. Patient was a clever, but quiet, sensitive young man. The illness began about 2 weeks before admission, when he became very confused and rambling in his talk. He seemed very well-pleased with himself and talked of going away from home. Physically, he was a thin, under-developed young man, in poor condition.

He was admitted in a typical manic state, restless, talkative and showing a flight of ideas. He masturbated freely and talked continuously of sexual subjects.

Treatment was commenced on 6/6/35. He reacted favourably to the somnifaine and as a rule slept deeply. At times he would waken up between injections and talk in a rambling confused fashion, saying among other things, that he was a plant, that the Russians were after him, or that the Irish were persecuting him. He imagined that he was in various parts of the world; at one time in Germany, at another time in Russia. Four c.c. were required on the first, second, seventh and thirteenth days; 6 c.c. from the third to the sixth, and on the eleventh, twelfth and fourteenth days; and 8 c.c. on the eighth, ninth and tenth days. The temperature remained normal from 97°F. to 98°F. The pulse-rate varied from 70 to 80 per minute. At times his colour became

poor and the pulse weak and of low tension. Blood pressure at commencement was 110/75 mm.; fell on the third day to 95/65 mm. Ephedrine gr. $\frac{1}{2}$ thrice daily was given and the pressure improved slightly to 100/70 mm., at which level it remained throughout the course. He required catheterisation on the fourth, fifth and sixth days. From the seventh to the fourteenth days he was incontinent. On the eighth day the pulse volume was very small, although the rate remained at 74 per minute: one c.c. of coramine was given and repeated thrice daily till the eleventh day. As a result the pulse quality improved considerably.

Urinary findings. Output was 20 to 30 oz. per day: a trace of albumin was present on the eighth day: acetone was found in definite quantity from the third to the sixth days. The urinary acidity increased to 52° on the fifth day, but following alkaline treatment it fell gradually and was 3.5° on the eighth day.

The patient began to emerge 12 hours after the last injection and following that was decidedly quieter than he had been before the treatment. For a week he remained in a curious state during which he had periods when he was perfectly clear and composed, alternating with spells of mild confusion. During these latter spells he would become dull and almost stuporose, mutter away to himself and pay no attention to anyone else in the room. This state lasted for a week. By 2/7/35 his condition became uniformly good: he remained peaceful and composed, slept and ate well and behaved normally. He realised that something had been

wrong with him, but had no idea of the nature of his illness. He had a complete amnesia for the whole of his stay in Gartnavel.

He left the Hospital on 9/7/35 and remained well for a fortnight, after which he began to show signs of relapsing. He became restless again, did not sleep at nights and would roam about the house. He seemed completely out of touch with his surroundings. He would laugh foolishly, shout odd phrases for no apparent reason and was evidently hallucinating. He was readmitted to the Hospital on 29/7/35 in the above state. He would lie in bed all day muttering away to himself incoherently. His habits were faulty; he would shout and laugh loudly.

In a fortnight he gradually began to settle down and in a month had completely recovered. Since then he has remained very well.

CASE 29. Involutional melancholia of a month's duration. Treatment followed by slight temporary improvement.

J.K., a railway worker aged 42 years, was admitted to the Glasgow Royal Mental Hospital on 29/3/35. He had always been a steady reliable man, but reserved and of a worrying disposition. His illness had been of a month's duration and had followed on the death of his brother. He gradually became more and more depressed. He refused to go to bed, saying that it was of no use as he would not sleep. He believed that he was being punished by God for some crime which he would not disclose and for which he was going to suffer a cruel, lingering death. He had been married 6 years, but has had no family.

On admission, he was very depressed. He refused to take food, saying that it would collect in a large sack in his abdomen and gradually pile up there. He believed that his stomach was sealed up and that there was no way for the food to get out. He felt that he had committed a great crime and that God was killing him slowly as a punishment for it. After 4 months no improvement had taken place and tube-feeding had to be resorted to. He believed that he was the reincarnation of the Devil and that he had lost the souls of everybody in the world. His guilt had branded him and he would be seen by everyone outside the Institution.

It was at this stage that treatment was commenced on 18/7/35. Physically, apart from some pyorrhoea, no abnormality was detected. On the first day 6 c.c. were given. He slept well.

but from time to time was awake, very depressed and agitated. On the second day 4 c.c., and on the third day 6 c.c. were given. On the latter day he was troubled with persistent hiccough. On the fourth day the temperature rose to 101.8°F. at 2 p.m. The pulse-rate also rose rapidly to 132 per minute, and at times the pulse was weak and almost imperceptible. Ephedrine gr. $\frac{1}{2}$ 4-hourly, and strychnine gr. 1/60 thrice daily were given.

Somnifaine was withheld for 72 hours. Nothing in the physical examination accounted for the pyrexia. By the fifth day the temperature had returned to 97.4°F. and the pulse was much stronger at 88 per minute.

On 24/7/35 treatment was resumed. Four c.c. were given on that day and a further 4 c.c. the following day, with which he slept very well, though he continued to be troubled with severe hiccough. On 26/7/35 further treatment was stopped on account of a progressive leucopenia which had taken place during the previous 72 hours. On 22/7/35 the white blood cells numbered 7,270 per c.mm.; on 24/7/35 they were 6,600 per c.mm.; and by 26/7/35 they had fallen to 4,790 per c.mm. This leucopenia in association with the pyrexia, decided us to stop the treatment.

Urinary findings. He required catheterisation on the fourth day following 36 hours' retention and 24 oz. of urine were withdrawn. No abnormal constituents were discovered on examination of the urine at any time during the course. Following the last injection, he remained asleep for 48 hours.

On his emerging, he appeared slightly improved and continued so for 6 weeks. During that period he was able to get up and go about the ward and he took his food himself. He still continued to worry about his bowels, though this subject did not engage his conversation as much as formerly. After 6 weeks he gradually relapsed. He became very depressed again, felt that he was the Devil's representative and that he had come to destroy the world.

The one permanent improvement which treatment did bring about in this patient was in the matter of feeding. For some time previous to treatment, he required a tube-feed thrice daily, but following treatment, he continued to take his food by himself.

On 12/11/35, he was transferred to Hartwood Asylum.

CASE 30. Catatonic schizophrenia. Treatment followed by an episode of acute excitement lasting 3 days, after which he returned to the former state.

A.G.K., a clerk aged 20, was admitted to the Glasgow Royal Mental Hospital on 5/7/35. The illness had been of 6 months' duration. He refused to take his food properly and became erratic in his behaviour. He would go out at all hours during the day or night and refused to talk to anyone. A week before admission, he suddenly jumped out of bed and attempted to rush out into the street in his night attire.

On admission, he was mute and inaccessible. He would not utter a single word. He kept his handkerchief firmly clutched in his right hand and resisted any attempt to take it away from him. For 3 weeks he became more and more negativistic and had to be tube-fed on occasions. He lay in bed all day taking no interest in his surroundings. Physically, he was thin and undernourished, but no signs of organic disease were detected.

It was in this condition that somnifaine was started on 24/7/35. He reacted very well and remained in a deep narcosis during the first week, but during the second week he became more and more disturbed. On the evening of the eleventh day, a complete change came over him. From being quiet and easily narcotised, within a few hours he became very noisy, talkative, excited and attempted to get out of bed. On the twelfth day, in spite of 6 c.c., he slept at intervals only of a few hours. On

the sixth day, he was actively sick. He required catheterisation on the third and twelfth days. Feeding was always difficult with this patient, and on the eleventh day he ceased to take fluids at all, and this refusal continued until the thirteenth day, when a tube-feed became necessary.

