A PSYCHO-PHARMACOLOGICAL STUDY OF SCHIZOPHRENIA, WITH PARTICULAR REFERENCE TO THE MODE OF ACTION OF CARDIAZOL, SODIUM AMYTAL AND ALCOHOL IN SCHIZOPHRENIC STUPOR.*

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> " The difference in sensitivity between that portion of the central nervous system which is most easily affected by a poison and all others is often so great that only a single point of action need be considered, in its practical use in therapeutics."
>
> H. H. MEYER and R. GOTTLIEB
> (*Experimental Pharmacology*).

THERE is already a comprehensive literature on the convulsion treatment of schizophrenia, and it is not the purpose of this paper either to attempt to assess these results, or to claim therapeutic success, or failure, in the cases mentioned here.

The work to be described owed its inception to the results obtained by Cook (2) in chronic cases of schizophrenia, and reported by him at a meeting of the Royal Society of Medicine in January, 1938. Of 26 schizophrenic patients, ill for a period of over two years, 2 recovered, 2 showed " very good remissions " and 7 showed " striking improvement " as a result of cardiazol treatment. The present series also includes 26 cases, of whom only 5 were of between one and two years' duration. The average duration of illness for the group was $5\frac{0}{1-2}$ years. In the face of evidence presented by continental workers, it was from the first difficult to be optimistic about these cases. Angyal and Gyarfas (3) had reported that of 18 schizophrenics of more than one year's duration, only 4% had recovered. Brousseau (4) reported no remissions in 6 patients, ill for more than 5 years, and Sorger and Hofmann (5) treated 100 cases of schizophrenia, and obtained a remission-rate of approximately 25% in cases ill over one year. At their face value these results are poor, and when compared with the spontaneous remission-rates of 23·6% given by Pullar Strecker (6) and of 33% given by Harris (7), they do *not* appear to warrant this treatment in chronic cases. As will be seen by the case-histories,

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the majority of the cases selected were of the stuporous catatonic type of schizophrenia. This type of case was selected because it had been stated by most workers (8, 9, 10, 11, 12) that it responded more favourably than other types (simple, hebephrenic, paranoid) to cardiazol treatment.

In my own cases, it was almost constantly observed that during, and for a considerable period after, the completion of treatment hitherto stuporous patients became overactive, impulsive and often violent. Mutism gave place to incoherent speech, and indifference to food was replaced by a gluttonous appetite. This observation has already been made by others. Thus Harris (7) states: "The most profound effect (of cardiazol) was obtained in cases of catatonic stupor, which passed into a state of catatonic excitement or hebephrenia, if they did not recover completely." Again he writes: "The change from a state of stupor to a state of excitement cannot be regarded as beneficial, and those patients in whom it occurred were rendered much more difficult to care for, and more troublesome." He does not, unfortunately, state the duration of the illness in the cases where this reaction occurred. Nightingale (13) also mentions this phenomenon, and states "The occurrence of this aimless excitability has been rather a troublesome feature in the course of treatment, and a number of previously lethargic patients have become extremely mischievous and interfering. In some cases this has been a passing phase, but in others, despite prolongation of treatment, this behaviour train has persisted".

It seemed that there was a similarity between this "post-cardiazol" hyperexcitability and impulsiveness, and the post-convulsive irritability and impulsive conduct of the average epileptic in a mental hospital. Before commencing cardiazol treatment I had been treating cases of catatonic stupor, with sodium amytal, and two cases, in which I had been able to produce a lucid interval with this drug, shortly afterwards received cardiazol treatment at the hands of a colleague, recovered and were discharged. It therefore naturally occurred to me to consider whether there might be some common mode of action of these drugs, which would explain on the one hand the temporary remissions to normality or quasi-normality, and on the other hand, the complete remissions. The effect of alcohol on catatonic stupor was also investigated, since I felt, for reasons which will be explained later, that its results would tend to prove or disprove my hypothesis as to the mode of action of cardiazol and sodium amytal. Thirty-four cases of schizophrenia were investigated. Some of these cases presented some difficulty in diagnosis, but it will, I think, be made clear by the case-histories that as time passed the diagnoses became certain. I refer to cases V. W. W—, T. S—, A. M. K— and E. M. B—, who were at first diagnosed as depressive states. Only 3 cases could be said not to have been stuporous, namely cases R. M—, G. F. D— and H. F—. These 3 cases were impulsive, often violent, and actively hallucinated, but though at times quiet and sullen, were never stuporous.

The cases are divided for convenience into five groups :

Group I comprises 6 cases, who received at different periods cardiazol, sodium amytal and alcohol.

Group II : 10 cases who received cardiazol and sodium amytal.

Group III : 6 cases who received sodium amytal and alcohol.

Group IV : 10 cases receiving cardiazol alone.

Group V : 2 cases receiving sodium amytal alone.

For physical reasons all the cases could not receive cardiazol, and in some it was thought inadvisable to administer the large quantities of alcohol necessary to produce lucid intervals.

Technique.

The technique of cardiazol treatment has been adequately described elsewhere by Meduna (14, 15), Cook (2), Kennedy (9) and others. It will suffice to state, therefore, that the method employed here was, with two exceptions, identical with that advocated by Kennedy. These exceptions were :

(1) The patients were treated in an open dormitory, and not in side-rooms, though screens were placed between the beds.

