A STUDY of the CONVULSION THERAPY in MENTAL DISORDERS.

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Historical Introduction.

In 1929 Nyiro and Jablonozky published a series of observations on the treatment of epilepsy. One important point which emerged from these observations was that the recovery rate of epileptics in the series of cases which they studied was 1.05% but rose to 16.05% if schizophrenic features were present. This suggested the possibility that some biological antagonism exists between the two conditions - a suggestion which received support from G. Müller's description in 1930 of two cases in whom schizophrenic symptoms disappeared after the onset of idiopathic epilepsy. Continuing on the same lines Glaus in 1931 pointed out that the combination of schizophrenia and epilepsy was a rare one and could find only eight cases showing symptoms of epilepsy out of 6,000 schizophrenics investigated. Of these eight, four recovered from their schizophrenia shortly after the appearance of the epileptic fits. Finally Steiner and Strauss in 1932, after examining 6,000 cases of schizophrenia, concluded that the rarity of

epileptic seizures suggested a mistake in diagnosis in those cases in which the fits did appear.

In 1933 Sakel (1) published a report on four cases of schizophrenia which he had treated by insulin shock therapy. In three of these, epileptiform convulsions occurred at intervals during the treatment and were followed by marked improvement in the condition of the patients. On the basis of this observation he expressed the view that the epileptiform convulsion was an essential factor in producing improvement by hypoglycaemic shock. (It must be admitted that he modified this view later and now believes that the convulsion plays only a minor part and indeed may be harmful in some cases.)

At about the same time von Meduna commenced experiments on guinea pigs in order to discover a safe and reliable convulsant drug. For this purpose he used 25% bromide of camphor in oil and found that this, without damaging the vessels of the nervous system, would produce convulsions which resembled closely genuine epileptic attacks. He then proceeded to treat with this preparation a number of cases of schizophrenia who had been in hospital for years and were regarded as hopeless. He soon discovered, however, that camphor in oil was not a satisfactory

agent because the convulsant action was variable and the drug tended to induce a prolonged deliriform state with active hallucinations and impulsive tendencies and because the excretion of camphor into the lungs and stomach invariably caused nausea and vomiting. Further experimentation on animals led to the use of cardiazol as a convulsant agent and this preparation has now superseded camphor for this purpose.

Chemistry and Pharmacology.

Cardiazol is the European, and metrazol the American, trade-name for pentamethylenetetrazol which is a light water-soluble substance similar to camphor in chemical structure and possessing similar therapeutic properties. It is readily soluble in nearly all solvents, including lipoids, and is thus rapidly absorbed if given intramuscularly. In water it forms a stable, almost neutral, solution. If injected into the circulation it is eliminated rapidly so that, according to Biehler[3], two doses of 1 c.c. each injected shortly after one another produce a much smaller effect than a 2 c.c. dose in experimental animals. There is no satisfactory evidence as to how the drug is excreted from the body.

In small doses (1 c.c.) given either intramuscularly or intravenously, it has been used for some time in general medicine as a cardio-respiratory stimulant. According to Camp[4] it acts specifically on the medulla and Burn[5] states that it stimulates the vasomotor and respiratory centres in the medulla and is thus of value in barbiturate poisoning. It has no direct action on the heart but it may, by acting through the medulla, increase the force of the heart beat and raise the blood pressure.

Convulsive Effect.

There is a gap between the ordinary therapeutic dose of 1 c.c. and the convulsive dose. The latter depends upon the susceptibility of the subject but is usually about five times the therapeutic dose. It is interesting to note that epileptics are often particularly susceptible to cardiazol - indeed in one of a small series of epileptic patients who were tested during the course of this investigation the intravenous injection of 1 c.c. of a 10% solution of cardiazol, that is the ordinary therapeutic dose, was followed immediately by an epileptic fit. This was a true epileptic fit and differed in one or two points from the typical cardiazol convulsion. In the latter the

general course of events is as follows. Within the first five seconds after the injection the patient gives a slight cough - this is followed, almost immediately, by rapid twitching of the eyelids and pallor of the face. Myoclonic movements begin in the face and spread to the arms and legs and a short clonic phase develops which is cut short after one or two seconds by the appearance of a marked tonic phase with loss of consciousness. In this the head is retracted, the eyes move upwards and to the side, the mouth opens widely with such force that the lower jaw may dislocate and the arms and legs are tetanically contracted, usually in extension, with the wrists and fingers flexed and the thumbs held between the first and second fingers. Opisthotonus may be present. This phase lasts about twenty seconds and then clonic movements begin in the fingers and spread rapidly to involve the whole body. These movements are at first rapid but gradually become slower and more severe and finally cease after about twenty to thirty seconds. During this stage the nipples in the female are erect and ejaculation may occur in the male. Incontinence of urine may also occur but this happens rarely. The patient becomes deeply cyanosed with widely dilated and inactive pupils and

positive Babinski reflexes. One or two seconds after the last clonic contraction the patient takes a deep, stertorous breath and respiration remains stertorous for the next minute or two, gradually returning to normal. The reflex changes disappear almost immediately and the cyanosis vanishes after the first few breaths. (It is interesting to note that in one case of this series who was known to have an old tuberculous lesion the cyanosis persisted for fifteen minutes). Shortly after the end of the clonic phase the patient may become restless and noisy and roll about in bed but as a rule he remains drowsy and may sleep for a short time. His attention may be attracted usually about five minutes after the convulsion but amnesia persists for a period of thirty minutes or more. This amnesia covers the convulsion and sometimes even the injection but it does not obliterate the aura which in many cases precedes the convulsion. This aura is nearly always of an unpleasant nature, e.g. one patient described it as follows: "You feel ghastly, as though you were floating about in the air with hundreds of microbes" while another said that she felt as if a bomb exploded inside her head. It will be seen from the above description that the cardiazol convulsion differs

from an epileptic fit in two major points - firstly the preliminary clonic phase and secondly the very forcible opening of the mouth to the point of dislocation of the jaw at the beginning of the tonic phase.

Subconvulsive dose. If the dose of cardiazol given is just insufficient to produce a convulsion the patient may show twitching of the lids and a few myoclonic movements but there is no loss of consciousness. Instead subjective symptoms of general malaise and intense anxiety appear and the patient may complain of sickness, hunger, thirst or a sensation of impending death. He is usually restless and agitated and may remain in this state for more than an hour. There is no amnesia and the recollection of the experience remains unpleasantly vivid. Marked antagonism towards the treatment is produced and for this reason it is advisable that each injection should be followed by a convulsion.

Technique of Treatment.

In this series of cases the scheme recommended by Meduna[6] was followed with one or two minor modifications. The procedure was as follows. Each patient was given a thorough physical examination which included an examination

of the urine, and an estimation of the blood urea - the latter being used to eliminate the possibility of hidden damage to the kidneys. On the morning of the injection the patient was kept in bed and given only a glass of milk or a little glucose and water. This precaution was taken to minimise the risk of vomiting following the fit. The injection was given as rapidly as possible through a fairly wide serum needle which was pushed slightly up the vein to prevent any possibility of leakage round the vein. If this occurs it is apt to induce sclerosis of the vein. The speed factor is of importance because within certain limits the amount of cardiazol required to produce a convulsion varies directly with the time taken to give the injection.

Cardiazol is marketed as a powder and in 1, 3, and 5 c.c. ampoules of a 10% solution. Ampoules were used in this series of cases. The initial dose with females was 3 c.c., i.e. .3 gm. and with males 5 c.c. or .5 gm. In the majority of cases a fit occurred with the first injection: a few however proved resistant and in these the dose was increased by 1 c.c. on each treatment day until a fit occurred. In all cases it was found that resistance to cardiazol increased and that sooner or later

the patient failed to have a fit with the initial dose. To counteract this a practice was made of increasing the dose by .5 c.c. on alternate treatment days up to 2 c.c. above the initial fit dose and of continuing at this level. Occasionally even with this precaution no fit occurred - when this happened a second injection equal in amount to the first was given immediately and the dose was increased by 1 c.c. for the next injection.

Management of the fit. Single rooms were used so that no patient had the opportunity of seeing another have treatment. At the beginning of the tonic stage dislocation was prevented by holding the patient's lower jaw firmly with one hand while the other was used to insert a gag between the teeth and push the tongue out of danger. The gag used was a piece of solid rubber firm enough to prevent the mouth from closing and elastic enough not to damage the teeth. The patient's limbs were allowed free movement during and after the fit - it was necessary occasionally to have the patient held lightly in order to prevent him rolling out of bed, other-wise no form of restraint was used. This is a point of importance because the greater the restraint employed the greater seems to be the liability to fracture.

After the fit nausea and headache were frequent complaints and vomiting occurred in many cases but these symptoms were more severe in the early stages of treatment and tended to disappear as the treatment continued. The patients were allowed to get up, if they wanted to do so, four hours after the injection. In most of them all symptoms due to the injection had disappeared completely by the time.

Duration of treatment. Following V.Meduna's[6] recommendation, fits were induced twice a week. A shorter interval between the injections means that there is no period during which psychological treatment may be used because the patient has no sooner recovered from one injection than he begins to anticipate the next one - usually with some anxiety. On the other hand a longer interval may prevent the full effect of the convulsions being obtained. Frequent interviews were held with the patients so that a simple form of psychotherapy, consisting of explanation, reassurance and encouragement, could be used in those cases who were or became accessible to this. The object aimed at was that those patients who recovered should have some understanding of the factors which had produced their illness. The following rules governed

the stopping of treatment: (1) if the patient had received 20-25 injections without appreciable improvement; (2) if the patient had recovered five more injections were given to stabilise the recovery; (3) if the patient had improved treatment was continued until no further improvement showed during five successive injections; (4) if the patient's physical condition deteriorated; and (5) if the patient refused further treatment. The last group consisted of a few patients whose apprehension increased to such an extent that they finally refused to submit to treatment. To counteract this difficulty Cook (7) advised the use of hyoscine and morphia as a routine measure half-an-hour before the injection, stating that this allays apprehension and diminishes considerably the unpleasantness of the treatment while Georgi and Strauss (8) induce a light hypoglycaemic coma and give cardiazol while the patient is in this state. In the present state of our knowledge it seemed inadvisable to use either of the above precautions because the very unpleasantness of the treatment may be partly responsible for some of its beneficial effects. This question is discussed more fully later.

Azoman. In a small number of cases in this series 4-cyclohexyl 3-ethyl 1-2-4 triazol, which has the trade

name of azoman in Germany, was used instead of cardiazol. This has two advantages:- (1) the solution is less irritating than cardiazol and therefore can be used for intramuscular injection, and (2) the amount required to produce a convulsion is much smaller.

The technique as described by Walk and Mayer-Gross (9) is exactly the same as with cardiazol except that the initial dose is .6 to 1 c.c. of a 5% solution depending on the weight and general condition of the patient, increasing by .2 c.c. until the fit dose is reached. Another important point of difference is that azoman is excreted more slowly than cardiazol and therefore if the patient fails to have a fit any supplementary dose must be not more than half the original one.

The effect of a convulsive dose is similar to that produced by cardiazol except that the whole process is slowed down - the induction phase lasts longer, the preliminary clonic phase is frequently greatly increased in length and the fit may occur as long as five minutes after the injection. Further, a second fit may occasionally follow some time later but this does not appear to have any deleterious effect.

In patients whose veins are so poor that intravenous

injection is contraindicated azoman can be used by the intramuscular route. For this purpose one may start with 1.5 c.c. and increase by .2 c.c. each time until the fit dose is reached. The fit occurs 15-30 minutes after the injection and during the intervening period the patient usually displays psychomotor activity with symptoms of anxiety and complaints of hunger and thirst recalling the light hypoglycaemia of the insulin shock therapy. Here again multiple fits may occur. Azoman is clearly superior to cardiazol for intramuscular use because the latter requires about three times the intravenous dose, that is from 10-15 c.c.. It is claimed by Walk and Mayer-Gross that azoman is not so unpleasant as cardiazol for the patient and thus does not raise the same antagonism. In the few cases treated here this impression was not obtained and it appeared that azoman had no superiority over cardiazol in this respect.