On account of the restlessness and increasing tolerance to somnifaine, associated with the retention of urine and refusal of food, it was decided to suspend treatment on the thirteenth day. He was put on rectal salines and after 3 days, began to take some food himself.

Urinary findings. Output was from 20 to 40 oz. per day. There was an occasional trace of albumin and acetone in the various specimens. The urinary acidity increased to 46° and was treated by alkalis. The temperature remained normal from 97°F. to 98°F., and the pulse from 50 to 80 per minute. Blood pressure fell slightly from 120/75 mm. to 105/70 mm. Constipation was relieved by hydrogen peroxide enemata.

As mentioned above, a sudden change came over this patient on the twelfth day of treatment. He suddenly entered a manic phase, shouting loudly and using abusive language. In 3 days he quietened down, and in a week relapsed into his former state of inaccessibility and negativism. His habits have become more and more degenerate. He giggles and laughs away to himself - obviously hallucinating. He remains in Hospital in that state.

CASE 31. Anxiety neurosis of 12 months' duration. Treatment followed by temporary improvement lasting a week.

G.S., an engineer aged 38, was admitted to the Glasgow Royal Mental Hospital on 13/10/35. His sister had suffered from an acute depression and had been under treatment in a mental hospital. He had always been an active and energetic man, a good mixer and above average intelligence. His illness began a year before admission. He became dissatisfied with his job and could not settle down to do his work properly. He was very nervous and restless and became afraid of some disaster overtaking him. He would sit about the house looking very gloomy and even weeping. He complained that something had snapped in his brain, and that this had destroyed his reason and power of concentration. He felt that he would never recover, and that he would end his days in an asylum.

On admission he was extremely distressed. He said that he never slept and complained of profuse sweating. He was subject to frequent attacks of acute agitation during which he rolled about in bed and wept bitterly. He felt that his memory was leaving him. Physically, he was a well-built man. Nothing abnormal was detected on physical examination, apart from a tendency to sympathetic over-activity, evidenced by frequent flushing of his face and profuse sweating.

Treatment was commenced on 18/10/35 and lasted 14 days.

A satisfactory narcosis was difficult to obtain even with pushing

the dose to from 6 to 8 c.c. per diem. Sleep was interrupted and he would waken up occasionally in a talkative, restless and distressed condition and complain of severe headache and profuse perspiration. The temperature rose on the ninth day to 99.4°F. At 10 p.m. on the tenth day, a further rise occurred to 101°F. For the following 8 hours somnifaine was withheld. By 10 a.m. on the eleventh day, the temperature had returned to normal. The pulse varied from 76 to 100 per minute and was of good quality. Blood pressure at commencement was 130/85 mm.; fell gradually to 105/72 mm. on the fourth day and 95/65 mm. on the sixth day. From the seventh day onwards it remained at the latter level. From the fourth day onwards he was incontinent. He complained of nausea on the twelfth and thirteenth days, but without actual vomiting.

Urinary findings. Output measured from 20 to 30 oz. per day. There was a trace of albumin on the fourth and eighth days and a trace of sugar from the seventh to the eleventh days. No acetone was present.

Following the conclusion of treatment there was a definite improvement in the patient, and for a week he remained very well, quite free from anxiety and full of hope for the future. He slept soundly and admitted that he did so. He felt that he had conquered his obsessions which had been making his life so miserable. He described the last year of his life as being in the nature of a bad dream which he did not remember too clearly and was trying to forget. This state, however, lasted only for a week, and at the

end of that time he showed signs of relapsing. He began to complain again of lack of sleep, loss of memory and mental confusion: in fact his condition became exactly as it had been before treatment was commenced. On 20/11/35, he escaped by climbing the wall. During treatment he lost 3 lbs. in weight.

... his wife and ...
 ... in the winter. ...
 ... his illness had been brought ...
 ... before admission. ...
 ... he said he had ...
 ... with water. ...
 ... through the ...
 ... of ---oOo--- ...
 ... he was very ...

CASE 32. Involitional melancholia of 6 months' duration. Treatment was complicated by a cardio-vascular collapse on the fourth day. Temporary improvement lasting a week followed the course.

W.M., an engineer aged 50, was admitted to the Glasgow Royal Mental Hospital on 4/9/35. His father had suffered from an attack of severe depression 10 years before his death. Five years ago, he began to suffer from rheumatoid arthritis and this progressed steadily until, at the time of admission, he had marked limitation in movement of both elbow joints. In the summer of 1935 he gradually became more and more irritable. He told his brother that he thought his wife was mad, and that she would be unable to look after herself in the winter. He said that he had ruined his firm and his illness had been brought about by his own fault. Five months before admission, he gave up work. He went off his food saying that he could not eat it because it was dirty. For a time even he refused to drink water, or to wash himself as he believed there were mice in the water tank. He said his children were guilty of misconduct in bed with each other. Later he had developed ideas that his bowels never moved and that his skin was peeling off.

On admission, he was very depressed, stated that he felt sad and hopeless and that he never slept. He felt that he had come into Hospital to be punished for his sins. He believed that he was surrounded by dirt, that the water was tainted and that his bowels had not moved for 2 weeks. His memory and orientation were

good. Following on admission, he showed no improvement. It was very difficult to get him to take sufficient nourishment as he said that food was collecting inside him, and that sooner or later he would burst. Physically, he was in poor condition. There was arthritis of both elbow and ankle joints. The heart was normal in size, but sounds were poor in quality.

Treatment was commenced on this patient on 18/10/35 and lasted 14 days. He reacted very well to the drug and remained deeply narcotised with a very small dose. Two c.c. were given on the first, fourth, fifth, tenth, eleventh and thirteenth days, 4 c.c. on the sixth, seventh, eighth, ninth, twelfth and fourteenth days, and 6 c.c. on the second and third days. The temperature remained normal from 97°F. to 98°F. On the fourth day the pulse became very rapid, averaging 120 per minute and was at times slightly irregular. His colour became poor. Two c.c. of icoral were given subcutaneously, and with it his cardio-vascular state improved considerably. Somnifaine was withheld for 24 hours. By the afternoon of the fifth day, the pulse-rate had diminished to 92 per minute. Blood pressure to commence was 130/90 mm.; on the fourth day, associated with a rise in pulse, it fell to 90/65mm.; under the influence of the icoral and also ephedrine gr. $\frac{1}{2}$ thrice daily, it improved and reached 110/75 mm. by the sixth day.

He was incontinent throughout the treatment and his urinary output was difficult to estimate, though well-maintained. There was a trace of albumin on the eighth day; sugar was present from the sixth to the tenth days. Reactions to acetone were negative during

the course. Urinary acidity remained low at 11°. Constipation was relieved by hydrogen peroxide enemata. He took his fluids well.