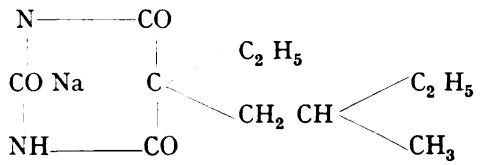
(2) No attempt was made to thread the needle up the lumen of the vein, as this may tend to favour thrombosis (Harris and Birnie, 16).

A table of the injections given is included in each case-history, together with the latent periods in seconds, from the completion of the injection to the onset of the fit, and the duration of the fit itself, i.e., from the onset of the tonic spasm until the final clonic spasm. A course of 30 fits was aimed at, in cases who responded favourably, and of at least 20 fits, before relinquishing treatment in unresponsive cases. Occasionally, however, accidents, thrombosis of veins, etc., occurred, which resulted in earlier cessation of treatment.

Sodium Amytal.

As far as I am aware, no account has appeared in British journals of the action of sodium amytal on catatonic stupor. It seems therefore justifiable to consider this drug and the technique of its administration in detail.

Sodium amytal is a synthetic drug of the barbiturate series, first prepared by Shonle and Moment (19) in 1923, and first used in animals by Page and Coryllos (20) in 1926. It is sodium iso-amylethyl-barbiturate. Its chemical structure is best represented thus :



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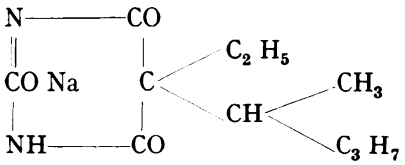
It is closely allied to nembutal (sodium-ethylmethyl-butyl-barbiturate) :



The psycho-pharmacological action of these drugs may also be similar, though nembutal would appear to be less effective in its action on catatonic stupor, according to MacMillan (21).

Stability of Solutions.

It is advisable to use the solution immediately it is prepared. Zerfas (22) has shown that when a solution of sodium amytal is left standing at room temperature, the barbituric acid ring breaks open, with the elimination of carbon dioxide, forming iso-amyl-acetyl-urea. This latter product further breaks down, forming iso-amyl-ethyl-acetamide, ammonia, and carbon dioxide.

Pharmacology.

Amytal has a shorter action than most other barbiturates, because it is rapidly broken down in the body (23). Thus Campbell and Shonle found no trace of the drug in the urine, after large doses had been given intravenously (22, quoted by Zerfas), and Broder (24) was unable to detect any of its decomposition products in the urine. Henwick (25) states that "sodium amytal is quantitatively destroyed in the body, no trace of it appearing, even in the first twelve hours. In contrast barbitone appears in the urine in from 15–20 minutes after intravenous administration in dogs".

On the other hand, Koppanyi and Krop (26) claim to have recovered 8% of a dose of amytal in the urine.

Contra-indications.

Broder (24), who used the drug in 58 cases of various psychoses, gives a long list of toxic manifestations, including convulsions, retention of urine, cyanosis, emesis, hiccough, dysphagia, headache and slurred speech. His average dose, however, was 13 gr. daily over an average period of 11 days. From my own experience I feel it safe to say that, excluding cases of marked hypertension, or hypotension, generalized arteriosclerosis and gross pulmonary or cardiac disease, the drug as used in the treatment of catatonic stupor is without danger. Care must be taken, however, when administering the drug intravenously, to inject it slowly, and in fairly dilute solutions. Zerfas and

McCallum (27), for example, state that with rapid intravenous injection there is a prompt fall of blood-pressure (30 mm. Hg., average) with prompt recovery, but add, " even hypnotic doses may paralyse the respiratory centre, if they are injected too rapidly ".

Sollman (28) gives the average drop in blood-pressure as between 50 and 70 mm. Hg., and I am inclined to accept these latter figures, since in 16 cases of my own, where the injection speed was 1 c.c. per minute, the average fall in systolic pressure, immediately after the injection, was 24 mm. Hg. Garry (29) goes so far as to say that " too rapid intravenous injection may lead to fall in blood-pressure, heart-block, ventricular fibrillation and death ".

Basal Metabolism.

Dameshek, Myerson and Loman (30) found that the intravenous administration of 1 grm. of sodium amytal in animals, caused a marked diminution in the basal metabolic rate, averaging 26%.

Temperature.

Dewel, Chambers and Milhorat (31) (quoted by Meerloo) describe a fall in temperature averaging 1° F. in animals after intravenous administration of 1 grm. of sodium amytal. Meerloo (31) states that " the barbiturates appear to have an intracerebral toxic action, to which the variations in temperature must be ascribed. They affect the temperature curve, causing an equilibration of temperature ".

Site of Action of Sodium Amytal in the Nervous System.

With one exception I can find no reference in the literature to experiments attempting to determine the site of action of sodium amytal itself, but there are several important references concerning the site of action of other related barbiturate compounds.

Masserman (32), working on cats, stated that " sodium amytal, when injected parenterally . . . in a dose of 20 to 50 mgrm. per kilogramme of body-weight caused . . . a marked diminution, or total abolition of the vegetative and emotional mimetic reactions to faradic stimulation of the hypothalamus ".