Physiological Effects of Cardiazol Convulsion.

The extreme muscular action in the fit is associated with certain physiological changes which, as a rule, are transient in nature. The pulse rate usually rises but not to the extent which might be expected from the activity

shown and rarely exceeds 120/minute, returning to normal within five minutes after the fit.

The blood pressure usually increases slightly - blood pressure observations on twenty patients in this series showed an increase in the systolic pressure of 5-30 mm.Hg. in sixteen of them while in the other four the pressure was slightly lowered after the fit.

The effect of the convulsion upon the myocardium may be considered conveniently at this point although it involves pathology to some extent. In none of the cases of this series was there any clinical evidence of myocardial disease before treatment commenced but in five cases irregularities of rhythm appeared during the course of treatment. The point at which the irregularity first appeared varied in the different cases from the first to the fifth injection - once it had appeared it tended to become more pronounced with successive convulsions. In four of them the irregularity consisted of extrasystoles occurring immediately after the fit and lasting for a period which varied in the different cases but never exceeded one hour - the normal rhythm was always restored within an hour of the fit. In the fifth the arrhythmia appeared after the first injection and became worse so that after the seventh injection this

patient had an attack of fibrillation lasting twenty-four hours. Treatment was discontinued on account of this. Three of the five cases were women over forty years of age - it seems possible therefore that the effect of the convulsions was to unmask and increase pre-existing cardiac lesions. Geraudel[10] has made an extensive investigation on this particular point. He studied by means of the electrocardiograph, twenty-one patients who were undergoing treatment, taking one tracing in each before treatment commenced and one after each fit - in all 189 electrocardiograms were studied. His results were as follows: (1) in 8 cases the only effect was to accelerate the heart rate for two or three minutes, (2) in 11 cases a transient alteration of rhythm lasting not more than five minutes followed the injection - this being due to auricular extrasystoles in 9 cases and to ventricular extrasystoles in the others, (3) in 2 cases an inversion of the T-wave developed and in these treatment was suspended. In all cases the electrocardiogram was normal before treatment. In no case was it affected when the patient received a subconvulsive dose suggesting that the above changes were due to muscular effort and not to any inherent effect of cardiazol. These results raise the possibility that the

repeated convulsions can damage a previously healthy myocardium, but further investigation is required on this point. Meduna denies this possibility, stating that none of his patients showed any evidence of abnormality after treatment, and giving the opinion that the treatment is absolutely harmless if the patient's heart is sound. Clinical experience tends to favour this conclusion. There is no doubt, however, that the treatment may cause serious damage if any heart lesion already exists and the last two cases of Geraudel's series show that the routine use of the electrocardiograph in the early stages of treatment would diminish considerably any risk from this source. This point is stressed by Wexberg[11] one of whose patients, who had shown no clinical abnormality previously, suffered a cardiac collapse after the third injection of cardiazol. Further evidence is given by Dick and MacAdam[12] who report the onset of auricular fibrillation in three cases undergoing treatment, and heart-block in a fourth.

Blood picture and blood chemistry. Meduna carried out a series of blood counts on 100 cases and found that in the course of cardiazol treatment the total number of white blood corpuscles does not change but that an increase takes place in the number of the leucocytes and a decrease

in the lymphocytes. The increase in the polymorphs is from right to left so that the Arneth Index moves to the left. He also found a greater shift to the left in patients who were remitting than in those who were not and adopted this as a prognostic point.[13] Harris, repeating this investigation, found an actual as well as a relative leucocytosis and confirmed the shift to the left but was unable to draw any distinction between remitting and unremitting cases. The change in the blood picture occurred even when no fit was produced and seemed to be a direct response to the cardiazol itself and not to the fit.[14] Muller's work tends to show that a similar change takes place in the blood when any noxious substance is introduced into the circulation and consists of a withdrawal of leucocytes from the peripheral circulation into the blood vessels of the liver and their replacement by immature forms from the bone marrow.[15] The findings of Low and his co-workers agree with those of Harris.

Low also carried out a careful investigation of the p.H. and the calcium and carbon dioxide contents of the blood in 10 patients undergoing treatment, taking readings before the fit and ten minutes, one hour and two hours after it and comparing them with 10 controls in whom readings

were taken at similar intervals. They found that in all cases the value for the p.H. and calcium and CO_2 contents fell immediately after the fit, showing a change towards acidosis. This change was reversed gradually and the return to normal was completed in two hours after the convulsion.

A study of the blood sugar in these same patients showed an increase immediately after the fit, returning to normal in two hours - a finding which agrees with that of Georgi (18) and Strauss and Harris (13). The former, however, state that there is a transient but definite hypoglycaemia in the preparoxysmal stage, that is between the injection and the actual fit, followed by a hyperglycaemia after the fit. Clemens (16), after a study of 13 patients, taking readings in each before the injection, before the fit, during the fit and after the fit, denies this statement and says that there is no preliminary fall in the blood sugar but on the contrary an immediate rise. He also notes that this rise occurs even without a fit and seems to be due to the cardiazol itself.

An ingenious biochemical investigation was carried out by Himwich and his co-workers (17) who, in a series of 7 patients, collected samples of blood from the femoral arteries and

the internal jugular veins during various stages of the convulsion and studied the oxygen content. They found, as expected from the diminished breathing, CO_2 retention plus diminished O_2 content. The latter reduced the haemoglobin saturation ($\frac{O_2 \text{ content}}{O_2 \text{ capacity}}$) from the normal of 95% to as low as 50% at the end of the seizure. As soon as breathing recommenced the O_2 content returned rapidly to normal. The anoxaemia and muscular effort resulted in an increase in the blood sugar and blood lactic acid - a finding which agrees with Bömer's[18] experiments with cardiazol on animals. They conclude that the convulsions depress metabolism by decreasing the oxygen available for the combustion of sugar.

It is interesting at this point to recall the work of Loewenhart, Lorenz and Waters,[19] who used a high percentage of CO_2 in the treatment of patients suffering from catatonic stupor and found a definite but transient improvement in the mental state. D'Elseaux and Solomon[20] repeated this experiment, beginning with the administration of 10-15% CO_2 and increasing each minute by 5% until 30-40% CO_2 was being given. They found an increase in the depth of respiration and the rate of ventilation, a rise in the systolic blood pressure, cyanosis of the face, and a state of acidosis

of the tissues associated with partial saturation of the tissues with CO_2. The O_2 saturation of venous blood fell. In all cases where the concentration of CO_2 in the inspired air rose above 25% they obtained improvement in the mental state which, however, never lasted more than a few minutes. The similarity between their findings and those of Low and Himwich is apparent.

Urine. The investigations of Meduna showed that after a fit there was an increase in the acidity of the urine and in the ammonia and phosphate contents with a reduction in the chloride content. None of these changes was produced by subconvulsive doses of cardiazol.

It may be concluded, therefore, that the cardiazol convulsion causes a violent and sudden disturbance of metabolism which alters the acid-base equilibrium in the direction of acidosis.

Mechanism of the Convulsion.

A certain amount of work has been carried out to determine how cardiazol causes a convulsion. Denyssen and Walterson (21) found that a dose of cardiazol which usually caused a fit could be rendered subconvulsive by the previous administration of a vaso-dilator such as amyl nitrite or

histamine and concluded that the convulsion was due to vascular spasm. V. Anzyal (22) supports the same theory and states that the working mechanism of the convulsion is a cerebral vasomotor constriction. (23) Wilson and Rees Thomas, noting that the occurrence of the fit depends to some extent on the speed of the injection, suggest that speed shock may be a predisposing factor to the convulsion. Speed shock is the name given to a number of symptoms such as flushing of the skin, sweating, excitement and anxiety, caused by the rapid intravenous injection of almost any substances.

Study of the Literature.

(1) Results.

In the comparatively short space of time which has elapsed since cardiazol treatment was introduced a very large volume of literature has accumulated and the study of even a part of this is rather confusing because there is no common basis on which the results given by different authors can be compared. Very few of these give any detailed indication of the criteria used in the diagnosis and classification of their cases. As a result of this there are two obvious sources of error when an attempt is

made to compare the results obtained by different workers. (24) In the first place, as Leroy and Clemens point out, the term schizophrenia does not convey the same meaning to the French and Belgian psychiatrists as it does to the Germans and Swiss - the former tending to limit it to well established cases while the latter have a much wider conception of the illness. In the second place, bearing in mind the diagnostic difficulties in acute mental disorders, the suspicion arises that there has been a tendency to treat all acute mental disorders with cardiazol and to compress them into the schizophrenic group for this purpose.

The matter is complicated further, when the results themselves are studied, by the multitude of terms employed to indicate degrees of improvement. These range from 'complete remission', the meaning of which is obvious, through 'social remission', 'partial remission', 'improved', and several others down to 'unchanged'. This difficulty, however, is not so great as would appear on first sight because in many cases exact definitions are given of the terms employed.

Finally there is one small point which is worthy of mention - this is that the cases treated are usually classified according to the duration of their illness. Now

schizophrenia is frequently so insidious in onset that it is difficult to understand how this period is computed in many of the cases. As a basis for comparison it might be more useful if patients were classified instead according to the duration of their stay in hospital.

The results obtained by some of the authors are given at this point so that some idea may be gained of the value of the treatment. The results chosen form a representative group ranging from the best to the worst. Meduna (2) treated 110 schizophrenic patients the duration of whose illness varied from one week to ten years and secured remission in 50%. Sixty-two of the cases had been ill for less than one year - of these 51 or 80% recovered. He describes the remaining 11 cases as 'hereditary schizophrenics' in whom the actual disease had been inherited and he concludes that it is not possible for such cases to remit. He calls those who did remit 'symptomatic' as opposed to the 'hereditary' group. This division, however, suggests the 'post hoc' fallacy.

Briner (25) gives the results obtained in 111 schizophrenics treated at the Berne clinic. Thirty-four had been ill for less than one year and of these 50% recovered, 9% were discharged relieved, 24% were improved but unfit for discharge

and 17% were unchanged. In 24 cases who had been ill for from one to five years the corresponding figures were 13%, 0%, 65%, and 22%, and in 53 cases of over five years' duration the corresponding results were 5%, 4%, 52%, and 39%. Pullar Strecker (26) combines the results obtained by several authors, including the two already mentioned, and finds that out of 103 patients whose illness had lasted less than one year 69% showed complete or incomplete remission while a further 10.7% showed improvement. In 75 cases of one to five years' duration the corresponding figures were 25.4% and 22.6%, while in 87 cases of more than five years' standing the figures were 10.5% and 33.5%.

Wilson and Rees Thomas (23) give a summary of the results obtained in 29 American hospitals as follows: out of 1244 cases treated the acute and subacute cases showed 59.7% of full remissions while the chronic cases showed 10% remission. Remission and improvement in all cases amounted to 59%.

Brousseau (27) out of 110 cases treated had improvement in 50%. This figure rose to 82% in those treated within six months of the onset of their illness.

V. Angyall and Gyarfas (28) had 44.4% remissions in 45 cases treated but raised this figure to 66.7% by treating

the unrecovered cases with insulin. It is interesting to note that the converse to this is shown by Goldstein (29) who treated 10 cases who had already received insulin treatment without improvement and obtained 5 recoveries. It seems, therefore, that insulin and cardiazol treatment may supplement each other but further investigation is required on this point.

Finally Winhelman (30), who treated 35 cases, had full remission in 20% and improvement in a further 33%.