He emerged from the somnifaine 24 hours after the last injection. At first he was confused, asked where he was and what had been done to him. The effects of the drug wore off completely in about 36 hours and when seen at that time, he appeared extremely well. He was bright, happy and talked cheerfully about his past life and his future intentions. For 10 days he remained in this state of well-being. He read the papers daily, slept well and had an excellent appetite. His depressive ideas had vanished completely. After that period, however, he gradually began to relapse. Depressive features became prominent again; he went off his food, slept badly at night, and began to lose weight. The old ideas concerning his food and bowels returned. Up till the present he has remained in a depressed state.

Contra-indications.

Since the early days of induced narcotic therapy, efforts have been made to eliminate serious complications as far as possible, by the proper selection of patients. Kooy⁽²³⁾ states that cardio-vascular, renal, pulmonary and hepatic disease are all definite contra-indications and, since the treatment is drastic, it should not be given in the arterio-sclerotic, senile or debilitated. Similar views are expressed by most of the writers, including Klasi⁽⁸⁾ and Müller.⁽¹⁰⁾ Wagner⁽³⁰⁾ says that it is dangerous in the obese and in those with a very low blood pressure, or with a tendency to respiratory trouble.

In order to avoid complications, a careful physical examination should be carried out before treatment is commenced, and special attention must be paid to systems where trouble is likely to accrue. With regard to the chest, Magnus⁽²¹⁾ even advocates complete isolation of the patient for forty-eight to seventy-two hours before the first dose of narcotic, in order to make sure that no respiratory disease is in process of incubation and to prevent him from being infected during that period. He recommends also a detailed blood examination, with special reference to the white cell count, as a rise in this would indicate the presence of a fairly acute infective process. According to Maier⁽⁵⁰⁾, physically very weak patients and those with tuberculosis, liver, kidney and metabolic diseases and

marked anomalies of the circulation are unsuitable. During menstruation it should be avoided, since at that time the tendency to pyrexia and collapse is increased.

Nevertheless, a completely negative physical examination does not preclude the possibility of complications developing. Continuous observation of the case is the best safeguard, with the immediate cessation of treatment should untoward symptoms arise. Those "danger signals" have been already discussed.

Post-narcotic Reactions.

Following the conclusion of treatment, definite changes take place in the individual. Magnus⁽²¹⁾ describes the state of emerging very fully. Consciousness is gradually regained, the patient begins to recognise people round about him, but retention remains poor. Such a state of amnesia lasts up to seventy-two hours. The speech is inarticulate, the movements slow and ataxic and Romberg's sign is frequently positive :-

"In many the picture bears semblance to a mild toxic state, with visual hallucinations and confabulations."

The amnesia gradually ebbs away; the patient smiles and, at the same time, endeavours to explain what was once oddly said and done. He concludes by saying that during this period the physician should keep in close touch with his subject, as there is no better opportunity for psycho-therapy.

Bleckwenn⁽¹⁷⁾ found that after a dose of amytal, on the

return to consciousness, there was a prolonged period of physical relaxation and drowsiness. When aroused, the speech is slow and thick; there is marked inco-ordination and the eyelids droop. The patient responds to commands automatically and with a slow reaction time. It is during this stage that catatonics have striking episodes of normal existence.

The events following on treatment are called "abstention symptoms" by Meerloo⁽²²⁾. He states that one of 5 reactions may appear :-

- (1) A sudden change in the psychotic symptoms resulting in cure
- (2) Epileptiform attacks
- (3) Anomalous moods
- (4) After several days, a temporary, repressed psychosis may break through, with renewed fury
- (5) A variation in the temperature, with fever on the seventh or eighth day.

Strom-Olsen⁽²⁴⁾ found that four or five days were often necessary for withdrawal symptoms to subside.

In my series, the condition of the patient during the days following the cessation of treatment proved to be very much an individual matter. Some had completely lost the effects of the drug in forty-eight hours, but in others a week elapsed before one could say definitely that they had emerged from the narcosis. The usual sequence of events was as follows: for some hours sleep continued, and then the patient gradually roused. He was confused, spoke in a slurred voice, wondered where he was and appeared bewildered. During that stage, outstanding

psychotic symptoms which had been present previously, often persisted. The confusion passed off after a varied time, leaving the patient either improved or unchanged. Let us take, for example, Case 3, an involuntional melancholic. For two days, she remained very emotional and agitated, but on the third morning the weeping and distress had vanished, she was correctly orientated and spoke in a clear, relevant fashion. In another case (No. 8) the psychotic symptoms persisted for a week. She remained resistive, distressed and muttered and sobbed incoherently. Between two visits her condition had completely changed; her tenseness and distress disappeared, she requested food and talked in a perfectly intelligent manner. The most interesting case, however, is No. 1. For three days, she was confused, emotional and suffered from intense hallucinations. On the fourth day, an epileptic seizure took place. Two further fits occurred after a period of four days, and in the interval between them she had attacks of vomiting and frequent muscular twitchings. Following on the seizures, a rapid improvement was noticed. The confusion lessened, the hallucinations quickly vanished and in three days the change from her previous disordered mental state was remarkable.

It was impossible to state what result would take place until one had allowed several days to elapse. Certainly, observing the patient mentioned above, one would have thought that the outlook was very poor, judging by the persistence of her psychotic symptoms; yet eventually, she proved one of the

best results of the whole series.

A few cases showed a complete change in their signs during the emerging period. Thus, in Case 26, the patient - a paranoid schizophrenic - was hypomanic for three days; and in Case 23, the patient - an acute mania - was depressed and emotional for a similar period. As a rule complete amnesia remained for the period of narcosis. At the most, the patients had a hazy recollection about receiving the injections, but were quite oblivious to the time they had been under treatment.

The response of the different cases to somnifaine varied considerably, as did that of each individual at different periods of the narcosis. Some lay perfectly still in bed; others remained resistive, restless and noisy, yet in all these states they were deeply under the influence of the drug and had complete amnesia afterwards. Any psychotic symptoms evidenced during treatment were usually in accordance with the patient's original mental state, though occasionally depressive features would be noticed in a manic case and vice versa. For example, in Case 6 - a manic - there were occasional spells of sobbing and weeping. In 2 cases alteration occurred during the narcosis (Cases 26 and 30). The former became excited and happy during the last few days, and the latter suddenly passed into an acute manic state on the eleventh day.

A marked change, therefore, takes place in the whole

organism during the stage of detoxication. The period required for this differs widely, and it appears that the alteration which does occur is much more important than the actual sleep in bringing about beneficial results.

Results following upon Treatment.

Since the introduction of this form of therapy, workers have varied considerably in their views on its efficacy in mental disorder. Thus, Ragg⁽⁴⁾ in 1900, described complete resolution of symptoms in a manic depressive following on intensive bromide therapy; and in the same year MacLeod⁽³⁾ reported good results in several cases treated by the same means. In Klasi's⁽⁸⁾ series, out of 26 schizophrenics who had been given somnifaine, 8 showed immediate relief of their symptoms and 4 were discharged well two months later; 11 of his cases were unimproved and 3 died during the treatment. The improvement consisted in their quietening down, gaining in rapport and sometimes in repudiating their delusioned material.

Dawson and Barkas⁽¹¹⁾ were not enthusiastic over its results, and after treating their 18 cases - 5 of which had to be stopped on account of complications - came to the conclusion that any improvement was quite transitory and that the improved contact claimed by Klasi was not conspicuous. Oberholzer⁽¹³⁾ found that manic depressives and cyclic types of schizophrenics reacted very favourably. In his opinion good issues could be obtained where there was a tendency to period-

icity. Likewise Müller⁽¹⁰⁾ regarded manic depressives as the type which showed the best result after narcosis. Out of 20 manias treated, he had only 3 failures. Involitional melancholics, he felt, did not react well and as regards schizophrenics, the most favourable were the acutely excited and hallucinatory forms of the disease.