However, in another paper, published later (33), he found that after destruction of the hypothalamus by electro-coagulation, faradic stimulation of contiguous structures produced responses similar to those of the intact hypothalamus, and that sodium amytal, given parenterally, also diminished or abolished these responses. He concluded therefore, that " sodium amytal, when injected intravenously or intraperitoneally, not only modifies the

sympathetic and emotional mimetic functions of the hypothalamus, but affects corresponding functions, mediated by the perihypothalamic part of the diencephalon, and probably by other portions of the nervous system ".

Various methods of study appear to point to an infra-cortical localization of the barbiturates. Hoff and Kauders (37) found, after experimental medinal poisoning in dogs, injury of the nuclei of the medulla oblongata, of the olives, and around the sylvian aqueduct. The injury was marked by chromatolysis, tigrolysis and acute swelling.

Pick (38, 39) found that decerebration in the larger animals heightened the hypnotic action of barbiturates. He concluded that the site of action of the barbiturates lies in the brain-stem, near the thalamus, between the diencephalon and the mesencephalon, in contradistinction to that of the inhalation anæsthetics which lies in the cortex. In veronal poisoning in man, Spielmeyer and Weimann (40) mention the following changes: Cerebral toxic phenomena, tigrolysis, etc., capillary hæmorrhages as in polio-encephalitis hæmorrhagica, purpura of the brain with ring-shaped hæmorrhages, round the capillaries, especially in the mid-brain.

Van der Horst (41) found the following changes in the case of a patient, who died after she had taken 8 c.c. of somnifaine daily for 4 days: degenerative changes in the ganglion cells of the respiratory centre; in the vagus nuclei, the cerebellum, and the thalami, locally there were metachromatic degeneration products, which were absorbed by glia, round the vessels.

Koppanyi, Dille and Krop (35), however, state that " various barbiturates, given intravenously to dogs, are recoverable from every part of the central nervous system, in approximately equal concentration, and from organs, and tissue fluids". They add: 'The classification of barbiturates as thalamic hypnotics is therefore not justified." They reaffirmed these results at a later date (36).

A considerable amount of work has been done on the distribution of barbiturates in the central nervous system. No conclusive evidence has been adduced to solve this problem. The Keesers (34) gave the iron and silver salts of luminal and dial in order to study possible precipitates of these narcotics post-mortem. They found precipitates in the thalamus, and to a lesser extent in the corpus striatum, but nowhere else.

Demole (42) has contrasted the effects of directly applying hypnotic drugs, to the cerebral cortex, and to the infundibular region, and finds that medinal affects both. He believes that the susceptibility of higher animals to barbituric derivatives indicates that the cortical mechanism of sleep has undergone development in the course of evolution.

It will be seen, therefore, that though the evidence is inconclusive, the greater amount of work done favours an infracortical site of action for the barbiturates. It is important to note however, that in all the experiments cited, large narcotic or even fatal doses of barbiturates were employed.

Psycho-pharmacology.

Bleckwenn (43) in 1930 was the first to use sodium amytal in the treatment of the psychoses. Being dissatisfied with the results of other hypnotics in restless psychotic cases, and noting Zerfas and McCallum's (27) results with this drug as an intravenous anaesthetic, he commenced to use it in "acute manias and agitated mental states". In this and a subsequent paper (44) he describes the production of a short lucid period in a case of catatonic excitement to whom he had administered the drug. He states that the patient "had a period of about two minutes, during which he seemed quite normal, and discussed his illness and future plans. Following the initial period of sleep, which lasted about four hours, he again seemed quite rational for a period of two hours". In his second paper, 15 cases of catatonia were studied. Four failed to talk, but all except one took food voluntarily where tube-feeding had been formerly necessary. The lucid periods varied from 2 to 14 hours, and were produced daily, by intravenous injections of from 10 to 15 gr. of the drug. Bleckwenn aimed in each case at producing "a profound narcosis"—the lucid period following the interval of sleep. Lorenz, Lovenhart, *et al.* (45, 46) had prior to this produced similar though less prolonged lucid intervals in catatonic schizoprenics, using small intravenous doses of sodium cyanide and by carbon-dioxide-oxygen anæsthesia. They ascribed their results to stimulation of cerebral oxidative changes. Later, however, Lorenz (47) proposed another theory, stressing the effects of deep narcosis as being the important factor in the production of these temporary remissions. Bleckwenn accepted Lorenz's theory as also explaining the mode of action of sodium amytal. It is as follows (quoted from Bleckwenn) (44): "An individual develops a psychosis, following normal mental life. Assuming that this psychosis, in the case of catatonia, is at a much lower level of mental existence than the normal, and may even be a subjugation to the more primitive fœtal existence, yet it is not so deep as real unconsciousness. If at this point one precipitates a catatonic patient into unconsciousness, by the use of a narcotic or anæsthetic agent, one pierces through this level of catatonic stupor and dislodges the catatonic mechanism. Upon the return from unconsciousness induced by the drug, the catatonic patient mentally approaches the so-called normal. After he has regained this normal mental life, the various factors and stimuli responsible for his original psychosis become effective, and after a period of hours he reverts back to this more primitive level, which is apparently a more desirable refuge."

Later it was shown by Lindeman (48), and by Lindeman and Malamud (49), that similar and equally prolonged temporary remissions could be produced by intravenous doses of sodium amytal which were insufficient to cause sleep. These results would appear, therefore, to make Lorenz's theory untenable, at any rate as applied to the action of sodium amytal.