All the above authors stress the importance of early treatment and comment upon the discrepancy between the results in early cases and those in late ones. And indeed this discrepancy is so pronounced that comment is inevitable. Two possible explanations of it present themselves - first the fact, referred to earlier, that in the treatment of acute schizophrenic patients belonging in reality to other groups and suffering from a type of illness with a good prognosis, might inadvertently have been included: and second the fact that the acute schizophrenic groups included patients who would have remitted naturally. The question now arises as to what proportion of the total recoveries is made up of these two groups. This is a question which it is practically impossible to answer. A study of the liter-

ature on natural remissions in schizophrenia reveals very conflicting opinions. Mayer-Gross[31] made a survey of 328 schizophrenics admitted to the Heidelberg clinic in the years 1912 and 1913. Fifteen years later he was able to trace 294 of these and he found that 89 or 30% were still in the community and apparently well. Briner[25] states that between 1933 and 1935 about 60% of the schizophrenic patients admitted to the Berne clinic with illnesses of less than a year's duration were discharged socially cured or greatly improved. Of these two-thirds remained able to work and free from symptoms some two years after their discharge. Braatoy[32] found that out of 298 schizophrenics 26% were recovered after six years. A recent work by Cheney and Drewey[33] gives interesting results. These authors studied the results obtained with 500 schizophrenics who were given intensive individual attention in an admission hospital in which the ratio of patients to medical staff was low. They found that at the end of about one year 63% were unchanged, 16% were improved, 14% much improved, and 7% recovered, i.e. that the improvement rate without specific therapy was 37%. This figure comes close to those obtained by several authors with cardiazol although it falls far short of those obtained by others. The only

conclusion, therefore, that one can draw from the statistical evidence is that it raises a presumption in favour of cardiazol being able to effect a cure in certain cases of schizophrenia which would not remit without it, but that it does not prove this point.

There is, however, a different type of evidence to be taken into account - namely the impression created by this treatment on those actually carrying it out. Several authors comment on the fact that cardiazol produced striking improvement in cases which they had regarded as most unpromising. For example Briner states that no one who has witnessed the change in patients who have been given up as hopeless can doubt the value of the treatment. No one has committed himself to the statement that the treatment is useless and at the moment the position appears to be that opinion is divided equally between those who feel that this treatment can raise the spontaneous recovery rate and those who feel that it merely shortens the duration of illness.

(2) Theories of Action.

It is pertinent at this point to consider the question of what one might call the mechanism of improvement with Cardiazol therapy. There are, as might be expected, numer-

ous speculations on this point - speculations which depend upon the particular theory held of the causation of schizophrenia and obviously, since the cause of schizophrenia remains in doubt, the theories of improvement must remain conjectures.

Meduna,(2) arguing from the alleged antagonism between epilepsy and schizophrenia, believes that the schizophrenic process produces changes in the chemical milieu of the patient and that unless these changes have progressed so far as to be irreversible the cardiazol convulsions reverse the process in the direction of return to normal. However, the theoretical basis of his theory is attacked by Gibbs et al.(34) on two main grounds, (a) that the electro-encephalogram is similar in schizophrenia and epilepsy, and (b) that in a series of cases of schizophrenia studied by Jasper epilepsy occurred in 15%. Similarly Harris found that the incidence of epilepsy in 924 schizophrenics was 1% - a figure which is higher than that obtaining in the general population.

Friedman(35) follows Meduna's theory a little further and, ppstulating the existence of changes in the metabolic and chemical processes in schizophrenia in the direction of general sluggishness, suggests that there may exist a functional barrier to facile absorption or assimilation of nutri-

tive elements in the brain of schizophrenics and concludes that the treatment breaks down this barrier and that it does so because cardiazol unites with the cell-bound toxin responsible for the barrier and is eliminated with it - the idea being, apparently, that the drug acts as a sort of neuronic purgative.

The same author[36] calls attention to the analogy between the deep cyanosis with decreased O_2 tension during cardiazol treatment and the similar change brought about by the anoxaemia treatment of Loewenhart. This point is fully discussed by Wilson and Rees Thomas[23] from the viewpoint that deprivation of the brain cells of oxygen is beneficial in some way. Gellhorn[37] develops the theory another step. He assumes that the cause of schizophrenia is a dysfunction of the autonomic nervous system, drawing support for this view from the fact that tumours in the region of the third ventricle produce severe changes in the personality, and from the work of Cannon on the effect of hypothalamic lesions on the emotions. He then examines insulin therapy, cardiazol therapy, prolonged narcosis, and inhalation of CO_2, and states that the common factor in all these is a state of anoxia of the brain cells, caused in the first method by a fall in the blood sugar depressing the oxidative processes

in the brain, in the second by the cessation of respiration, and in the third by the direct effect of barbiturates in inhibiting oxidation; he shows that any lowering of oxidation produces excitation of the sympathetic system, and concludes that the various forms of treatment enumerated above are effective because they produce, by profound alteration in the metabolism of the brain, a strong and lasting excitation of the sympathetic nervous system.

Humbert and Friedemann (38) approach the problem from a different angle. They consider that the sudden descent into unconsciousness, which characterises the convulsion, awakens in the patient the primitive conflict between life and death and that the violent call on the life instinct submerges the autistic indifference of the patient. In support of this theory they stress the infantile reactions shown during the fit, e.g. eroticism and assumption of foetal postures, and suggest that the patient reintegrates from the infantile level. They consider that this process occurs in insulin therapy and in prolonged narcosis as well and that it is the only common denominator of the three - the difference between the treatments resting essentially on the speed at which, and the degree to which the above antagonism is stimulated.

There are other biochemical theories such as that the improved tissue respiration, or that an alteration in the water-salt regulation is responsible for the therapeutic efficacy of the treatment. The defect of such theories is that one part of the total change produced in the organism by the convulsion is exalted, without sufficient reason, into the position of being the effective factor.

It will be seen therefore that the mechanism of improvement remains a matter of theory only, and that there is not enough evidence at the moment in favour of any one theory to warrant its acceptance.

Role of psychotherapy in cardiazol treatment. The importance attached to this varies in different articles. Some writers emphasise its importance - Meduna (39), for example, insists that psychotherapeutic talks at frequent intervals with the patients undergoing treatment are necessary in order to effect a complete cure, while Briner (25) looks upon cardiazol simply as a means by which contact may be established with the patient, and states that the variations in the results obtained in different clinics depend upon the amount and kind of psychotherapy used. Ellery (40) holds similar views. Other writers make no specific mention of any psychotherapeutic regime during treatment and fail to make

it clear whether they obtained their results with the help of psychotherapy or without it, although it is probably safe to assume that in the majority of instances some form of this was used. This assumption is made because, unless the belief is held that psychological factors play no part in the causation of mental disorder, it seems only reasonable that some attempt should be made to discover such factors and to remedy them in order to produce a complete and lasting recovery.

(3) Dangers and Complications.

The number of deaths reported is surprisingly low when the severity of the treatment is considered, and the mortality rate appears to be about .5%. A total of ten deaths can be traced. Of these four are reported by Pameijer (41) as occurring in a total of 1200 cases treated in the mental hospitals of Holland. Two of the deaths were due to cardiac trouble, one to pulmonary tuberculosis, and one to interlobar empyema. Meduna (42) had one death due to aortic incompetence and myocardial degeneration out of 500 cases treated. Angyal and Gyarfas (28) had one - again from aortic incompetence and myocardial degeneration - out of 45 cases treated. Briner (25) had two deaths in 111 cases - one being due to pulmonary embolism from old thrombo-

phlebitis of the pelvic veins, and one to the presence of a deep-seated goitre causing narrowing of the trachea. Leroy and Clemens[24] state that Kraulis of Riga had one death but do not give the cause.[9] Finally Walk and Mayer-Gross report a case in whom the first convulsion caused fracture of the neck of the femur on both sides - this patient died on the following day.

It will be seen that in the majority of instances quoted above a lesion had existed before treatment but had not been accessible to clinical examination. There is no definite evidence that cardiazol itself produces a lesion 'de novo' as it were. But these fatalities serve as a warning that the preliminary physical examination of the patient must be thorough and that such examination should be repeated at frequent intervals during the course of the treatment.

The effect of cardiazol on the heart has been dealt with earlier. The importance of ruling out every case showing evidence of heart disease is clearly demonstrated by the fact that at least four of the deaths reported were due to the strain imposed by the convulsions on a damaged myocardium.

Activation of pulmonary tuberculosis in six cases is

also reported by Pamaijer and the occurrence of pulmonary abscess in another seven. (43) Bookhammer and Saxe, similarly, report acceleration of the disease process in a case of pulmonary tuberculosis which had not been diagnosed.

The other complications reported consist chiefly of fractures and dislocations. Dislocation of the lower jaw is noted in nearly all series of cases. Dislocation of the humerus at the shoulder joint occurred next in frequency - Winhelmann (30) uses a special apparatus which is applied to the patient before treatment and which prevents abduction of the arm thus removing the danger of dislocation. It seems doubtful, however, whether the advantage obtained by this would outweigh the discomfort which the patient is bound to feel. Fracture of the femur is the next in order of frequency, followed by fracture of the humerus and of the scapula. The total number of such fractures reported amounts to about twenty and represents a morbidity rate of about 1%. The suggestion has been made that these fractures were due to vitamin D deficiency but at present there is no concrete evidence in favour of this hypothesis.

Contra-indications. It follows from what has been said above that patients should not be given this treatment unless they are in good physical condition. Cardio-

vascular and pulmonary diseases are special contra-indications.

Scope of this Investigation.

This investigation was undertaken to test the validity of the claims made on behalf of cardiazol treatment, and to find out exactly what type of case reacted most favourably to the treatment. At first only schizophrenics, in whom the diagnosis was beyond dispute, were included and the first group tested consisted of 6 patients who had been in hospital for more than twelve months and 6 who had been in hospital for a period less than twelve months. The rapid disappearance of some acute symptoms in certain of the latter group led to the extension of the treatment to cases suffering from other types of mental disorder but showing symptoms which had been influenced in the schizophrenic group by cardiazol. Finally two cases of hysteria, both of whom had been bedridden for a long period of time and had proved resistant to psychotherapy, were given cardiazol as a therapeutic last resort. In all 52 cases were treated of whom 43 were diagnosed as schizophrenics, 4 as involutional melancholics, 3 as manic-depressives, and 2 as hysterics.

For reasons stated earlier in this paper psychiatric

classification has always been a stumbling block to the exact comparison of results from any form of treatment. The elasticity of the nomenclature renders it difficult for any clear picture to be built up from the statement that a certain number of paranoid schizophrenics, a certain number of hebephrenics and a certain number of catatonics have undergone a course of treatment. On account of this it has seemed advisable to introduce at this point a very brief summary of each case giving the predominant symptoms present, the diagnosis, the duration of treatment and the maximum dose used, and a commentary giving the result obtained with any point of interest arising during the treatment. The family history has been represented in each case as 'good' where no trade of psychotic symptoms could be found in the immediate antecedents on either side or in the siblings, 'indifferent' where such traces were evident in the antecedents on one side, and 'bad' where such traces were present on both sides or were very marked on one side. Apart from this no attempt has been made to introduce aetiological factors and the patients have been presented as they appeared in the wards.

Case No.1. Female - age 37. Family history indifferent. Had been excitable and strange in manner for some

days. On admission stated that she was in love with the manager of the shop in which she was working and that this man used to dope her, come into her room at night, and massage her body, changing her into a Dresden china figure. She was hallucinated and stated that this man talked to her through the walls and through the ceiling. During the next three months her condition remained unaltered - she was very suspicious and refused her food at times because she thought it was poisoned and her hallucinations remained vivid.

Diagnosis. Paranoid schizophrenia.

Treatment commenced three months after admission and consisted of 14 convulsions - maximum dose 4 c.c.

Commentary. She showed immediate and steady improvement and was discharged recovered two months after her treatment had finished. She was interviewed at a clinic six months later and had remained well, with full insight into her illness.