The results in a series of 179 courses of narcosis administered to 175 patients in 1927 and 1928 have been published by Meerloo⁽²²⁾. Twenty-six of these were considerably improved and, with the exception of one confusion, were all circular states. A group of 15 including 3 schizophrenics improved, but not completely; 57 were favourably influenced; 70 were unchanged and were chiefly schizophrenics. In 11 instances the course had to be interrupted on account of complications. He describes how the clinical picture of catatonia may be modified by barbitol therapy. One patient who previously had been very excited, hallucinated, cataleptic and allowed no physical contact whatever, during narcosis became quiet and the psycho-motor disturbance and catalepsy disappeared. Only stereotyped remarks and vague delusions remained. This lady kept well for a week after treatment, but very soon relapsed into her old condition.

Using sodium amytal, Bleckwenn⁽⁵¹⁾ indicated that, with its employment, more rapid recoveries could be anticipated in acute mania; that normal lucid intervals were seen in protracted cases of catatonia, that status epilepticus and acute deliria

could be controlled and that periodic narcosis would break down the stubborn insomnia met with in the more severe psychoneuroses.

Speaking of narcosis by the use of sodium amytal, Ettleson⁽²⁹⁾ also states that it causes an immediate disappearance of tension in some and induces prompt sleep in all. In one case it apparently shortened a manic attack; in a few others it rendered mute patients accessible, particularly catatonics, thus making it possible to obtain an idea of their mental content.

Kooy⁽²³⁾ treated 133 cases by means of somnifaine up to 1934. He divided them into 4 groups :-

- (1) Recurrent manic depressives
- (2) First attacks of depression
- (3) Schizophrenics
- (4) Various minor psychoses.

The curative effect was practically confined to the manic depressives. Out of 44 manic depressives so treated, he had 29 cures; out of 36 first attacks of melancholia, he had 14 cures; 9 cures resulted out of 29 cases from his minor psychotic group; but of 24 schizophrenics, no case was observed which became permanently well after treatment, though he had several instances where a remarkable temporary change occurred in the mental picture. He reports the case of a schizophrenic girl who, during the last part of her treatment, changed from an apathetic, autistic and resistive patient into a normally bright, keen and

interested person, only to relapse in a few days. Later, he gave a further course of three days of somnifaine which produced the same result, and for some time further he continued giving her 40 drops of somnifaine per day by mouth. This time her improvement was maintained, and she was discharged practically normal. He found that very often a manic phase changed into a mild depression and a depressive phase into a slightly euphoric state, both of which cleared up in a short time, leaving the patient well.

In 1930 Schrijver⁽⁵²⁾ treated a case of dementia paranoides by means of somnifaine for three weeks. Five days after the end of treatment, the patient was very restless, but seven days later he suddenly became normal, and had remained so six months later. On the eighth day he had 2 epileptic attacks, one in the morning and one in the evening.

Palmer and Paine⁽²⁰⁾ reviewing the results of 26 cases using sodium amytal for a period of from seven to ten days, state that 10 of their cases recovered, 4 were permanently improved, 7 were temporarily improved and 5 were unchanged. All their 5 cases of acute mania cleared up. The highest recovery rate was in those patients who had been subjected to the most heroic methods of treatment, where the administration of amytal had been combined with injections of luminal and hyoscine and by induced pyrexia :-

"That form of treatment which was most debilitating and produced the greatest degree of

"toxaemia and physical prostration resulted in the largest number of recoveries."

Out of 38 cases treated by dial, Magnus⁽²¹⁾ reported 14 improved, 9 who had lucid intervals and 12 who showed no change. One case was undetermined and 2 died. He considered that frankly involuntional cases and long-standing deteriorated patients did not respond well.

Murray and Burns⁽¹⁹⁾ found that in their series of 24 cases treated by sodium amytal narcosis, 16 showed some degree of improvement. Of 12 of these who were treated for five days or more, 10 were benefited; yet they believed there was only one case where the course of an acute mania seemed definitely shortened. They did not feel that the drug affected the fundamental course of the psychosis except by improving the physical condition of the patient, by diminishing the activity and producing a better contact with the environment.

Strom-Olsen's⁽²⁴⁾ series of 107 cases included schizophrenics, manic depressives, a number of chronic demented patients and 13 psycho-neurotics. Out of 49 schizophrenics 4 cases recovered, 19 were slightly improved and 26 showed no change. The catatonics were particularly disappointing; none recovered and only 3 improved. He agrees with Müller and Oberholzer, that cyclic and autistic forms of schizophrenia are those in which the most favourable result can be expected. Of 45 manic depressives, 17 recovered, 13 improved and 15 were unchanged. Of 13 psycho-neurotics, 8 recovered, 2 improved and 3

remained as before. Anxiety states showed the most favourable response. Included in the manic depressives were a number of involuntional melancholics, the results of which were very poor (3 recoveries out of 17 treated). He considered that prolonged narcosis followed by psycho-therapy was frequently more effective than when the latter was employed alone, and that it was essential for schizophrenics to commence occupational therapy at the earliest possible moment after the conclusion of treatment.

Wright⁽¹²⁾ who treated 85 psychotics by massive doses of potassium bromide up to 300 gr. per day, reports that 4 of his cases recovered, 2 were much better, 37 improved, 21 slightly improved and 21 showed no change. Deteriorated patients became cleaner in their habits and less destructive, agitated states quietened and violent patients were better adjusted to their environment. Most of his failures occurred in "states of apathy."

Maier⁽⁵⁰⁾ attributes much of the lack of success met with by some workers in the use of somnifaine and other barbiturates, to the neglect in carrying out the proper technique, the improper selection of cases, and failure to make good use of the period immediately after wakening for psycho-therapy :-

"The best prognosis in schizophrenics appears to be in the acute catatonic and hebephrenic attacks where, after some weeks in hospital, the acute stage lessens, but the patients are unable to find rapport with the environment. In such cases the sleep treatment is able to break up the vicious circle. Favourable also

"are those schizophrenics with a strong manic or depressive component in the symptom picture, provided that chronic catatonic elements are not in the foreground."

The 32 cases in the present series consist of 14 manic depressives, 6 schizophrenics, one paraphrenic, 8 melancholics, 2 chronic anxiety states and a final case where obsessional symptoms of a depressive nature had been present for many years, and which could not be placed in any of the other categories. Of the manic depressive group, 3 were acutely maniacal, 9 were depressed and 2 were of a mixed type where short spells of distress and emotion alternated with longer periods of restlessness and excitement. Of the schizophrenics, 4 were definite catatonics and 2 were of the paranoid type. In a few of the cases, the diagnosis was not very clear. For example, in Case 1, many of the features were distinctly schizophrenic, and in Case 15, though the main state was one of depression, marked paranoid trends were also present. Ten of the patients in the manic depressive group had suffered from one or more previous attacks which had cleared up after a varied period of time. In the remaining 4, no history of a former mental illness was elicited.

The melancholic group includes patients where the symptoms were of the involuntional type, and in each case it was the patient's first attack.