In this connection it will also be remembered that Bleckwenn's first case had a lucid period of two minutes as the narcosis was being induced.

The second attempt to explain the mode of action of this drug was made by Bancroft *et al.* (50, 51, 52) in 1931. Briefly, he suggested that in maniacal and agitated states there existed in the cells of the central nervous system a state of increased agglomeration of the colloids, whereas in catatonic states there existed a state of over-dispersion of colloid material in the cells.

He further suggested that sodium amytal promoted agglomeration of colloids in the cells, and that sodium thiocyanate promoted dispersion of colloids. He suggested that these two drugs might therefore be used for treatment and for differentiation of the two classes of psychoses, since each drug would either aggravate or improve the psychosis, according to the state of colloidal aggregation present in the cells of the central nervous system.

Several workers have administered these drugs to the two types of psychoses, but have been unable to substantiate Bancroft's theory (53, 54).

A third school puts forward the theory that sodium amytal produces temporary remissions in catatonic stupor, by virtue of its action on the brain-stem. The leading supporters of this theory are Gildea, Hubbard, Himwick and Fazekas (55). They confirm Bleckwenn's work, and adhering to the theory that the main symptoms of schizophrenia are due to "a disturbance of function, in the centres in the mid-brain which control the vegetative system", conclude on the evidence of the Keesers and of Pick that sodium amytal interrupts catatonic stupor by virtue of its "changing the activity of the brain-stem". Harris and Katz (56) support this theory.

That the arousal from stupor is not due solely to a temporary improvement in the cerebral circulation by capillary dilatation has been shown by Gildea *et al.* (55). They administered sufficient histamine to three catatonic patients to cause "a marked flushing of the face, dilatation of the pupils and a fall of 20–30 mm. Hg. in the blood-pressure" without a remission of symptoms. These same patients, at a later date, showed no response to the inhalation of 6–7% carbon dioxide administered for 20 minutes, yet subsequent intravenous administration of from ·5 to 1·5 grm. of sodium amytal produced lucid intervals, lasting from 1 to 24 hours. They further demonstrated that sodium amytal can produce marked changes in catatonic patients, with "practically no fall in pH, or rise in carbon dioxide content of arterial blood".

As far as I am aware, M. W. Thorner (17, 18) is the only worker who has attempted to show that the effect of sodium amytal on catatonic stupor may be due to its action on the cerebral cortex. He states that—"In nine patients in whom an intravenous injection of sodium amytal was halted just short of unconsciousness, we have been able to elicit Babinski responses to plantar stimulation. In none of these patients was the unusual response present before injection, and it disappeared shortly after the injection was made in all. It was reproducible, on subsequent injection, in eight". He designates the

experimentally produced remissions as "release phenomena", and explains their production as being due to "the inhibition of higher inhibitory centres."

In this connection the experiments of Wolff and Horsley Gantt (57) are of especial interest. Conditioned responses were measured according to Pavlov's technique, using the salivary reflex as the unconditioned response. The subjects were dogs, with salivary fistulæ. Small (7½ mgrm. per kg.) and large (15–30 mgrm. per kg.) doses of sodium amytal were given intraperitoneally in 10% aqueous solution. The large doses induced a prompt and relatively deep narcosis; the small doses produced a light narcosis or sleep that was of short duration. "For a few minutes after the injection the dog was overactive and gave an exaggerated salivary response to the conditioned stimuli. It then became more relaxed and lethargic, went to sleep, and gave no appreciable salivary response to any of the stimuli for about 5 hours. At the end of 10 hours the animal could be roused from its stupor, and again became overactive, passing through another period of exaggerated responses. This overactive condition persisted for several hours. About 10 hours after the dog's rousing from the lethargy, the salivary response was still increased in amount over the maximum response observed during the control period, . . . The initial increase in responses was not limited to the salivary response. The general motor overactivity was clearly apparent from the behaviour of the dog."

They therefore concluded that the reaction of the dog to sodium amytal could be divided into four phases, viz.:

(1) A phase of initial increase in conditioned responses.

(2) A phase of narcosis.

(3) A phase of recovery from narcosis.

(4) A phase of post-narcotic, or secondary increase in conditioned responses.

The similarity of these reactions to those seen in man is very striking. Sodium amytal has been used with some success to produce prolonged narcosis in many types of psychoses (58). Thorner (18), however, states that "sodium amytal fails to act as a 'sedative' to quiet an excited state in patients properly classified in this group".

Hermann (59) finds that it is often more effective than other methods, including hypnosis, in recovering the "lost" memories of psychogenic amnesic states, and it has been much vaunted in the treatment of *status epilepticus* (43, 60).

Technique of Administration.

In attempting to effect a temporary remission in catatonic stupor, workers at first aimed at producing an immediate profound narcosis, in order to obtain a lucid interval in the post-narcotic stage. For this purpose they injected from 10–15 gr. of sodium amytal intravenously in a 10% aqueous solution at the rate of 1 c.c. of solution per minute. In the cases described in this paper it was at all

times attempted to produce remission by the injection of amounts of sodium amytal insufficient to induce narcosis. With one exception (case T. S—) the dose did not exceed 7½ gr. At first, as will be observed in the case-histories, a 10% solution of the drug was used, but later the concentration was reduced to 5%, though the original injection rate of 1 c.c. per minute was maintained. During the injection the patient was continually questioned, and close observation was made of any spontaneous movements, lessening of negativism, change of expression or the appearance of tears in the eyes (often a first sign of remission). Employing a 5% solution, it was found that a remission could often be produced with less than 7½ gr. of the drug, whereas with the 10% solution there was a tendency to inject more than was necessary, and thus to produce a slight clouding of consciousness, with physical signs of intoxication (e.g., slurred speech), which marred the initial period of remission.