Case No.2. Female - age 21. Family history indifferent. History of epileptic fits between the ages of 9 and 14. Was always very shy and timid and could never make friends. Six months before admission she suffered from sleeplessness and became irritable and peculiar in manner -

turned against her relatives - tried to injure her sister's baby - gradually became worse and on admission was in a stuporose state - dull and retarded and answered questions only after long hesitation. Admitted hearing voices which told her sometimes that she was good and at others that she was bad. A month after admission she was mute, difficult with her food, defective in habits and mildly resistive to all attention.

Diagnosis. Catatonic schizophrenia.

Treatment commenced one month after admission and consisted of 23 convulsions - maximum dose 8.5 c.c..

Commentary. She showed intense fear of the injections the whole time. She improved slowly until the 14th convulsion - the next injection given produced no fit but made the patient acutely maniacal so that a second injection could not be given - following this she relapsed completely into her stupor but emerged from it with the next convulsion on the following day. From this point onward she improved steadily and at the end of the course she was cheerful and well occupied, and denied hallucinations saying that the voices she had heard were 'imagination'. At the same time she remained shy and timid and seemed to be an unstable personality. She was discharged recovered and was back at

work when interviewed four months later.

Case No.3. Male - age 32. Family history good. Eccentric behaviour for some years - had worked on a farm in Canada but was directed by voices to return to England. On admission he was quiet and introverted - did not speak spontaneously but was willing to answer questions - admitted hearing voices continually but would not disclose what these said but felt that they were sent to guide him. Was well-behaved but did not occupy himself.

Diagnosis. Hebephrenia.

Treatment commenced two months after admission and consisted of 20 convulsions - maximum dose 8 c.c..

Commentary. Showed no appreciable change - he remains in hospital, unchanged.

Case No.4. Female - age 37 - married. Family history good. Admitted to another mental hospital twelve years ago after the birth of her second child. Remained there for ten years and was then transferred to this hospital. Since her transfer she has remained solitary and unemployed, dirty in her habits and vividly hallucinated - resistive and aggressive at times and elated and foolish at others. Her conversation was incoherent at times and her response to ques-

tions quite irrelevant.

Diagnosis. Hebephrenia.

Treatment commenced twelve years after admission and consisted of 25 convulsions - maximum dose 7 c.c..

Commentary. Her behaviour and her mental state were unaffected.

Case No. 5. Female - age 25 - single. Family history indifferent. On admission was very foolish, giggling and laughing to herself - said she had been eating a lot but was always hungry. Her appetite was excessive and perverse and she was completely irresponsible in her behaviour. During the next four years her condition varied - at times she could occupy herself and talk reasonably - at others she was very silly, hallucinated, irresponsible and defective in her habits and ate everything she could lay her hands on, including her own clothing. For the last year she has been in the latter state.

Diagnosis. Hebephrenia.

Treatment commenced four years after admission and consisted of 20 convulsions - maximum dose 8.5 c.c..

Commentary. Her condition remained unchanged.

Case No. 6. Male - age 19. Family history bad. Had

behaved in an irresponsible fashion for six months during which time he had lost several situations. On admission he was talkative, elated and excited and had frequent outbursts of laughing and giggling. Said that he had gone to the police station for protection against his mother who, he felt sure, was quite mad - that he was frightened by her face and that she used to tap on the wall at night to drive him mad. He lay in bed muttering constantly to himself and smiling foolishly - at intervals moved about in bed, explaining that he did this because the movements protected him. During the next month he remained noisy, hallucinated and foolish and was impulsive at times. Persisted in his magic movements and became very suspicious and aggressive if questioned.

Diagnosis. Hebephrenia.

Treatment commenced one month after admission and consisted of 24 convulsions - maximum dose 7 c.c.

Commentary. He became quieter after the first six injections and improved steadily until by the fifteenth convulsion he had apparently lost his hallucinations and was behaving reasonably although he showed no insight. He did not improve beyond this point and his discharge from hospital was ordered by his mother as soon as the treatment

had been discontinued. One month later he returned, having relapsed completely - again talkative - hallucinated and suspicious. He was given six more injections which had the effect of removing his acute symptoms but after which he remained devoid of insight, lazy, vain and obstinate and quite unfit to look after himself outside hospital. Improved - unfit for discharge.

Case No. 7. Female - age 20 - single. Family history good. A week before admission became excited, sleepless and talkative. On admission was acutely excited and extremely noisy - her conversation was incessant and incoherent - she was dirty in her habits, exposed herself and showed erotic tendencies. After two days in this state she lapsed into a stupor and became mute and resistive - she remained in this state until treatment was commenced.

Diagnosis. Catatonic schizophrenia.

Treatment commenced four weeks after admission and consisted of 15 convulsions - maximum dose 7.5 c.c..

Commentary. Showed immediate and rapid improvement. After five convulsiosn talked freely and behaved normally - after another five appeared quite normal with good insight into her illness. She was discharged recovered. She

returned to her previous work and six months later she remained quite well.

Case No. 8. Female - age 24 - single. Family history indifferent. Had been apparently normal until the age of 20 - after that became solitary and irritable, neglected her appearance and her work and gradually lost interest in her surroundings. On admission was in a state of stupor - dull, apathetic, mute and resistive. During the next two years she showed no change. Showed stereotypy and, at times, flexibilitas cerea. Dirty in her habits and unoccupied.

Diagnosis. Catatonic schizophrenia.

Treatment commenced two years after admission and consisted of 20 convulsions - maximum dose 6 c.c..

Commentary. Condition unchanged.

Case No. 9. Female - age 32 - married. Family history good. A solitary introverted and suspicious type of individual with a history of two previous breakdowns. On admission was dull and apathetic and said that she heard voices telling her silly things and annoying her - very vague and discursive and unwilling to discuss her symptoms. During the next two years remained asocial, hallucinated

and suspicious. Became convinced that her husband visited the hospital and had intrigues with other patients. Very resentful of her detention and at times excited and abusive - made several efforts to escape.

Diagnosis. Paranoid schizophrenia.

Treatment commenced two years after admission and consisted of 30 convulsions - maximum dose 5 c.c..

Commentary. After the first 15 injections she was brighter and more active, and appeared to lose her hallucinations and her suspicious attitude. Did not progress beyond this point and never showed any insight. Relapsed a month after her treatment had finished, so that the final result showed no improvement.

Case No. 10. Female - age 29 - single. Family history good. Had been odd and peculiar in her behaviour for about a year before admission. On admission was excited and noisy and said that she saw her sister in her coffin, that her mother was dying in agony and that she heard drops of blood falling all round her. During the next seven years she showed no improvement - at times she was very excited, impulsive, and actively hallucinated - at others was quiet but incoherent in speech, dirty in habits and unoccupied. Showed evidence of dementia.

Diagnosis. Hebephrenia.

Treatment commenced seven years after admission and consisted of 12 convulsions - maximum dose 8 c.c..

Commentary. After the first few injections she became more excited and difficult to manage - objected strongly to the treatment which was given up after 12 injections with the patient showing no improvement.

Case No. 11. Male - age 33 - married. Family history good. A week before admission became silent and rather moody - slept badly and neglected his work. On admission was elated and excited - hallucinated and showed grandiose delusions. Stated that he was the chosen instrument of God to perform a great task - namely to see that no one worked more than eight hours a day - later showed delusions of persecution, saying that people were trying to poison him and were shooting at him. For the next three months he remained impulsive, noisy, and vividly hallucinated, and disorientated and expressed numerous fantastic delusions of persecution.

Diagnosis. Paranoid schizophrenia.

Treatment commenced three months after admission and consisted of 12 convulsions - maximum dose 9 c,c..

Commentary. His mental state improved immediately.

He quickly regained touch with his environment and lost all acute symptoms. He insisted on leaving hospital after he had had 12 injections. At that point he showed residual mental impairment in that he was very simple and had no real grasp of his illness but no other abnormality could be demonstrated.

Case No. 12. Male - age 21 - single. Family history indifferent. Had gradually become quiet, solitary and reserved - eventually attempted suicide by jumping through a window. On admission was quiet and correctly orientated but stated that his mind was controlled by an evil influence which gave him messages by voice, that two huge eyes followed him about, and that a filthy smell came up from the floor and filled his body. Said his whole family had changed their bodies. Gradually became quieter and more introverted - was excited and impulsive on one occasion but finally lapsed into a stupor in which he was mute, and resistive, and showed flexibilitas cerea. Was given a course of insulin shock treatment without benefit.

Diagnosis. Catatonic.

Treatment commenced two years after admission and consisted of 15 convulsions - maximum dose 7 c.c..

Commentary. He showed great fear of the injections

but did not resist them. The treatment produced no improvement.

Case No. 13. Female - age 29 - single. Family history good. Received an injury at work one month before admission - was convalescent from this when her symptoms developed suddenly. On admission she was very excited, restless, and emotionally unstable, laughing and crying alternately. Talked incessantly, showing marked flight of ideas with external ideation so that her speech was incoherent. Was hallucinated and aggressive. During the next seven months she became a little quieter but showed no other change. She was dirty in her habits, impulsive and hallucinated and had to be kept in bed on account of her mental state. Showed distractibility, elation, and flight of ideas.

Diagnosis. Acute mania.

Treatment commenced seven months after admission and consisted of 9 convulsions - maximum dose 5 c.c..

Commentary. Her mental state improved immediately and after five injections she was quiet, reasonable, well-behaved and able to occupy herself, although still rather excitable. She gained full insight into her illness and was discharged recovered two months later. Six months

after her discharge she was still well and at work.

Case No. 14. Male - age 26 - single. Family history good. Had developed symptoms while on service in Egypt as a soldier. Transferred home to a military hospital and persuaded to come to this hospital as a voluntary patient. On admission was depressed and hallucinated. Said that he heard voices from all over the world plotting his destruction. His conversation was rambling and pointless and his behaviour impulsive. For the next ten months remained very suspicious and impulsive. Had periods during which he refused his food and was mute: did not occupy himself in any way and was frequently aggressive towards those around him - on several occasions smashed windows, and on one swallowed a key. Said that everyone else in the ward was a detective set to watch him.

Diagnosis. Catatonic schizophrenia.

Treatment commenced ten months after admission and consisted of 20 convulsions - maximum dose 8 c.c..

Commentary. His mental state showed improvement after the first six injections - he began to occupy himself and lost his hallucinations and his suspicions. At the end of the course behaved normally but had not recovered insight, saying that he no longer heard voices but

that he had done so in the past. Discharged himself and was considered improved. Four months later had recovered - showed good insight, and had returned to his previous occupation.

Case No. 15. Female - age 24 - single. Family history bad. Only child - apparently well until the age of 21 but always very shy and had no friends. Unable to work because she disliked meeting people. Later developed psychotic symptoms and on admission to hospital was simple and childish - did not speak spontaneously - showed numerous ties and complained that people stared at her and talked about her - was unable to occupy herself to any extent because she was very slow in everything she did, taking about an hour to each meal. Was solitary and very timid.

Diagnosis. Simple schizophrenia.

Treatment commenced one month after admission and consisted of 16 convulsions - maximum dose 6 c.c..

Commentary. Her condition remained unchanged.

Case No. 16. Female - age 24 - single. Family history good. History of having been indulged by parents and considered delicate. Admitted to hospital in an acutely excited condition in which she struggled violently and shouted that she must kill herself because she was no use

to anyone. Became quiet after two days but remained rather depressed and showed ideas of unreality - stated that she had no joy in life and was incapable of feeling or expressing affection for anyone and had come to the conclusion that she would never be normal and that she ought to kill herself.

Diagnosis. Simple schizophrenia.

Treatment commenced two months after admission and consisted of 8 convulsions - maximum dose 8 c.c..

Commentary. Improved at once - after four injections was apparently well and stated that her emotions were quite normal, that she could feel joy again and that her previous ideas were absurd. Maintained this improvement and left hospital one month later, recovered.