The most outstanding results occurred in the manic depressive group. Out of the 14 cases treated, 8 recovered.

Two of the acute manias cleared up after treatment and in the third case the same thing happened, to be followed only by a complete relapse in two weeks. Five of the 9 depressions recovered and were able to leave the Hospital. One case, following treatment, passed into an acute manic state which resolved spontaneously in three months. Two showed slight, temporary improvement and one was unchanged. One of the mixed states recovered completely and in the other a slight amelioration of the symptoms was noted for a few weeks.

By cure in the manic depressive group is meant recovery from the existing attack. A course of somnifaine, though it may be effective in cutting short an acute mania or depression, does not prevent the development of a further attack at a later period. Case 23 is a good example: each course of narcosis brought about a resolution of symptoms, but a further acute mania occurred after a short interval. Similarly, in Case 22, the depression cleared up after treatment, only to recur when the patient was faced again with professional and financial responsibilities. Also in Case 9, the patient remained well for some months until the death of her mother caused a return of her old symptoms.

A course of intensive narcosis by means of somnifaine or other suitable drug, would seem to be an excellent form of therapy in those recurrent or cyclical manic depressive cases, especially if it is known from previous experience that the

attack is likely to be protracted. In these seven to fourteen days' treatment will probably be effective in curtailing the illness. In any case, in a patient of that type sedatives are usually required; in mania, to diminish excitement and in depression, to promote sleep. A course of somnifaine will do both of these and, at the same time, help to bring about improvement of a more lasting nature.

In the melancholic group, the most striking feature was the remarkable improvement often amounting to apparent cure which frequently took place after they had emerged from the narcosis. It occurred in 4 of these patients. In each case, however, this change was only temporary and every one ultimately relapsed into the former depressed state. The period of well-being varied considerably: in one case relapse occurred after three days, while in another the patient remained extremely well for two months. In some of these cases, the suddenness of the relapse was almost as marked as the rapidity with which they got well during the period of emerging from the somnifaine. This was observed in Case 3. In the morning, she had been bright and cheerful, but as the day went on, she gradually became emotional and agitated, and by the evening she was exhibiting practically all her former symptoms. In others, the relapse was not quite so sudden, and it occurred gradually over the space of several days.

None of the 4 catatonics recovered; one was slightly improved for ten days; another became acutely excited for three

days towards the end of the narcosis and 2 showed no change after emerging. The 2 former cases reverted into their previous state and have since remained so. Both the paranoid schizophrenics were more approachable and less deluded for a short period afterwards. In the paraphrenic patient, an apparent cure was obtained and lasted for four weeks. During that time her mental state differed little from normal, but it was followed by a gradual re-development of her previous symptoms.

One feels in these cases where a complete temporary recovery has taken place, that the re-development of symptoms is a type of rapid and condensed picture of what occurred at the very commencement of the illness.

In neither of the chronic anxiety states was any definite benefit obtained, and the obsessional depressive case also was unaltered by the treatment.

In those who improved, it was very interesting to hear their views concerning their previous mental state. The majority remembered their symptoms, but were unable to give a logical explanation of their behaviour and ideas. For example, in Case 3, the patient remembered that she had wept all day, bitten her clothes, worried over the burying of a Bible, but could not explain why she had done so. Similarly, in Case 22, the patient could not understand why he had brooded so much and taken such a gloomy view of things. A number of the manic depressives appreciated the fact that the treatment had brought about an improvement, and a few expressed their gratitude to

those who had attended to them. On the other hand, during the temporary improvement in the melancholic patients, a marked feature was the extreme lack of insight into the nature of their original state. They admitted their old ideas and behaviour, but had no realisation that they had been suffering from a mental illness, or that the narcosis had been instituted as a therapeutic measure.

Summary of Results.

<u>Manic Depressive Group.</u>			<u>Result.</u>
<u>Mania</u>	<u>Depression</u>	<u>Mixed</u>	
<u>Case Nos.</u>			
		1	Complete recovery.
	5		Slight temporary improvement lasting a few weeks.
6			Gradual recovery following treatment; complete in 6 weeks and permanent.
	9		Recovery from present attack.
		12	Temporary improvement lasting 4 weeks, followed by complete relapse.
	13		Complete and permanent recovery.
	15		Slight amelioration of symptoms for 2 to 3 weeks, followed by complete relapse.
	17		No definite change occurred in this patient.

Manic Depressive Group.Result.Mania Depression MixedCase Nos.

	19	Improvement for 2 weeks, followed by sudden change to acute mania. Complete recovery in 3 months.
	21	Complete recovery.
	22	Recovery from present attack.
23		Complete recovery from each attack in the 6 courses given.
	24	Gradual recovery which has been maintained.
28		Recovery lasting 2 weeks, followed by relapse which cleared up spontaneously in 4 weeks.

Melancholia - First Attack.Result.Case Nos.

	3	Complete recovery lasting for one week, followed by a rapid return to former state of depression and agitation.
	7	No change.
	8	Complete absence of symptoms for 2 months, followed by relapse.
	14	Slight temporary improvement which was not maintained.

Melancholia - First Attack.Result.Case Nos.

18	Death from pneumonia 5 days after commencement of treatment.
25	Marked improvement which lasted only 3 days, followed by complete relapse.
29	Slight improvement of 6 weeks' duration, with return to former condition.
32	Marked improvement with complete absence of depressive ideas for 10 days, followed by relapse.

Chronic Anxiety States.Result.Case Nos.

27	No change.
31	Slight temporary improvement lasting one week.
11	This case could not be placed in any of these groups. She was a chronic obsessional depressive state of many years' duration. Treatment resulted in no change whatever.

Schizophrenic Reaction Type.Result.Catatonic Paranoid ParaphrenicCase Nos.

2

Slight temporary improvement lasting a few weeks, followed by complete relapse.

4

No change.

10

Marked improvement lasting 4 weeks, during which delusional ideas and hallucinations disappeared. At the end of that time a complete relapse occurred.

16

No change.

20

Slight improvement lasting 10 days.

26

Slight temporary improvement lasting one week.

30

Sudden change to manic state lasting 3 days, followed by return to previous symptoms.

Rationale of Treatment.

Three points have here to be considered :-

- (1) Why should a barbiturate like somnifaine produce sleep
- (2) In what region of the brain does it act
- (3) How can any beneficial effect following treatment be explained.

The derivatives of barbituric acid have been known for some time to possess anaesthetic and analgesic properties when administered orally or parenterally⁽⁵³⁾, but little is understood about their absorption. They are eliminated slowly and have a cumulative effect. In diseases with fever less barbital is eliminated, and even small doses inhibit diuresis⁽²³⁾.

Katzenelbogen⁽³⁵⁾ believes that the essential property of narcotics is that of inducing important disturbances in cell permeability, and the lowering of cellular sensitiveness so produced may be one of the conditions inducing sleep. Being easily absorbed, narcotics interfere with a normal absorption of hormones and this is deemed to be the most important preliminary condition of induced and natural sleep.

In the opinion of Meerloo⁽²²⁾, these drugs act on the brain-stem and he quotes the numerous bulbar symptoms which may arise as corroborating this viewpoint. The anuria which occurs is not necessarily the result of toxic irritation of the kidneys, as a similar condition is found in cases of subcortical or ventricular tumour, showing that barbital also have a tendency to-

wards these subcortical areas.