The actual amount injected was a matter of assessment in each individual case. As a rule the injection was stopped when any of the above signs were noted, or when the patient spoke, either spontaneously or in reply to questioning. As a rule the remission would progress from this point, without the necessity of a further injection. In those patients who exhibited no response the injection was continued until narcosis was effected.

Alcohol.

Until the publication of Thorner's paper (17, 18), the theories put forward to explain the mode of action of sodium amytal in catatonic stupor had appeared unconvincing. From clinical observation it appeared that Thorner's theory was the most likely to be correct. It will be remembered that this theory was based solely upon his clinical observations, plus his findings, as regards the change of plantar response in the pre-narcotic stage. It seemed that if it could be shown that a drug which was known to exert a depressant effect on the highest (inhibitory) levels of the nervous system could produce a similar remission in catatonic stupor, then additional evidence would have been established in support of this theory.

In 1936 Kantorovitch and Constantinovitch (61) published from Leningrad a paper on the effect of alcohol on catatonic stupor, in which they reported that alcohol given by mouth, as 40% brandy, or (in resistive cases) intravenously, as a 20% aqueous solution, caused "general disinhibition, with resumption of speech, in 7 cases out of 15", the effect lasting for several hours. In the experiments reported here the Russians' technique has been followed, but there have been no cases so resistive as to necessitate intravenous administration.

40% brandy was administered orally at the rate of 15 c.c. every 5 minutes until the patient commenced to speak, either spontaneously or in reply to questions. If he became somnolent or exhibited signs of nausea the administration was stopped.

The depressant action of alcohol on nervous tissue has been conclusively proved (62), and it has been made clear that its action on the central nervous system takes place according to the law of dissolution. That is to say it acts in inverse order to that of the phylogenetic development of the nervous system, the comparatively recently developed (and mainly inhibitory) functions of the cerebral cortex being first affected, and the older and more stable functions of the mid and hind-brains being next affected in that order (63, 64, 65, 66).

In the concluding argument the mode of action of alcohol on the central nervous system will therefore be taken as having been proven.

CASE MATERIAL.

GROUP I.

Case 1.

A. G. C. M—, single, aged 23, admitted on 16.vi.34.
Occupation: Ex-soldier.
Heredity: No history of insanity in ascendants.

Personal History.

A clever, sociable, athletic boy, top of his class at age 13. Left school at 14. From 14–15 worked as messenger for a boiler-works. At 15 joined army (Dorset Regiment). and after serving at home 2 years was sent to Germany and stationed at Wiesbaden and at Cologne from age 17 until 19. He was then transferred to India, where he served for 4 years. Rank: Private.

Pre-psychotic Personality.

He was described as being sensitive, quick-tempered, excitable; he talked rapidly, drumming with his fingers on the table. Was " always going out of his way to seek a fight ". Yet he was described as " on the whole good-natured, rather reserved, and very fond of music ". Unlike the rest of the family he was gifted in this direction, and " played the piano, violin, flute, mandoline and drums ".

His mother states that she found she had to treat him differently from the other members of the family. He could not be brusquely told to give a hand with the work at home, as he would then obstinately refuse, but if spoken to more gently would try to be helpful. He was a keen amateur boxer.

History of Present Illness.

When in India his letters home had been cheerful, and the first intimation of any change was when his relatives received a letter from the authorities stating that he had been transferred home to Netley Hospital, because of " dullness and lack of interest ". On 6.vi.34 they were given the option of receiving him home on their own responsibility. They did so, but soon realized that he was mentally ill. When he first saw his mother he cried and stated that he had " been done out of promotion ". He was restless, excited, and would not talk of anything else. He brooded, stared at objects for a long time, muttered to himself and held his hands to his ears. A few days later he became worse, chased his relatives with a knife, injured the cat, and accused his mother of being " in the Secret Service and against him ". He was transferred to an observation ward on 12.vi.34, and admitted to West Park Hospital on 16.vi.34.

On admission: *Physical state:* Nothing abnormal detected. *Serum Wassermann:* Negative. *Mental state:* " He lies in bed completely disinterested in his

environment. He does not speak spontaneously. When questioned, he states that his mind is a blank. In spite of this, however, he can answer questions relevantly and give a fair account of himself."

The following abstracts of notes indicate his progress in hospital:

30.vi.34: He is now inaccessible. He sits with his head and eyes turned towards the ceiling, his face expressionless. Answers "Yes" to every question asked. He is unco-operative, and has to be prompted to eat his food.

17.v.35: He is detached from his environment to an extreme degree, and is quite inaccessible. He is unemployable, no reply can be elicited to questioning, and he spends the day alternately pacing up and down in soldier fashion, and adopting fixed attitudes.

25.vii.35: Impulsively struck another patient to-day.