Case No. 17. - Male - age 27 - single. Family history good. Always reserved and rather solitary - three months before admission lost his job and began to complain that he could not swallow because his head and his stomach did not work together - became depressed and moody and retired to bed, refusing to get up. On admission was in a stuporose state - appeared apathetic but said that he was rotten, that he had ruined his body by masturbation and that he was going to die - that his throat was closed up and his

face changed and that there were ringing noises in his ears. During the next nine months he showed little change but remained dirty, untidy and solitary, talked very little and refused to occupy himself - retained his hypochondriacal delusions.

Diagnosis. Catatonic schizophrenia.

Treatment commenced nine months after admission and consisted of 20 convulsions - maximum dose 11 c.c..

Commentary. At first showed improvement and after ten injections looked cheerful, spoke freely and spontaneously and had lost his delusions. He had no insight, however, and he did not gain this with further treatment. He began to relapse shortly after treatment was stopped and eventually returned to his previous condition so that the final result was unchanged.

Case No. 18. Female - age 31 - single. Family history indifferent. Typically spoiled child - considered delicate. Was trained as a school teacher but never worked - remained at home helping her mother. First admitted to hospital 1934 with delusions and hallucinations - prominent ideas of reference. Improved and returned home. Readmitted to hospital four years later complaining that she felt ill - had frequent outbursts of weeping

for no apparent reason - said she had noises in the head and that people stared at her - was asocial, introverted and unoccupied and admitted that she liked to spend the whole day thinking.

Diagnosis. Simple schizophrenia.

Treatment commenced one month after admission and consisted of 12 convulsions - maximum dose 7 c.c..

Commentary. Showed some improvement in that she became cheerful and talkative but she gained no insight into her illness. Discharged herself against advice - relapsed at home and returned to hospital - final result unchanged.

Case No. 19. Female - age 35 - single. Family history indifferent. History of several attacks of mania and depression since the age of 22. Present attack commenced with depression a week before admission. On admission was mildly depressed but soon changed and became elated, talkative and overactive. Remained rather unstable for the next six months changing from hypomania to simple depression - then passed into a state of acute mania in which she was confused, noisy, hallucinated and dirty in her habits. Showed extreme manic overactivity with flight of ideas to the stage of incoherence. Required to be kept in bed and needed sedatives frequently. Re-

mained in this state for five months.

Diagnosis. Acute mania.

Treatment commenced eleven months after admission and consisted of 7 convulsions - maximum dose 4 c.c..

Commentary. Became much quieter after the first four injections. The seventh injection produced a severe and apparently typical fit but respiration was not re-established after it, the cyanosis became deeper, the pupils remained widely dilated and fixed, rigidity disappeared and the pulse became rapid and feeble. Oxygen and artificial respiration were given and after five minutes natural respiration recommenced. The patient became extremely restless and struggled violently for about twenty minutes - consciousness returned forty minutes after the fit. Her mental state returned to normal after this convulsion and a week later she was cheerful, well-occupied and stable and had been given parole. In view of her previous history she has been kept in hospital since but is considered to be recovered.

Case No. 20. Male - age 32 - single. Rigid, conscientious type of individual with few friends. Six months before admission had an attack of influenza - since

then very moody and appeared to lose all sense of enjoyment. On admission was very depressed saying that he had betrayed God by self abuse and that he heard voices inside his head accusing him of sinning and telling him that he was responsible for all the unnatural things happening in the world, such as the war in Spain. He gradually became almost mute and passed into a stuporose state in which he lay in bed muttering to himself and paying no attention to his environment.

Diagnosis. Catatonic schizophrenia.

Treatment commenced three weeks after admission and consisted of 20 convulsions - maximum dose 11 c.c.

Commentary. Improved slowly and after the tenth fit was much brighter and was able to talk naturally and to occupy himself. At the same time he was very quiet and diffident and retained the conviction that his behaviour had been much worse than that of normal people. Beyond this point he did not improve but he showed no relapse after treatment was stopped - improved, unfit for discharge.

Case No. 21. Female - age 27 - single. Family history bad. Previous breakdown six years earlier. Present attack commenced suddenly. On admission she was excited,

talkative and elated. She talked incessantly and at times incoherently and her speech showed distractibility and flight of ideas. She exposed herself and showed erotic tendencies. During the next nine months she remained noisy, restless, impulsive and hallucinated - muttered constantly to herself and on several occasions attacked other patients. Her habits were dirty and her mental state was such that she had to be confined to bed.

Diagnosis. Acute mania.

Treatment commenced nine months after admission and consisted of 18 convulsions - maximum dose 9 c.c..

Commentary. She showed rapid improvement - after ten injections was quiet and reasonable and had lost her hallucinations although she retained a tendency to laugh immoderately. Stated that she could remember very little of what had happened while she was in hospital. Discharged recovered after another eight injections and when interviewed six months later had kept well.

Case No. 22. Female - age 22 - single. Family history good. Admitted to hospital for the first time seven months before treatment commenced - was simple and facile and masturbated constantly - kept on repeating that she could not stop herself doing this. Discharged herself after six

weeks. Five months later attempted to commit suicide by gas poisoning and was re-admitted. This time she was still very simple and childish - smiled pleasantly and showed no appreciation of the seriousness of her act. Her memory was impaired and she was unable to say anything about her previous stay in hospital. Apparently not hallucinated.

Diagnosis. Simple schizophrenia.

Treatment commenced two weeks after admission and consisted of 16 convulsions - maximum dose 8 c.c..

Commentary. Made some progress at first - regained the ability to concentrate and seemed to lose her emotional instability while her memory improved. During the last six convulsions showed no further change and on her discharge was still rather childish but was bright, cheerful and able to occupy herself. Classed as recovered. Interviewed four months later was back at work and had remained well.

Case No. 23. Male - aged 15. Family history bad (younger brother developed schizophrenia at the age of 10). History of breakdown while at school a year previously - recovered to some extent but was unable to return to school. A fortnight before admission became very quiet

and would not speak. On admission he was dull, retarded and apprehensive - he seemed to be terrified of something - after great persuasion he admitted that he heard voices speaking to him. During the next week he became more stuporose and finally was mute and defective in his habits.

Diagnosis. Catatonic schizophrenia.

Treatment commenced one week after admission and consisted of 12 convulsions, - maximum dose 4 c.c..

Commentary. Was very frightened by the treatment but did not struggle against it - began to show improvement after the fifth injection and gradually became active and lost his appearance of apprehension. Started to talk freely but developed a stammer. At the end of treatment was simple and suggestible and childish in his behaviour and speech - his mental age was ten. He showed a tendency to repetition and was quite unable to think for himself or to look after himself. Left hospital a month later and went to live on a farm. Interviewed four months later - showed the same characteristics. Classed as improved, fit for discharge.

Case No. 24. Male - age 31 - single. Family history good. Long history of seclusiveness. On admission was quiet but very vague in his conversation - eventually

admitted that an invisible man spoke to him about his past life and that he was under the control of some influence which made him do the opposite of what he intended. Grinned foolishly for no apparent reason and was obviously constantly hallucinated. Remained in this state - solitary and introverted.

Diagnosis. Paranoid schizophrenia.

Treatment commenced three weeks after admission and consisted of 7 convulsions - maximum dose 7 c.c..

Commentary. Objected strongly to the treatment, saying that he was being given injections by wireless so that a needle was unnecessary. Was so terrified of the injections that he began to resist them - treatment was stopped for this reason. Condition unchanged.

Case No. 25. Male - age 35 - single. Family history good. Only child - grew up to be shy, solitary and self-conscious. First breakdown at age of 25 - afterwards always irritable and unstable. Gave up work two years ago and since then had gradually become more peculiar. On admission was cheerful, vague and hallucinated - had shaved his head because a voice told him to do so to let the atmosphere get inside it - said he was troubled by spirits - could not occupy himself in any way.

Diagnosis. Hebephrenia.

Treatment commenced 14 days after admission and consisted of 15 convulsions - maximum dose 6 c.c..

Commentary. He showed no change - remained foolish, hallucinated and unoccupied. Transferred to another hospital - unchanged.

Case No. 26. Female - age 25 - single. Family history indifferent. Home life rather unhappy - strict parental control which patient resented. Symptoms appeared one week before admission. On admission was in a state of stupor, the degree of which varied - at times mute and resistive - at others talked a little saying that the world had treated her badly and that she hated everyone in it - was hallucinated saying that voices told her she was going to have a baby. During the next month was mute, resistive and defective in habits most of the time but had impulsive outbursts in which she laughed and cried and attempted to smash windows - masturbated constantly - admitted hearing voices and said that she saw visions in the sky sent by God to comfort her.

Diagnosis. Catatonic schizophrenia.

Treatment commenced six weeks after admission and consisted of 30 convulsions - maximum dose 5 c.c..

Commentary. Her behaviour began to improve after six injections and she commenced to occupy herself although her hallucinations remained. These had apparently disappeared after 20 convulsions and she behaved in a normal fashion except that she was rather silly and unstable. A fortnight after treatment had finished she suddenly became wildly excited and hallucinated again - was given another short course of 7 injections and returned to her previous state. Relapsed a second time a month after this and was given a third course of 5 injections. Four weeks after the end of the course she was discharged by order of her parents. At this point she showed no acute symptoms but was childish, irresponsible and devoid of insight. Classed as improved, unfit for discharge.

Case No. 27. Female - age 24 - single. Family history good. History of mild attacks of depression for a year before admission ending in a suicidal attempt. On admission was very depressed and cried bitterly - said ~~only~~ that she had lost her mother and that her sister was unkind to her. During the next twelve months she lost any obvious sign of depression but passed into a state of stupor in which she was mute and defective in her habits. Picked her skin constantly - showed flexibilitas - and at

times smiled foolishly to herself for no apparent reason.

Diagnosis. Catatonic schizophrenia.

Treatment commenced twelve months after admission and consisted of 11 convulsions - maximum dose 5 c.c..

Commentary. Showed immediate improvement and after the third fit was able to talk and to occupy herself and had stopped picking her skin. At the end of the course was cheerful, simple and suggestible; was able to work but was very slow in everything she did. Discharged a month later as improved, fit for discharge. Returned to hospital as a voluntary patient two months later saying that she could not work outside because she was too slow and because she was afraid of what people would say to her. Now shows no active symptoms, but is very slow and devoid of initiative. Final result - improved, unfit for discharge.

Case No. 28. Male - age 39 - married. Family history good. Long history of obsessional ideas over a period of twenty years - for some time before admission his ideas had been more troublesome and vivid. On admission was deluded - said he was Judas Iscariot - was very depressed because he was sure that he had interfered with his daughter (aged 2 years) and that she was going to have a baby. For the next nine mo nths showed a curious swing from an obsessional

to a delusional state - at times saying that his ideas were absurd - at others that they were true. There was a tendency for the delusional stage to increase in length.

Diagnosis. Paranoid schizophrenia.

Treatment commenced nine months after admission and consisted of 15 convulsions - maximum dose 7 c.c..

Commentary. Made slow but steady progress - after ten injections was cheerful and settled and had lost his anxious worried expression. Stated that the ideas which had troubled him so much no longer came into his head - showed good insight and appreciated the explanation of his symptoms given to him. Discharged recovered. Three months later was still well and was back at work.

Case No. 29. Male - age 19 - single. Family history poor. Had been a backward child - always rather unstable and unable to stick to any kind of work. A week before admission became talkative and excited - masturbated openly and asked his sister to have intercourse with him. On admission was excited, noisy and actively hallucinated - his conversation was incoherent and his answers to questions irrelevant - had attacks of screaming. Remained confused, noisy, destructive and defective in his habits.

Diagnosis. Hebephrenia.

Treatment commenced ten days after admission and consisted of 10 convulsions - maximum dose 6 c.c..

Commentary. Showed immediate improvement - after three injections his behaviour was normal - at the end of the course showed no symptoms but was rather simple - appreciated that he had been ill but showed no depth of understanding. Discharged recovered. Three months later was still well and had returned to work.