In experiments on rabbits, Keeser⁽⁵⁴⁾ found that, when barbital products are injected intravenously, they are discovered post mortem chiefly in the thalamus and in lesser amounts in the striate body.

Von Economo⁽⁵⁵⁾ in an endeavour to localise the sleep centres, examined the brains of patients suffering from epidemic encephalitis, in 85 per cent. of which there is trouble with sleep function. Inflammatory lesions were found in the cup of the mid-brain at its junction with the thalamus, suggesting that a centre in this region co-ordinates the changes occurring in sleep.

Kooy considers that the drug acts on the cerebellum like all veronal preparations, with a resulting tendency to dysarthria inco-ordination and nystagmus, and on the medulla oblongata. He suggests that, as somnifaine affects the temperature curve, and since the temperature centre like the sympathetic centre and that for carbohydrate metabolism, is supposed to be in the neighbourhood of the third ventricle, it is possible that the narcotic acts also in this region. He wonders if somnifaine affects the regions of the brain which are involved in manic depressive insanity. He makes a sweeping statement by saying that the central grey substance round the third ventricle may play some rôle in this disease, and that that is why prolonged narcosis is chiefly beneficial in this type of illness.

Following experiments on sodium amytal, Thorner⁽⁵⁶⁾

believes that the action of the drug is partly upon the autonomic neurones, since changes in the pupils, respirations, pulse and blood pressure are common accompaniments. Small doses appear to act chiefly on the cortical cells and larger doses are necessary to cause appreciable change in the function of the autonomic nervous system.

Horst and Hasselt⁽⁵⁷⁾ report a case which had died from cardio-respiratory failure following large doses of somnifaine. The post-mortem showed extensive degeneration of ganglion cells in the nucleus dentatus, the thalamus, the striate body and in the medulla.

Isenberger⁽⁵⁸⁾ points out that barbiturates act by depressing vegetative centres in the hypothalamic portion of the diencephalon.

Pick⁽⁵⁹⁾ divides hypnotics into two sets: the barbital group which act on the thalamus, and ether, alcohol, chloral and bromide which are cortical depressants.

The balance of opinion, therefore, is that somnifaine exerts a profound effect on the subcortical areas, and this is further borne out when one attempts to correlate the varied bodily disturbances met with during and immediately after narcosis. Brain⁽⁶⁰⁾ indicates the widespread systemic results which follow disturbance in the region of the hypothalamus. This part of the brain is intimately related to the involuntary nervous system and to the function of the endocrine glands. His statements may be summarised as follows :-

- (1) Lesions in the region of the tuber cinereum may lead either to persistent somnolence, or to paroxysmal attacks of sleep.
- (2) Disturbance of sugar metabolism has been produced by experimental lesions of the hypothalamus.
- (3) Irregular pyrexia may occur in patients with a lesion in the region of the tuber cinereum, and the hyperpyrexia which not uncommonly follows operation in this region is probably the result of injury to a hypothalamic, temperature-regulating mechanism.
- (4) It has been shown that stimulation of the hypothalamus causes a liberation of adrenalin: therefore, it seems obvious that depression of this area (by somnifaine) would diminish the output of adrenalin, with a corresponding fall in blood pressure and a tendency to cardio-vascular collapse. It has been mentioned that the reduction in pressure takes place rapidly after the first injection which points to its being most likely of a nervous origin and not to a toxaemia which would take longer to develop.

Other findings, such as excessive sweating and rapid pulse, are known to occur during an increased activity of the sympathetic, the action of which is, as previously mentioned, built up with the hypothalamus. On the other hand, a fall in blood pressure and flushing of the skin are usually associated with a diminished sympathetic activity.

The most likely cause of these changes would seem to be due to a dysfunction of the hypothalamic nerve centres, resulting from the effects of somnifaine in that area. Meerloo also explains abstention phenomena on similar lines. He says that the habitual use of a toxic substance such as a barbiturate produces a change in the vegetative hormonal system, resulting

in disturbance of the vaso-sympathetic system which is afterwards re-established on a new level :-

"Abstention phenomena may thus be explained by the disturbance of this new and less stable equilibrium."

"The treatment brings about a non-specific pharmacological alteration in the onto-genetically and phylo-genetically oldest parts of the brain."

One then wonders if the cause of the epileptic seizures could be founded on similar lines. The theories of epilepsy are still very indefinite, but the following impresses one as explaining the attacks which occur during the detoxication phase.

Hartenberg⁽⁶¹⁾ suggests that the initial feature in epilepsy is a cerebral inhibition, with sudden release phenomena due to the over-action of the lower centres. Now, it has been shown that somnifaine depresses the subcortical parts of the brain, with the result that during the period of narcosis there is no need for cortical control over these centres. However, after the patient emerges, the subcortical areas again become active and the cerebral control which has virtually been in abeyance for the duration of the narcosis, is unable to prevent these release phenomena, with the result that fits may occur during that period. The view is certainly very hypothetical, but it is in agreement with the facts.

One has now to consider the reasons why an alteration in the mental state should occur following the prolonged adminis-

tration of a hypnotic drug. According to Meerloo⁽²²⁾ treatment by barbitals originated in the idea that long-continued sleep on the part of the sufferer would facilitate contact between him and the psycho-therapist, a contact which had proved impossible in the face of motor restlessness, hallucinations and similar phenomena. In 1900 MacLeod⁽³⁾, reviewing his intensive bromide therapy, stated that during the period of narcosis, the higher centres are rested to an extent which cannot be obtained in any other way, and that the prolonged sleep may cause the patient to forget his delusions or psychotic trends. Klasi's⁽⁸⁾ original plan was to give rest to the diseased parts of the brain. A second result which he pointed out was that of rendering the subject more approachable on account of his comparative helplessness during narcosis and more dependent on his environment, thus making possible a closer contact between him and the physician and facilitating psycho-therapy. He compares his results with the improvement observed in schizophrenics during an acute infection and believes that in both cases it is due to the closer contact with the physician, and the increased attention given him during the illness, rather than to any physiological effect of the drug or infection :-

"When physically incapacitated, a schizophrenic would experience a certain feeling of helplessness and dependence which would increase his contact with the environment."

Klasi attributes his improvement in schizophrenics to

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psycho-therapy during and after treatment. He utilised the twilight state between the periods of sleep for this purpose. One feels that the narcosis which he induced must have been very light as, with the recommended 4 to 6 c.c. per day, the patient is rendered quite out of touch with his surroundings and contact with him is well-nigh impossible. After treatment there is practically always a complete amnesia for the period of the course, and it is difficult to see how any reassurance of the patient during that stage could prove of permanent benefit.

Palmer and Paine⁽²⁰⁾ believe that anything which will prostrate the patient, lower his general resistance and make him more dependent upon others, will render him more accessible to psycho-therapeutic endeavours :-

"The mechanism of recovery or improvement seems to be psychological rather than bio-chemical. A psycho-dynamic formulation seems not only more reasonable and more tenable, but is readily correlated with, and supported by psychological and psychiatric observations."

Bleuler⁽⁶²⁾ feels that the schizophrenic with part of his personality at least, craves help and is dependent on others for it. The narcosis causes a breaking through of the schizophrenic's defence and gives him a chance of contact with his environment :-

"It prevents the schizophrenic peculiarities from becoming fixed and helps to form a new and better adaptation."