15.xii.35: He remains mute, but will work mechanically at simple tasks. He requires supervision with his dressing, washing and eating.

5.iv.36: Attacked a nurse to-day.

16.v.36: Is now unemployable, mute and inaccessible.

From 11.iii.37 until 6.iv.37: Records of impulsive, restless behaviour; striking out at other patients.

16.vi.37: Now stands like a statue all day, unless moved. Incontinent of urine and fæces. Requires hand-feeding.

Reaction to Sodium Amytal.

On 3.ix.37, 8 c.c. of 5% sodium amytal was injected intravenously. As the last cubic centimetre of the drug was being injected he commenced to weep softly, and ceased struggling with the nurses, who had up to that moment been forced to hold him down on the bed. He immediately commenced to soliloquize on his life prior to admission to hospital. At first he did not appear to be addressing his remarks to anyone in particular, but later on he addressed me personally. A sample of his speech was as follows: "I'm happy when I'm alone—I'm happy when I'm looking at things—I've never done a thing in my life—I like working when I'm alone—I'm no good—I'm insane, ain't I?—They called names after me in the army, because I like being alone." He complained of hunger, and ate six thick slices of bread and butter so voraciously that it was deemed inadvisable to give him more at the moment though he asked for it. He answered questions promptly and relevantly, and showed a good memory for events prior to his admission to hospital. Of his coming to West Park or of his life in the hospital since that time he appeared to have little knowledge. He admitted that he had been mute and resistive up to this moment, but did not offer any explanation for this. Of his usual reluctance to eat, however, he said, "I want to eat, but I can't". He looked at the beds around him and expressed a wish to do dormitory work. On being questioned, he said that he would never get better. He stated that I appeared familiar to him, and that he thought he had once met me "in a chemist's shop in the Queen's Road". The most recent incident he appeared to remember was when he was taken from his home to the observation ward in June, 1934. He could not give any idea of the present date, nor where he was now living. He was very polite, rather apologetic in manner, and co-operative, dressing himself, etc., quickly and neatly. He remained in this state for 3 hours, until he went to sleep (at bed-time). The following morning he had reverted to his former negativistic, mute and inaccessible condition. There was at no time any physical evidence of intoxication (ataxia, slurred speech).

Reaction to Cardiazol.

From 20.x.37 until 21.xii.37 he received 20 injections of 10% cardiazol. Treatment had then to be postponed owing to extensive thrombosis of all visible veins in both arms, but was again resumed on 13.iv.38. Unfortunately his resistance became so great (he is a very powerful man) that even with the assistance

of 8 nurses and a preliminary injection of morphia gr. ¼ and hyoscine gr. $\frac{1}{100}$, it was found impossible to continue the injections. These had again to be stopped on 14.v.38 after a further 8 injections. The results are tabulated below:

Date.	Dose in c.c.	Duration of time in seconds from completion of injection to onset of fit.	Duration of fit in seconds.	No. of fit.
20.x.37	5	Not recorded	75	1
22.x.37	5	Anxiety state	..	..
23.x.37	6	Not recorded	120	2
25.x.37	7	Anxiety state	..	..
26.x.37	8	Not recorded	150	3
29.x.37	8	10	42	4
31.x.37	8	No reaction	..	..
2 mins. later	5	Anxiety state (spoke spontaneously, saying " I am full up—I don't want any more ")	..	..
mins. later	5	Anxiety state	..	..
3.xi.37	5	No reaction	..	..
2 mins. later	5	Anxiety state	..	..
2 ,, ,,	7	Not recorded	60	5
6.xi.37	6	Anxiety state	..	..
2 mins. later	7	No reaction	..	..
9.xi.37	7	,,	..	..
13.xi.37	8	Not recorded	40	6
20.xi.37	8	25	45	7
13.xii.37	8	No reaction	..	..
21.xii.37	5	,,	..	..
2 mins. later	5	18	37	8

SECOND COURSE.

Date.	Dose in c.c.	Duration of time in seconds from completion of injection to onset of fit.	Duration of fit in seconds.	No. of fit.
13.iv.38	5	40	78	1
15.iv.38	5	No reaction	..	..
2 mins. later	5	111	145	2
18.iv.38	5	No reaction	..	..
2 mins. later	5	,,	..	..
2 ,, ,,	7	,,	..	..
20.iv.38	7	,,	..	..
2 mins. later	7	,,	..	..
2 ,, ,,	5	Not recorded	Not recorded	3
23.iv.38	10	15	52	4
25.iv.38	10	No reaction	..	..
12.v.38	10	17	59	5
14.v.38	10	No reaction	..	..

From the commencement of cardiazol treatment he became apprehensive, though he still assumed fixed attitudes and was practically mute. He did, however, dress himself, and would eat without prompting. On each occasion before injection time, holding himself stiffly " to attention " as usual, he would gradually move to the furthest end of the ward by a process of almost imperceptible sideways shuffling of his feet. When approached by the nurses, in order to put him to bed, he would put up a tremendous struggle, exhibiting great strength. The general impression

was gained that he would have shown more improvement could the treatment have been continued.

After cessation of treatment he again required attention to induce him to eat.

Reaction to Alcohol.