Case No. 30. Female - age 23 - single. Family history indifferent. In hospital at age of 19 - very depressed and had attempted suicide - frequent outbursts of crying and extreme agitation - required tube feeding frequently. Recovered after one year and was discharged. On her second admission was very depressed and hallucinated - trying to get out of bed and break windows - said the devil was appearing to her and taunting her - refused food because this would make her body fatter and fatter until she burst. During the next few months remained extremely difficult with frequent attacks of extreme agitation during which she always tried to injure herself. Aural and visual hallucinations present - tube-feeding necessary at times.

Diagnosis. Hebephrenia.

Treatment commenced six months after admission and consisted of 20 convulsions - maximum dose 8 c.c..

Commentary. Was terrified of the treatment and always very agitated on the morning of the injections. Apart from this she improved and became quiet and stable, losing her agitation and her suicidal tendencies. Appeared rather childish but occupied herself well. Was transferred to another hospital at the end of treatment and discharged from there four months later. Classed as improved, fit for discharge.

Case No. 31. Male - age 28 - single. Family history indifferent. Long history of general ineffectiveness - had not worked for three years. On admission was vague and uncertain - gave a long and rather involved account of his history and his symptoms, stating that his mind was working wrongly, that everything had become unreal, that his emotions had gone, and that words had lost their meaning for him. He retained these symptoms but behaved quite normally and was able to carry out most efficiently clerical duties in the store-room. A course of insulin treatment was given without benefit.

Diagnosis. Simple schizophrenia.

Treatment commenced fifteen months after admission and

consisted of 14 convulsions - maximum dose 7 c.c..

Commentary. At the end of the course he was still unable to face life outside hospital. Condition unchanged.

Case No. 32. Female - age 42 - single. Family history good. Symptoms commenced in 1937. On admission to hospital one year later she was depressed, showed retardation of thought and speech and expressed depressive delusions, e.g. that she had committed the unforgivable sin, that she was unfit to eat, etc. Soon became agitated, and remained agitated, depressed and difficult with her food for the next nine months - unoccupied and completely obsessed by delusions of guilt. No hallucinations and not confused.

Diagnosis. Involutional melancholia.

Treatment commenced nine months after admission and consisted of 25 convulsions - maximum dose 7 c.c..

Commentary. Lost her agitation, recovered her appetite and commenced to occupy herself during the first ten injections. Made no progress beyond this point and at the end of the course she still had ideas of guilt and showed no insight. Classed as improved, unfit for discharge.

Case No. 33. Female - age 27 - single. Family history indifferent. Long history of eccentric behaviour with outbursts of impulsiveness - never able to work - several previous periods of residence in a mental hospital. On admission seemed to be mildly demented - did not speak spontaneously - in answer to questions stated that she had returned to hospital because she disliked people so much that she had to throw stones at them - showed ideas of reference and appeared to be mildly hallucinated at times.

Diagnosis. Simple schizophrenia.

Treatment commenced one week after admission and consisted of 21 convulsions - maximum dose 8 c.c..

Commentary. She was very antagonistic towards the treatment, which produced no improvement. Result unchanged.

Case No. 34. Female - age 28 - married. Family history good. History of nervous breakdown seven years earlier on the death of her mother. Recovered quickly and married some six months later. Had one child two years after marriage and on admission was seven months pregnant - was depressed and full of ideas of guilt - said she had used birth control and that the baby inside her was simply an inanimate mass of corruption and was giving off a horrible smell. Delivered of a normal child two

months later - no improvement in her mental state. For the next two years continued to express nihilistic ideas and to show fantastic delusions. Insisted that the baby which had been born was the child of the devil and had taken away her inside leaving a mass of corruption - had ideas of guilt and said that she was going to be punished in a horrible fashion. In spite of these ideas remained cheerful and well-occupied and smiled when describing her symptoms.

Diagnosis. Hebephrenia.

Treatment commenced two years after admission and consisted of 20 convulsions - maximum dose 9 c.c..

Commentary. Showed great fear of the injections and was persuaded each time with difficulty to submit to them. Between the fifth and the tenth injections her mental state improved considerably - she lost the ideas noted above and for the first time consented to see her younger child towards whom she behaved normally. During the treatment she showed a definite impairment of memory which had not existed previously - this passed off later. At the end of the course she was cheerful, quite normal in her conversation and behaviour, and appeared well balanced. Discharged recovered. Three months later had remained well.

Case No. 35. Female - age 28 - single. Family history good. Had been strange in behaviour for some six months. On admission was dull and retarded, spoke very little and resisted all attention - appeared to be hallucinated. During the next four years she remained asocial, moody, and self-absorbed with periods of impulsiveness during which she attacked others. Admitted hearing voices. At times became stuporose and refused her food - at others occupied herself but never spoke spontaneously.

Diagnosis. Catatonic schizophrenia.

Treatment was commenced four years after admission and consisted of 30 convulsions - maximum dose 6 c.c..

Commentary. In the early stages showed some improvement - became more active and spoke a little but still remained solitary. Made no further progress and had relapsed into her previous state a month after the end of the treatment. Result - unchanged.

Case No. 36. Female - age 34 - married. Family history good. Illness developed one month after the birth of her first child. Became excited and confused - very distressed, saying that she was wicked and was being punished by electricity in the wires of the mattress. Admitted to hospital in this state and remained excited,

hallucinated, and deluded for six months. Improved and developed into a simple individual with emotional instability and complete lack of insight. Retained a vague idea that she was kept in hospital because she had once worked in a solicitor's office - apparently not hallucinated. Had no emotional depth.

Diagnosis. Simple schizophrenia.

Treatment commenced two years after admission and consisted of 18 convulsions - maximum dose 6 c.c..

Commentary. Was very frightened of the injections. Showed no improvement at any stage. Result - unchanged.

Case No. 37. Female - age 29 - single. Family history indifferent. A quiet sensitive individual who had had an unhappy home life - deeply attached to her mother who committed suicide when the patient was 25. After this the patient became even more reserved - three months before admission became depressed and eventually tried to commit suicide by swallowing aspirin. On admission was depressed and showed ideas of unreality - complained that she had no feelings and that people had ceased to mean anything to her - felt she would be better off dead. Showed a half-resentful, half-fatalistic attitude: 'Everything I have ever loved, I have lost - if I became fond of a cat or a

dog it very soon died.' During the next nine months her attitude did not change - she obtained a measure of security in hospital and seemed content to stay there indefinitely - retained her ideas of unreality, became depressed at times and said she would commit suicide if she left hospital.

Diagnosis. Simple schizophrenia.

Treatment commenced nine months after admission and consisted of 14 convulsions - maximum dose 5 c.c..

Commentary. Objectively had lost all trace of emotional instability after the first ten injections. Maintained that her feelings of unreality had gone and that she had regained her self-confidence. Discharged recovered. Six months later had remained well and was back at work.

Case No. 38. Male - age 15. Family history indifferent. A mentally defective boy - only child - home conditions very unsatisfactory owing to differences between the parents. Illness started acutely and on admission three days later he was very excited and talkative - was visually and aurally hallucinated, defective in habits and incoherent in speech. During the next six months was excited, noisy and destructive most of the time, with a few quiet intervals.

Diagnosis. Schizophrenia with Mental Deficiency.

Treatment commenced six months after admission and consisted of 7 convulsions - maximum dose 7 c.c..

Commentary. Showed improvement at once and had lost all acute symptoms after four injections. Became happy and obedient although very backward in every way. Has remained in this state ever since, that is for six months. Result - recovered from schizophrenia.

Case No. 39. Male - age 24 - single. Family history bad. Three years before admission had tuberculosis of lung and was treated in Switzerland - made a good recovery. Returned home and was apparently normal for the next two years - then became depressed and worried - gradually became solitary and suspicious and finally locked himself in his room and refused to speak. On admission was dull and depressed - said he had taken a vow not to let food pass his lips - was fed nasally for a few days - after this passed the tube himself, saying that this did not break his vow. After six months improved and began to eat and to occupy himself but was very slow and hesitant - a year later became excited, restless and destructive and started picking his face and arms. His condition deteriorated and for the last nine months he has been confined to bed - noisy,

destructive, defective in habits and incoherent in speech.

Diagnosis. Catatonic schizophrenia.

Treatment commenced four years after admission and consisted of 8 convulsions - maximum dose 5 c.c..

Commentary. Evidence of lung damage appeared on the fact that he remained cyanosed for about fifteen minutes after each fit. Treatment was cut short for this reason. The mental state showed rapid improvement - at the end of treatment he was quiet and well-occupied although he still showed retardation, apathy and ambivalence. Has remained in this state for the last six months. Result - improved unfit for discharge.

Case No. 40. Female - age 29 - single. Family history good. Had been showing symptoms for about eight months - chiefly ideas of reference. On admission was in a state of delirium - muttering unintelligibly to herself, picking at the bedclothes and tossing about in bed. After two days she passed into a state of stupor in which she was mute and resistive. Improved slightly during the next few weeks but retained a severe degree of thought-blocking, spoke only in monosyllables, and wandered round in an aimless, puzzled fashion - admitted hearing voices.

Diagnosis. Catatonic schizophrenia.

Treatment commenced three weeks after admission and consisted of 32 convulsions - maximum dose 6 c.c..

Commentary. Showed little change at first - after 15 injections was brighter and more communicative - still rather lost but apparently not hallucinated. After the 21st fit relapsed suddenly and became noisy, excited, and hallucinated. Lost these symptoms after the next injection. At the end of the full course was quiet and reasonable - rather silly in her behaviour and slow in her work but no acute symptoms left and realised that she had been mentally ill. Result - improved, fit for discharge.

Case No. 41. Female - age 21 - single. Family history indifferent. Acute onset of symptoms - on admission was mute and negativistic, tearing her clothes and refusing food. Improved during the next six months to the stage where she spoke a little and occupied herself a little but remained solitary and introverted. Admitted hearing voices of men saying nice things to her, and displayed erotic tendencies. For the next five years remained more or less in this state with occasional outbursts of excitement associated with destructive tendencies.

Diagnosis. Catatonic schizophrenia.

Treatment commenced 5½ years after admission and con-

sisted of 23 convulsions - maximum dose 6 c.c..

Commentary. Showed no improvement. Result - unchanged.

Case No. 42. Female - age 40 - married. Family history indifferent. Husband died two years before admission and patient developed tremor and weakness of hands and feet immediately afterwards. Was treated for rheumatoid arthritis. On admission had been in bed for one year, unable to walk - had coarse tremor of arms and legs - rigidity of all voluntary muscles with limitation of movement of all joints - inter-phalangeal joints of the fingers flexed and both ankles inverted. No evidence of any organic disease was present and the disability disappeared during sleep except that the right foot remained inverted. Had some emotional instability but no other mental symptoms.

Diagnosis. Hysteria.

Treatment commenced five months after admission and consisted of 12 convulsions - maximum dose 5 c.c..

Commentary. Very frightened of the treatment and refused further treatment after twelve injections. By this time she had almost lost her tremor, her hand had returned to normal and her left ankle was freely movable although the right remained inverted with apparent shortening of tendons on the inner side. Was able to walk with a limp

and to occupy herself. Result - improved, fit for discharge.

Case No. 43. Male - age 30 - married. Family history indifferent. Previous history good although he had always been a simple type. Three months before admission suffered from sleeplessness and seemed worried - began to behave queerly. On admission was depressed and stated he was going to be buried alive - his conversation was rambling and showed numerous vague delusions - he stated for example that he could make the birds whistle by thinking about it but that if the birds whistled three times he would be dead. Asked for a light so that he could see himself asleep. Said that everyone round him kept repeating: "He's gone - good riddance". His condition varied during the next few months - at times he was stuporose and lay in bed gazing fixedly at the ceiling - at others he was rather impulsive - hallucinated continually.