Again, Murray and Burns⁽¹⁹⁾ reviewing the results on amytal narcosis, state that the drug does not affect the fundamental course of the psychosis, except in improving the physical condition of the patient by diminishing activity and in producing a better contact between the patient and doctor :-

"The ideal situation would be to have the psychiatrist constantly with the patient during treatment and be able to devote considerable attention to the latter for some time afterwards."

They found that all their manic patients, while under the influence of the drug, became deeply depressed and cried most of the time. Those who were benefited by the treatment remained depressed until recovery or improvement. This, they say, points to the conclusion that the euphoric stage of the manic depressive is an over-compensation, and that the fundamental condition is a depression which must be faced by the patient before recovery can occur.

Bleckwenn⁽⁵¹⁾ considered sleep as a biologic reaction of defence. He imputed the chief value of sodium amytal to its ability to produce prolonged and unconscious states easily and safely. He concluded that the drug was apparently a cortical depressant.

Wagner⁽³⁰⁾ sums up the situation very well: the marked improvement noted after prolonged narcosis has been variously explained on a psychological, physiological and bio-chemical

basis. Undoubtedly the rest, both psychological and physiological, is an important factor. In addition to this, the phenomena at the time of awakening, when he is rendered more suggestible, when he gains a feeling of well-being and shows more confidence towards people in his environment, are important factors.

From a purely clinical standpoint, Strom-Olsen⁽²⁴⁾ says, it would seem that the therapeutic action depends on two phenomena; the first being the removal of inhibition which is clearly seen in the twilight states of the treatment; and the second, the actual state of narcotic sleep in which one may speak of a central anaesthesia in the true sense of the term. During this period there is a complete abolition of the effects of peripheral stimuli and a consequent amnesia for the interval of the narcosis :-

"In the majority of cases, a degree of narcosis is required which will be sufficient to produce a more or less continuous sleep for a twilight state alone is evidently inadequate in most cases."

The above theories are all based on a psychological explanation, but various factors suggest that something else may be at work to produce the beneficial effect. For example, Magnus⁽²¹⁾ found that the actual depth of sleep had no material bearing on the results; and similarly, Kooy⁽²³⁾ states that often those who do not sleep well recover after treatment. The latter reports a case at Sandpoort where van der Scheer⁽⁶³⁾ made

the experiment of keeping a manic in a continuous sleep by hypnosis without the improvement which somnifaine subsequently brought about.

Thorner⁽⁵⁶⁾ believes that a depression of the activity of some of the neurones of the cerebral cortex is the important factor.

Palmer and Paine⁽²⁰⁾ state that cellular rest and the opportunity afforded the cellular metabolism to store up reserve for subsequent expenditure seems acceptable.

Quastel⁽⁶⁴⁾ describes at some length his views on the therapeutic results on a toxic basis. If we judge a functional psychosis to be due primarily to a hyperactivity of certain nervous structures, or a depression to the activity of others, the results are the same. There will exist an abnormal production of certain metabolites in the brain, or possibly of harmful substances whose presence brings about a disturbance in the normal equilibrium of the nervous system. In prolonged narcosis a depression of nervous activity is secured, compared with which the disturbance due to abnormal metabolites is small. During the long period of narcosis these metabolites, or maybe toxic substances, are eliminated by the body and are not replaced because of the lowering of the activity due to the narcosis. After a sufficiently long period of narcosis, the body is allowed to recover, and assuming no permanent damage to the nervous system, this should become relatively free from the abnormal conditions present before the narcosis. Granting this view,

it would follow that organic psychosis should not benefit, or those which are due to the presence of an active septic focus, unless the latter has been eliminated.

This view brings out various questions. Firstly, have we any evidence that during a psychosis abnormal or harmful substances are produced in the brain? And secondly, if so, how and where are they produced, and what is their nature? Cruchet⁽⁶⁵⁾ has demonstrated the value of large doses of chloral and chloroform in diminishing the symptoms resulting from neurotoxicosis. He deals with tetanus chiefly, and believes that after the early stages of the illness the toxin becomes fixed to the neurones. By anaesthetising the patient deeply for a prolonged period with chloroform, which itself is a powerful neurotoxin, the latter fixes itself to the nerve cells, and in doing so the neurone loses its hold on the tetanic toxin. To this theory one gives the name of "phylaxis." Cruchet believes that by doing this and at the same time giving large doses of anti-tetanic serum, the toxin is neutralised as soon as it is freed from the nervous tissue under the action of the chloroform. This point will be discussed later.

That the type of drug is not a responsible factor is the view expressed by Hackfield⁽²⁵⁾. Good results have been obtained by other forms of sedatives. To begin with, he states that most of the drugs successful have a specific action on the brain-stem, and therefore the point of therapeutic attack must be on the central part of the vegetative nervous system. He

feels that this theory breaks down, however, when one considers that improvement has been obtained from chloral, morphine and hyoscine which act on the cerebrum. He expresses a further idea that, as a result of the many afferent stimuli, condition reflexes are established. These delicate mechanisms in the cerebrum are easily disturbed and a cycle of heterogenous, disorganised reactions follow. To effect a recovery this cycle must be broken and rest is the best agent to bring this about :-

"The use of a drug which breaks the cycle at any point either in the brain-stem or in the cerebrum, producing absolute rest, is the goal of this therapy."

He states that the affective syndrome does not constitute a psycho-pathological entity, but rather a psycho-physio-pathological one, and this is attested by the accompanying autonomic dysfunctions during the illness and their return to the physiologically normal, with recovery from the psychosis.

The opinion of Wright is that the influence of the bromides appears to be explainable by reference to their known influence as a sedative or quietening agent in the domain of the autonomic system :-

"In the psychotic by reason of regression, the erotic tension manifests itself at inferior or infantile levels. When the tension is freed, the libido is set at liberty to occupy itself with more socialised interests."

Reviewing again the detoxication theory, we find that

Schrijver⁽⁶⁶⁾, discussing the biological mechanism of somnifaine treatment, found that changes occurred in the blood serum, indicating an increased disintegration of body albumin and a shift to the left of the polynuclears, such as one finds in various non-specific stimulating treatments. He mentions sulphur and nirvanol as being examples of these.

Reference must be made here to the theory of Bancroft and Richter⁽⁶⁷⁾. This theory considers that alteration in function of the central nervous system might be due to a change in the state of dispersion of the cellular colloids. These workers have shown the effect on albumin and globulin colloidal solution when exposed to a variety of narcotic and anaesthetic drugs. In each case the colloidal states have been agglomerated. If, however, sodium or potassium chloride, iodide, bromide, or thiocyanate was exhibited, the process of agglomeration was reversed and the normal state of dispersion was obtained. Cell activity and irritability were observed to be increased as agglomeration increased, and decreased by the reverse process. They believe that the whole genesis of mental disorder can be reduced to the simple terms of colloid agglomeration and colloid over-dispersion. By giving a coagulating drug, such as sodium amytal, to a psychotic whose cell colloids are in an over-dispersed state, there follows a re-establishment of cellular equilibrium, ending in mental recovery. Similarly, a dispersing agent, such as sodium rhodanate, would produce equilibrium in a

psychotic whose cells were in an over-agglomerated state. They even went as far as to say that different drugs, such as these, could be used in differentiating as well as in treating the opposed types of mental reaction. The catatonics and hebephrenics are supposed to suffer from an over-dispersion of cell colloids, while manic depressives and paranoid schizophrenics suffer from an over-agglomeration or coagulation of cell colloids.