On 10.x.38, 40% brandy was given orally at the rate of 15 c.c. per 5 minutes. He would not enter the dormitory, putting up a severe struggle when it was attempted to lead him in, but stood at the door gazing vacantly ahead, and taking the brandy automatically as it was offered to him. He remained thus, mute and inaccessible, until he had consumed 270 c.c. He then addressed the nurse standing near him and asked if he " might walk around a little ". On receiving permission to do so, he walked slowly half-way down the ward and back again. He then sat down on a chair, first looking at the floor and then at those around him. His facial expression lost its usual immobility, and he appeared interested in his surroundings. He commenced to talk in a disconnected and rambling manner. It was difficult to interrupt his flow of speech or to gain his attention. After a few minutes he appeared to become aware that I was addressing him. He gave his present age correctly, stated that he had been 7 years in the army, etc., in reply to questions. I offered him a cigarette (his first for over 4 years), which he accepted, saying, " You don't mind me smoking, do you ? " I then looked at my watch; he looked at it and said, " I've never had a watch—I've never had nothing ". He repeatedly asked for " a piece of chocolate—some ice-cream, please—I'm hungry and thirsty ". He pointed to the green linoleum on the floor, and said, " Green is green—I'm green ". He stretched out his hand in a hesitant fashion, and touched my trousers, saying, " You don't mind me touching this? " He made unintelligible remarks such as, " My mothers me ", and " They may have thought I took a rise out of them in the dance hall, but I didn't ". When questioned on these remarks he did not reply. Given a broom he swept the floor industriously for 15 minutes. He was then put to bed. He showed no slurring of speech, but on one occasion on suddenly standing up he became slightly ataxic. Questioned an hour later he was found to have become mute and negativistic.

CASE 2.

J. B—, single, aged 28 on admission on 22.vii.35.

History.

School: Reached standard 7 at 14 years. Had worked as a machine winder since leaving school, until 14.ii.35. He was described as having always been " timid and reserved ". The first change in his personality was observed in November, 1934. At that time he complained of pains in his stomach, and consulted several doctors about it, but could get no satisfaction. He commenced to stare at his image in mirrors for long periods, and at length became very depressed, stating that he was " a married man " and was going to commit suicide. (One sibling is a chronic alcoholic).

Eventually he was admitted to the Maudsley Hospital as a voluntary patient on 14.ii.35. There he was described as being depressed and nervous, with vague delusions that he was " under the influence of others ". On 22.vii.35 he was certified insane and transferred to West Park Hospital.

On admission: *Physical state:* Nothing abnormal detected. *Serum Wassermann.* Negative. *Mental state:* " He is aimlessly restless, will not sit down, and refuses to answer questions, but repeats monotonously, ' Give me my clothes, I want to go home '. Hand-feeding is at present necessary, and he resists attentions of every kind."

The following abstracts of notes indicate his progress in hospital:—

22.ix.35: He remains negativistic and will not reply to questions, but repeats " Can I get into a main road—I want to go home ". He is continually making efforts to escape.

22.xi.35: He remains agitated, wanders about aimlessly, but shows no interest in events around him.

22.xii.35: He is in a state of semi-stupor, but at times becomes restless. He states that voices tell him "to go away". Practically inaccessible. He cannot be employed.

22.i.36: He is negativistic. It requires much effort to extract even a few replies from him. He tears his shirt, picks his skin, and is occasionally incontinent of urine.

22.v.36: He is now quite inaccessible, pays no attention to the environment, but mutters unintelligibly to himself.

20.vi.36: His lips continually move but produce no sound; he requires to be hand-fed and resists every attention.

22.i.37: He remains mute. He makes weird facial grimaces, and draws air in through his incisor teeth making a whistling noise. He is now frequently incontinent. Cannot be employed.

Reaction to Cardiazol.

A course of injections of 10% cardiazol was given as tabulated below:

Date.	Dose in c.c.	Duration of time in seconds from completion of injection to onset of fit.	Duration of fit in seconds.	No. of fit.
4.iii.38	5	20	65	1
7.iii.38	5	20	67	2
9.iii.38	5	15	20	3
11.iii.38	5	18	45	4
14.iii.38	5	23	70	5
16.iii.38	5	18	52	6
18.iii.38	5	15	75	7
21.iii.38	5	20	50	8
23.iii.38	5	35	75	9
25.iii.38	5	No reaction	..	..
2 mins. later	5	35	75	10
28.iii.38	6	12	45	11
30.iii.38	6	30	60	12
1.iv.38	6	No reaction	..	..
2 mins. later	5	,,	..	..
2 ,, ,,	5	16	48	13
4.iv.38	7	31	81	14
6.iv.38	7	15	60	15
9.iv.38	7	15	73	16
11.iv.38	7	16	54	17
13.iv.38	7	10	56	18
15.iv.38	7	24	70	19
18.iv.38	7	22	72	20
20.iv.38	7	No reaction	..	..
2 mins. later	5	15	20	21
23.iv.38	8	19	56	22
25.iv.38	8	17	45	23
27.iv.38	8	No reaction	..	..
2 mins. later	5	18	52	24
30.iv.38	9	16	65	25
2.v.38	10	12	55	26
4.v.38	10	20	35	27
7.v.38	10	11	56	28
10.v.38	10	11	72	29

25.vii.38: Following the course of injections he has commenced to work fairly well in the ward, is no longer incontinent, eats well, and attends to his dressing and

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toilet, without the prompting which was formerly necessary. He is also no longer mute, but will only reply in monosyllables. Will only say a few words at a time, and shows marked blocking of thought. He appears mildly confused and agitated, and his face becomes contorted when he speaks. He cannot state the name of the hospital, gives the date as 1932, and is unable to state how long he has been here. He appears to have no insight into his mental state, and cannot even hazard a guess as to the reason for his having had the cardiazol injections.