Diagnosis. Hebephrenia.

Treatment commenced six months after admission and consisted of 10 convulsions - maximum dose 8 c.c..

Commentary. He showed great fear of the injections and finally refused treatment after the tenth convulsion. At the same time he made some progress and became cheerful

and co-operative but gained no insight into his illness - remained hallucinated at times. Result - improved, unfit for discharge.

Case No. 44. Male - age 25 - single. Family history indifferent. Patient was abandoned by his mother at the age of two - brought up in an orphan home. Always rather unstable and had thrown up several jobs in fits of temper - two days before admission lost his last job and attempted to commit suicide by swallowing aspirin. On admission was rather depressed saying that his head felt as if there was an electric motor inside it and that for some time he had heard voices telling him he was no good - showed ideas of reference saying that the people whom he passed in the street despised him. Memory and orientation unaffected.

Diagnosis. Simple schizophrenia.

Treatment commenced two weeks after admission and consisted of 14 convulsions - maximum dose 10 c.c..

Commentary. He lost his hallucinations and his depression but remained simple and garrulous and showed no real grasp of his illness. Result - improved, fit for discharge.

Case No. 45. Male - age 29 - single. Family history

indifferent. Long history of instability with outbursts of temper - occasionally attacked members of his family. On admission was mildly depressed - said that his family and strangers he passed in the street were always saying rotten things about him and that this made him lose control of himself. Memory and orientation unaffected.

Diagnosis. Simple schizophrenia.

Treatment commenced two weeks after admission and consisted of 15 convulsions - maximum dose 9 c.c..

Commentary. Became more cheerful and appeared to lose his ideas of reference - had no impulsive outburst while in hospital. At the same time he remained rather slow and devoid of self-confidence. Result - improved, fit for discharge.

Case No. 46. Male - age 48 - married. Family history good. Previous personality good - successful in his career. Illness commenced twelve months before admission - suffered from sleeplessness, inability to concentrate, and mild depression - became gradually worse and on admission was depressed and agitated and had several sores on his face and chest where he had picked the skin. Was mildly confused and showed thought-blocking - numerous delusions of guilt - that he had allowed his brain to soften

and had murdered his wife and sister. Made no progress and attempted to swallow his artificial teeth in order to commit suicide. Three months later he remained in the same miserable, agitated state.

Diagnosis. Involutional melancholia.

Treatment commenced three months after admission and consisted of 10 convulsions - maximum dose 6 c.c..

Commentary. Made immediate and rapid progress and after five injections had lost all trace of agitation and was cheerful and active. At the end of the course his behaviour was normal and he had good insight into his illness. Discharged recovered.

Case No. 47. Female - age 38 - single. Family history good. Symptoms commenced after her father's death eight years before her admission. Commenced to have tremors in arms and legs which grew worse - confined to bed and unable to walk for the last five years. On admission showed marked tremor of the arms and legs which was exaggerated by voluntary movement - was unable to stand upright or make any effort to walk. Examination of nervous system showed no abnormality except exaggerated reflexes. She looked bright and cheerful but complained of feeling de-

pressed and miserable, and of pains in various parts of her body.

Diagnosis. Hysteria.

Treatment commenced one month after admission and consisted of 20 convulsions - maximum dose 6 c.c..

Commentary. Improved to the extent of being able to get out of bed and dress herself but at the end of the course still complained of various pains and was unable to walk without assistance. Result - unchanged.

Case No. 48. Female - age 33 - single. Family history indifferent. Several previous attacks - unstable personality who had never been capable of earning her own living. Present attack commenced a week before admission. On admission she was mute but after two days began to speak and stated that an evil influence had been exerted on her by means of electricity and that people, who lived miles away, were continually talking to her and abusing her. Was very suspicious and did not occupy herself.

Diagnosis. Paranoid schizophrenia.

Treatment commenced two weeks after admission and consisted of 18 convulsions - azoman used - maximum dose 1.4 c.c..

Commentary. Improved to some extent but remained rather unstable - excited at times - at others morose and suspicious. Treatment discontinued because she refused it. Shortly afterwards relapsed and became depressed and complained of the voices which abused her. Result - unchanged.

Case No. 49. Female - age 49 - married. Family history good. A month before admission began to suffer from loss of sleep and complained that she could not work. On admission was depressed and stated that she felt worried because she had repeated gossip about a neighbour and because she had neglected her religion. Her condition deteriorated rapidly and she became agitated, hallucinated, and expressed prominent delusions of guilt - felt she was going to be burned and developed suicidal tendencies.

Diagnosis. Involutional melancholia.

Treatment commenced 6 months after admission and consisted of 14 convulsions - maximum dose 6 c.c..

Commentary. At first showed no change, but between the fifth and the tenth injections, improved considerably - lost her agitation and commenced to occupy herself - her delusions of guilt receded into the background but she ad-

mitted that she still heard voices. Made no progress beyond this point. Result - improved, unfit for discharge. As a voluntary patient she discharged herself later. Two months afterwards had made further progress and was beginning to show insight. Final result - improved, fit for discharge.

Case No. 50. Female - age 27 - single. Family history bad. Personal history poor - always asocial. Definite symptoms appeared four years before admission - started changing her job frequently because she thought her employers were trying to kill her. On admission was suspicious and negativistic - admitted hearing voices and laughed and cried very easily. During the next two months remained hallucinated, solitary and introverted - occasionally noisy and abusive - occupied herself spasmodically.

Diagnosis. Paranoid schizophrenia.

Treatment commenced two months after admission and consisted of five convulsions - azoman used intramuscularly - dose 1.8 c.c..

Commentary. Was afraid of the treatment and very resistive to it - this had to be abandoned for this reason. Result - unchanged.

Case No. 51. Female - age 55 - married. Family history good. Symptoms commenced when her husband left her four years earlier. On admission was depressed and complained of headache, noises in the ears, inability to think, and a burning feeling in her limbs. Gradually got worse, developed agitation and hypochondriacal delusions - eventually confined to bed because she said that her legs were paralysed. Displayed delusions of guilt and refused her food. Required tube feeding but in spite of this continued to lose weight.

Diagnosis. Involutional melancholia.

Treatment commenced eight months after admission and consisted of 7 convulsions - azoman given - maximum dose 1.9 c.c..

Commentary. Was in poor physical condition and showed arrhythmia after each convulsion - developed fibrillation after the seventh fit and treatment was stopped on account of this. Her mental state improved considerably - she lost her agitation, began to eat and her delusions disappeared. After the fourth injection was able to walk again. At the end of treatment was well occupied but still looked rather worried and had not gained full insight. Result - improved, fir for discharge.

Case No. 52. Female - age 27 - married. Family history good. History of being emotionally unstable for about a year, with hypochondriacal ideas. On admission was agitated and depressed and cried bitterly - complained of voices talking to her and accusing her of various sins. Soon lapsed into a stupor in which she lay in bed with her eyes tightly closed and was mute except for an occasional screaming attack like a baby. Her habits were defective. Was difficult with her food. Remained in this state.

Diagnosis. Catatonic schizophrenia.

Treatment commenced two months after admission and consisted of 18 convulsions - azoman used - maximum dose 1.7 c.c..

Commentary. Soon emerged from her stuporose state - had an interesting transitional stage in which she talked and acted like a child of six and at the same time insisted that she was six years old - after the tenth injection she was normal in her behaviour but still rather simple and emotionally unstable. Made no further progress. At the end of treatment was no longer hallucinated, but had no real insight. Result - improved, fit for discharge.

Discussion of Cases.

1) Complications. Dislocation of the lower jaw occurred frequently in the first few cases treated - it was found, however, that this could be prevented by controlling the jaw properly at the beginning of the tonic stage.

No other dislocation or fracture occurred. Several patients complained of muscular pain in the arms and lower part of the back in the early stages of treatment but this passed off as they grew accustomed to the muscular exertion of the fit.

The effect on the heart has already been considered.

Two patients had intercurrent influenzal attacks which caused postponement of treatment for a short time. These attacks were uneventful and there was no other evidence that this treatment lowered the resistance of the patients in any way.

In Case No. 19 there occurred an alarming complication which has not been described in the literature. This took the form of a primary failure of respiration, suggesting that the respiratory centre had been temporarily paralysed. It is difficult to see why this happened. Both the accumulation of CO_2 and the lowering of O_2 tension in the blood

with each fit act as respiratory stimulants (Samson Wright)(44) and presumably determine the automatic resumption of respiration which normally takes place. It is possible, however, that in this case the O_2 tension was lowered to such an extent that the respiratory centre was paralysed from actual deprivation of oxygen. The alternative explanation is that cardiazol can, in a susceptible subject, act as a direct poison to the respiratory centre.

Several of the patients complained during their treatment of impairment of memory - examination showed that they mislaid articles frequently and could not be trusted to perform simple tasks because they forgot what they had set out to do. Remote memory was not affected and the condition seemed to spring from blunting of attention. In all cases the disability had disappeared within a fortnight of the end of treatment.

There is, however, another and more serious danger the importance of which seems to be generally minimised and that is the possibility that the repeated induction of convulsions may cause some intellectual deterioration. In this connection attention may be drawn particularly to two of the cases in this series - Nos. 26 and 6. The first of these received three separate courses of injections

- in the first 30 injections improved her to the stage of being quiet, simple and rather foolish - she showed no sense of responsibility and was rather childish, unreasonable, and vain. Her acute symptoms recurred and a second course of 7 injections reproduced the above state - similarly a second relapse was cut short by another 5 injections. Thus after 42 injections the patient showed a type of intellectual deterioration which was not quite characteristic of schizophrenia. Similarly in the second case the result of treatment was to produce a mild dementia which rendered the patient incapable of living an independent and useful existence outside hospital, but a dementia which had supervened earlier than would have been expected if the original schizophrenia illness had been allowed to run its course and which differed from the deterioration of schizophrenia in that the patient was not particularly solitary or introverted but was simply vain, lazy, obstinate and childish. In both cases typically schizophrenic symptoms could and did appear but these were removed by further injections of cardiazol leaving behind them this background of intellectual shallowness. The suggestion is therefore made that cardiazol may induce a certain deterioration of the personality which appears to differ from that resulting from a pure

schizophrenic process. It is admitted, however, that this suggestion is based entirely upon an impression and is not reinforced by any concrete proof. That this possibility exists is noted by Humbert and Friedmann (38) who, pointing out that the aura of cardiazol resembles that of epilepsy in suggesting a vascular disturbance in the hypocarpus and cornu ammonis, conclude with this sentence: "One cannot, therefore, exclude the possibility that the frequent fits will damage the neurones in a similar fashion to the alternation of ischaemia and hyperaemia in epilepsy."

2) Effect of the Convulsions on the Mental State.

(a) Direct effect: After each fit there is a period of confusion varying in individual cases from about thirty minutes to some hours - during this period the patient may show intense motor activity - shouting, struggling, and attempting to get out of bed. This may proceed to the point of exhaustion and is usually accompanied by what appears to be a state of extreme fear. Amnesia is present for the actual fit and for some time subsequently; for example if the patient is removed to another dormitory soon after the fit he does not recall how this change of environment took place. There is, as pointed out earlier, no amnesia for the aura and this seems to account for the

conscious fear of the treatment which was present in nearly every case although not shown to the same extent by all. An interesting point aboutn this fear is that, as a rule, it appeared to grow in intensity with each succeeding convulsion. Some patients managed to control it well and even stated that they did not mind the treatment - but even these greeted the end of treatment with undisguised relief even though they admitted that the treatment had been beneficial. It was not uncommon to find a patient, who had accepted the treatment for some time apparently without any great objection, suddenly refuse to have any more - in such cases the fear was usually rationalised and the patient stated that he or she felt that the treatment had done all the good it could and that further progress would be more rapid without it. In other cases the fear was quite obvious and was freely admitted, and in six patients it became so great that they refused to have further treatment. It has been affirmed that the unpleasant feeling tone induced is the result of unsuccessful injections - that is of injections which are not followed by convulsions. Actually this is not so because although a subconvulsive dose is more unpleasant at the time than a convulsive one, the latter may produce antagonism just

as surely as the former and in three of the six patients whose treatment had to be stopped on account of this antagonism all the injections given produced convulsions.