These theories have been refuted by other workers. Harris and Katz⁽⁶⁸⁾ proved that there was no diagnostic value in the contrasted use of sodium amytal and sodium rhodanate. Similarly, Schube⁽⁶⁹⁾, following experiments on 75 patients at the Boston Psychopathic Hospital, found that at no time did sodium rhodanate produce any change in the mental or physical picture, whereas, if Bancroft's theory were true, manic depressive forms should definitely have benefited, being due to an over-agglomeration of cell colloids.

It seems, therefore, that there are as many views on rationale of narcosis as there are writers on the subject. Meerloo admits this by saying that we do not know with any certainty how the treatment works, at what stage and to what disease it is best applied, what is the optimum dose and for how long the treatment should be continued.

Let us now discuss these views and attempt to correlate them with the clinical findings during and after narcosis. In

the first place, cure in the true sense of the word is met with only in the manic depressive psychosis. One wonders if, in some of Klasi's schizophrenic patients who cleared up after treatment, the diagnosis was really correct. It is well-known that there is often great difficulty in differentiating between an acute schizophrenic excitement and an acute mania. Frequently the only way is to keep the patient under close observation over a prolonged period of time, to ascertain the type of reaction. Even in the present series, as already mentioned, the exact diagnosis before treatment was uncertain in 2 patients. Practically all the writers have agreed that results "par excellence" are met with in the manic depressive group. The next point is that somnifaine, though it may cut short an acute mania or depression, has no power in preventing a further attack developing in the individual. It apparently does something which hastens the natural course of the illness, bringing it to an end sooner than it would do so spontaneously. There seems an analogy between its action and that of adrenalin in stopping in a few minutes an attack of asthma which would have lasted for several hours or longer. Yet, like somnifaine, a further attack would not be prevented as neither drug affects the respective underlying diathesis, and any fresh precipitating factors are liable to bring back the old symptoms. Klasi has compared the effects of somnifaine with that of an acute infection in bringing about improvement in schizophrenics. Now, the

latter fact, I think, is well-known to most psychiatrists. I remember the case of a catatonic youth at Gartnavel who developed an encysted abdominal abscess, caused by his swallowing a piece of cane which had perforated his duodenum. He made no complaint and it was only as a result of a gradually increasing pyrexia that a detailed physical examination was carried out and the condition discovered. Up till the time of his operation he remained in a typical catatonic state, but a week after the abscess had been opened and when it was draining freely, his mental picture rapidly changed. He began to eat his own food, talked intelligently and took an active interest in his surroundings. This state of well-being persisted for about a fortnight, when he soon relapsed into his former resistive and mute condition. Now, that is exactly what was observed in some of the more malignant psychotic types treated with somnifaine. In both, while the toxæmia was present from the barbiturate or from the staphylococcal infection, no change was discovered; but in both during detoxication a remarkable improvement took place, only to be followed by a complete relapse.

To quote again from Meerloo :-

"One gets the impression that something happens to the psychotic patient after the heavy somnifaine intoxication - something serious - a process which causes the psychosis to yield for a shorter or longer period, but at the same time a process which we cannot control."

It seems unlikely that Klasi's idea that the increased

attention given to the patient during narcosis helps to promote improvement. Many psychotics have repeated opportunities for contact with the physician during ordinary routine psycho- and physico-therapy, yet no beneficial effects follow. Actual sleep per se cannot be the main factor, as a number of patients who remained resistive and restless during treatment gave good results. This important fact has also been noted by Magnus and Kooy.

The views of Strom-Olsen are certainly feasible. No doubt the long period of amnesia during narcosis may cause a break in the abnormal thought processes. The latter in the manic depressive being naturally of a temporary and more superficial type than the normal mental trends, are more easily interrupted, whereas in the schizophrenic, in whom the illness has been in the nature of a progressive maladaptation over a prolonged period of time, they have virtually replaced all the normal ways of thinking and, therefore, cannot be changed. Those statements are, of course, hypothetical and do not bring into line the improvements following acute infection where the amnesia does not occur.

As has been previously mentioned, the most marked disturbances, clinically, during narcosis occur in the involuntary nervous system, and during detoxication there is a rapid return to normal. Now, in any acute infection one encounters a rise of temperature, rapid pulse, perspiration, fall in blood pressure

and flushing of the skin; these effects most likely resulting from the action of the toxin on the autonomic centres and the hypothalamus. If the infection is such that a rapid relief can be obtained (as in the case cited) improvement in the co-existing psychosis may occur. These views have definitely clinical proof, but beyond that one is dealing in theory only. Whether the rapid return to normal of a severely disordered autonomic system causes a break somewhere in the psychotic vicious circle it is impossible to say.

If one accepts the toxic theories of mental disorder, one naturally wonders if improvement could not be explained along those lines. Undoubtedly toxic states are present in many psychotics, and in the present series of cases, were dealt with radically before, during and after treatment. Teeth and mouth received attention; the throat was examined and an attempt made to detoxicate the alimentary tract. Constipation was carefully guarded against and in a number hydrogen peroxide lavage of the lower bowel was carried out. Many of the patients also received yatren (Bayer) up to 24 gr. per day. The idea of a specific neurotoxin being the cause of certain mental disorders is expressed by Ford-Robertson⁽⁷⁰⁾, and certainly, if this is the case, the views of Cruchet on phylaxis could be accepted; the somnifaine displacing the toxin from the affected neurones, resulting in cure or improvement of the psychosis. Nevertheless clinical proof of a toxin of this nature is not yet forthcoming, so the above viewpoint is extremely tentative.

Certain factors are definite :-

- (1) That sudden abstention from a severe toxaemia tends to produce a beneficial result in mental illness.
- (2) Somnifaine has the advantage of being a sedative in addition to a toxic substance.
- (3) The most profound effects of the drug are on the hypothalamus and the involuntary nervous system.
- (4) Sleep per se is not the main factor. Intoxication is much more important.

It would seem that one could discuss the question from any point, depending largely on one's views as to the aetiology of mental disorder. A course of somnifaine therapy apparently causes a break somewhere in the psychotic processes either in the physical or psychological sphere, resulting in amelioration of the symptoms.

CONCLUSIONS.

1. Prolonged narcosis with somnifaine is a useful but dangerous form of therapy.
2. Numerous complications are liable to occur, some of them being of a serious nature.
3. Careful selection of cases from a physical point of view is essential.
4. The treatment requires the most careful supervision.
5. The curative effect is confined to the manic depressive group.
6. Cure of acute mania or depression by somnifaine does not prevent the development of future attacks.
7. Marked temporary improvement may be expected in melancholia.
8. Catatonics are uninfluenced by the treatment.
9. The drug appears to have its most profound effect on the subcortical areas, the hypothalamus and the involuntary nervous system.
10. Improvement occurs after the drug has been stopped and not during the narcosis.
11. It would seem to be an excellent form of therapy in cases of recurrent or cyclical manic depressive insanity, where the physical state is satisfactory, and especially if it known from previous experience that the attacks are likely to be prolonged.

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