The fact that this aversion occurred so frequently suggested that the nature of it would repay study. In this series of cases the impression was gained that the unpleasant feeling tone had both a conscious and an unconscious component and that its exact nature varied to some extent, according to the symptoms of the patients. For example, in some of the involutional melancholics and of the schizophrenics who showed a strong guilt sense the treatment was interpreted as a punishment, which had to be endured, and which seemed to provide a means of expiation (it is interestint to note that picking of the skin disappeared after the first few injections) - thus one girl in the early stages of treatment used to repeat: "I have been wicked - I must have this torture". Similarly another patient used to say: "Punish me by death - not by this." In other cases the emotional reaction was frankly one of fear the exact nature of which could not be described by the patient. A few maintained that it was a fear of death and that they felt that each injection would prove fatal. Others described it variously as an "awful feeling"; "you felt something

terrible was going to happen"; or "the thought of it made me tremble all over." A third group appeared to be indifferent and stated that they did not mind the treatment but, as noted above, some of these eventually changed quite suddenly without being able to give any real explanation of the alteration in their attitude, suggesting that an unconscious aversion had been present and had appeared above the surface as it were.

The existence of this aversion is shown further by the fact that some of the patients frequently complained of palpitation, headache, or sickness on the morning of the injection with the obvious hope that the presence of such symptoms would cause treatment to be postponed - and yet a percentage of those who did this maintained quite genuinely that they did not mind the treatment in the least. After the injection there appeared, commonly, a state of euphoria and the contrast between this and the state of agitation which often preceded the injection was most striking. Finally it was noted that schizophrenics in whom the illness had lasted for a considerable time and in whom some dementia was apparent were, as a rule, less resistive than cases of short duration and the fear response could not be evoked in them with the same readiness.

There are two main arguments used against the theory that the unpleasant feeling tone evoked by the treatment plays any part in producing the beneficial results of the treatment. First that the old-fashioned 'fear' treatments such as, to give an extreme example, standing the patient in a dungeon and allowing water to rise up to his neck, produced no beneficial effect - and second that there is no correlation between the amount of fear shown by patients undergoing cardiazol treatment and the amount of improvement obtained in them. Both these objections must be admitted, but it may be pointed out that the amount of fear shown is no measure of the unconscious anxiety present and it is possible that it is this unconscious anxiety which is the important factor.

(b) General effect. It may be stated to begin with that cardiazol does not affect the underlying personality although it may remove psychotic symptoms. In the cases which responded the changes which took place in the mental state occurred gradually as a rule. Meduna describes three kinds of remission: (1) sudden, (2) progressive, and (3) intermittent - in the first the remission takes place early in treatment and is permanent, in the second it is gradual and in the third a series of remissions of

increasing length are seen, but the first and third types were seldom encountered in the cases described here. The details of the improvement in individual cases were so varied that it is difficult to describe anything resembling a typical course of events. However certain interesting similarities could be detected. It was noted, for example, that certain symptoms tended to disappear early in treatment - among these were refusal of food, agitation, picking of the skin, defective habits and manic overactivity and with the disappearance of these the patients became quieter, tidier, more co-operative, and sometimes accessible to psychotherapy. Improvement of appetite occurred very frequently and in association with this it was found that most patients gained weight during and immediately after their course of treatment. Further, unless some mental improvement could be discerned after the first ten convulsions it did not occur later - in view of this it seems unnecessary to carry on treatment beyond this point in cases showing no improvement. Hallucinations and delusions proved more resistant than the symptoms mentioned above - in favourable cases these also disappeared later in treatment. But it must be stressed that while the above order was frequently seen variations from it did occur. -

Minor degrees of improvement such as an increase in accessibility or an increased ability to work could be detected often even in some of the most chronic cases, but such patients usually relapsed quickly after the treatment was discontinued. This tendency to relapse is commented upon by various authors. At the same time it must be pointed out that early relapse is uncommon in cases who have recovered completely and that this tendency applies to degrees of improvement short of recovery. There is also another side to the picture. Some of the patients, who were discharged as improved, continued to improve at home and, when interviewed later, had full insight and could be placed in the recovered class.

3) Type of case affected. The question now arises as to what type of case may be expected to respond to this treatment. The literature contains several opinions upon this point - for example Briner (25) says that the best results were obtained with late catatonics and in paranoid schizophrenics with predominantly hypochondriacal complaints and visceral delusions while catatonic stupors and simplex cases did not improve. Angyal and Gyarfas (28) on the other hand, report that the simple schizophrenias and the stuporose catatonics responded better than any other class. Meduna believes that all groups are favour-

able and that the response depends on (a) the duration of the illness and (b) whether the illness is inherited or not. Winkelman (30) lays much less stress on the type of illness and the duration and states that the remission probability corresponds to the amount of deterioration present, explaining in this way the apparent contradiction that good results are obtained in some cases of long standing and bad results in certain cases of short duration.

The matter has been complicated further by the extension of this form of treatment to other kinds of mental disorder. For example, Matthews (46) says that a severe case of psychoneurosis recovered after cardiazol treatment while Verstraeten (47) reports that melancholics of the manic-depressive group respond well. Cook (48) gives similar results. In this series three cases of mania, four of involutional melancholia, and one of hysteria of such long duration as to be inaccessible to psychotherapy, all showed either recovery or marked improvement. This wide diversity of conditions influenced by cardiazol suggests that what really matters in case selection is not so much the diagnosis as the symptom complex. Symptoms such as severe agitation, picking of the skin, acute excitement,

and noisy and restless behaviour generally, responded whether they had a schizophrenic or a manic-depressive background. Further, such symptoms responded even though, as in one or two of the cases treated, they had lasted a considerable time. On this point it is interesting to refer to the work of Cohen (45) who treated a mixed group of 42 patients who had shown chronic excitement over a long period and found, generally, marked improvement in such symptoms as aggressiveness, destructiveness, and incontinence so that the necessity for sedation was greatly diminished. It is not made clear how long such improvement lasted but the author concludes that cardiazol has a definite administrative value in chronic cases. Case No. 39 in this series is an example of such symptomatic improvement - and this improvement has been maintained for six months. On the other hand what might be called exaggerated personality defects - for example symptoms such as ideas of reference - were not, as a rule, influenced. Similarly hallucinations and delusions occurring in a clear setting did not respond so well as those occurring in cases showing some of the symptoms mentioned above.

4) Classification of Results. It is always a most

difficult problem to assess the degree of improvement in dealing with mental illness and the criteria adopted by different authors vary considerably. In this series the patients have been divided into four groups: (1) recovered, (2) improved fit for discharge, (3) improved, unfit for discharge, and (4) unchanged. Patients were said to have recovered if they had lost all psychotic symptoms, had full insight in the sense of realising that they had been mentally ill and had returned to their pre-psychotic state as far as this could be determined from the history. But, as pointed out already, no change was produced in the fundamental personality in these patients and those who had shown schizoid tendencies before the definitely psychotic symptoms appeared retained those tendencies after these symptoms had vanished. However, so long as they fulfilled the conditions enumerated above they were considered to have recovered. In the second group are included those who lost their psychotic symptoms and reached the stage of being able to return home and even, in some cases, to work but who showed no insight into their illnesses. The third group contains those whose general behaviour had improved considerably but who retained symptoms such as emotional

instability, hallucinations or delusions and whose discharge could not be recommended. Some of the patients in this group actually did leave hospital against advice, but, of these, three returned within two months of their departure. The fourth group contains those patients who showed no improvement or whose improvement was either very slight or of very short duration. The period which has elapsed since the termination of treatment varies from one to ten months. With this classification the following were the results obtained: out of 52 patients, 17 recovered, 8 were improved, fit for discharge, 7 were improved, unfit for discharge, and 20 were unchanged.

The details may be tabulated as follows:-

Type	Total	Recovered	Improved fit for discharge.	Improved unfit for discharge.	Unchanged.
Simple sch.	11	3	2	-	6
Paranoid sch.	7	3	-	-	4
Catatonic sch.	15	3	3	4	5
Hebephrenic sch.	9	3	-	2	4
Sch. $\bar{c}$ M.D.	1	1	-	-	-
Involutional Melancholia	4	1	2	1	-
Manic Depressive	3	3	-	-	-
Hysteria	2	-	1	-	1

Finally, taking the schizophrenic group only and dividing them into those who had been in hospital for less than twelve months before treatment was commenced and those who had been in hospital more than twelve months, the results were:-

	Total	Recovered	Improved fit for discharge	Improved unfit for discharge	Unchanged
Over 12 months	13	1	-	2	10
Under 12 months	30	12	5	4	9

5) Detailed study of results. In the schizophrenic group there emerged certain particular prognostic signs apart from the general ones already given. In the first place the duration of the patient's stay in hospital, and therefore the duration of his illness, was of importance. There was only one recovery out of the thirteen patients who had been in hospital more than twelve months before treatment was commenced. Secondly an acute onset, with definite precipitating factors, was more favourable than a gradual one and therefore patients who had been well adjusted to their illness had a better chance of recovery than those in whom schizophrenic tendencies were pronounced.

Thirdly, a poor family history was an unfavourable sign. Now it will be seen at once that these are the points which favour a remission, apart from any form of shock treatment - this raises once more the question whether cardiazol has increased the remission late in schizophrenia. This question cannot be answered with any degree of certainty - the impression gained was that some of the cases who did recover would have passed into a chronic state without treatment. Whether this impression is accurate or not there is no doubt that the treatment was of value in limiting the duration of the attack in many of the patients.

Simple schizophrenics in whom the symptoms were not clearly defined but consisted of personality defects such as lack of application and attention, moodiness, irritability and a want of social consciousness, and in whom the illness developed gradually, did not respond well while those who showed acute emotional instability usually improved.

In the catatonic group those in whom excitement, restlessnes, and impulsive conduct predominated improved more than those in whom the stuporose periods were of long duration.

In the hebephrenic and paranoid groups a good result was obtained chiefly in patients who showed acute symptoms without evidence of marked deterioration and who retained emotional response. Apathy was an unfavourable sign in all groups.

The results in the manic depressive group were more striking. In each of the three cases treatment of the manic overactivity had lasted for some months without showing any sign of improvement. Yet all three responded immediately to treatment and recovered completely. The results obtained have suggested the advisability of using this treatment to cut short attacks of acute mania and it is proposed in future to treat such cases in this way if they do not show signs of improvement within a month of admission. It is possible that this treatment may have a useful application in cases of mania occurring for the first time relatively late in life and having a bad prognosis.

In the involutional melancholic group the results were again encouraging. The four patients treated all showed, in different degrees, refusal of food, agitation, hallucinations and depressive delusions. The immediate result of treatment was to remove the agitation, restore

the appetite, lessen the danger of suicide and enable the patients to occupy themselves. One patient recovered completely and two more improved sufficiently to be able to return home. Here again there appears to be a promising field for investigation.

The results in the two cases of hysteria were indefinite. One patient did improve to the extent of ceasing to be bedridden and of beginning to do useful work. In view of this it is considered that the treatment is worth a trial in refractory cases of this nature.

Conclusions.

(1) Cardiazol provides a safe and easily administered therapeutic method.

(2) This method is of value in the treatment of acute mental disorders in the schizophrenic and manic-depressive groups and of acute exacerbations in chronic mental disorders in the schizophrenic group.

(3) It has no effect on the underlying personality and is of no value in relieving personality deterioration.

(4) There is not enough evidence at the moment to show whether its effect is merely to accelerate recovery in the type of case mentioned above or whether it actually increases the recovery rate.

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