Reaction to Sodium Amytal.

On 30.v.38 he received 8 c.c. of 5% sodium amytal intravenously. Before the injection he was more " tongue-tied " than usual, opening and closing his mouth, wrinkling his forehead, and blinking his eyes, as if in a desperate attempt to speak. As a rule, since his course of cardiazol he had succeeded in doing so, but to-day he failed. He appeared nervous at the commencement of the injection, perhaps thinking that it was cardiazol, but soon became quiet. When 5 c.c. had been injected his lips commenced to move rapidly, appearing to form words, but produced no sound. When 8 c.c. had been given he suddenly " found his voice ", and it was then observed that he had been trying to tell the nurse standing beside him, that he (the patient) had once before been in another ward in his charge (correct). On being questioned he stated that he was still in the Maudsley Hospital. When asked if he knew the names of the nurses around him, he stated that he knew them all and proceeded to name them entirely incorrectly. He stuck resolutely to his misidentifications. He showed marked dilapidation of thought and gave evidence of being hallucinated, stating that a Mr. Burger had shouted down to him from an aeroplane that very morning as he was walking in the garden and had said, " Your time will be up on July 28th ". On the whole deterioration was much more marked than had been thought from his conduct since having cardiazol, his answers being so scanty before that it had been difficult to form a judgment. He talked freely in this manner for an hour, showing only a faint trace of his former grimacing, and none of his usual agitation. He appeared alert and interested. He showed no physical signs of intoxication.

From this date he spoke less and less and by 28.vi.38 became mute, though he continued to work and attend to his own dressing, etc. By October, 1938, he scarcely worked at all, and required prompting to attend to himself; he had practically drifted back to his pre-cardiazol state.

Reaction to Alcohol.

On 19.x.38 he received by mouth 405 c.c. of 40% brandy at the rate of 15 c.c. per 5 minutes. He became progressively drowsy, finally showed signs of nausea, and fell asleep. One hour later on being awakened, he mumbled indistinctly the words, " St. Giles' Hospital—five hundred pounds ". He did not reply to questions.

CASE 3.

K. B—, single, aged 27 on admission on 11.v.37.

Occupation: " Gemologist."

Heredity: Father became insane following a head injury and is in a mental hospital.

Previous History.

Intelligent at school, and described as being a cheerful boy. After leaving school he became a shop assistant in a jewellery establishment, studied hard, and became a Fellow of the Institute of Gemology. He left home in 1931 to take up work in London, and except for short holidays had not been home since that date. His personality appeared normal until 1936. During this year he became engaged to be married, but his fiancée postponed the marriage on three occasions (her mother being opposed to the " match "). His mother states that when he came

home on holiday after the first postponement of his marriage he appeared very "moody and depressed", and stated that the affair "preyed on his mind". On 24.iii.37 he was admitted to St. Ebba's Hospital as a voluntary patient. There he was described as being depressed, and unwilling to discuss his illness. He gave in his notice of discharge on 4.v.37, but being considered unfit to leave hospital, he was transferred to an observation ward, later certified and admitted to West Park Hospital on 11.v.37.

On admission: *Physical state:* Nothing abnormal detected. *Serum Wassermann:* Negative. *Mental state:* "He appears dull and uninterested. He lies in bed staring fixedly ahead, gives short non-committal replies to questions. He is correctly orientated and attends to his personal requirements, but expresses no wishes".

The following abstracts of notes indicate his progress in hospital:

25.v.37: He is almost inaccessible; occasionally for a moment he will rouse nimself and complain of his detention and request his discharge. He will not, however, enter into conversation on this subject. He puts up a passive resistance to ordinary nursing attention.

11.x.37: Is still stuporous but a little more communicative. He states that he cannot understand what sort of place he is in, or why he is here, and that he knows he is "needed in some other sphere". He knows vaguely about some "deep service to the country" which he has rendered. Is still resistive to attention, for example, has to be literally dragged to the table, or to the clinical room. Left alone, he slouches about, his hands in his pockets, his head bowed. He refuses to employ himself in any fashion.

11.xii.37: Has recently made a few feeble attempts to escape.

11.i.38: As a rule he remains mute when questioned, but sometimes "flares up" and asserts that he is "quite fit to work outside". Still unemployed, untidy in dress and disinterested in events around him.

Reaction to Cardiazol.

A course of injections of 10% cardiazol was given as tabulated below:

Date.	Dose in c.c.	Duration of time in seconds from completion of injection to onset of fit.	Duration of fit in seconds.	No. of fit.
7.ii.38	5	28	58	1
9.ii.38	5	20	64	2
11.ii.38	5	No reaction	..	..
2 mins. later	2	120	70	3
14.ii.38	7	14	57	4
16.ii.38	7	21	65	5
18.ii.38	7	25	76	6
21.ii.38	7	23	75	7
23.ii.38	7	23	48	8
25.ii.38	7	No reaction	..	..
2 mins. later	5	16	56	9
28.ii.38	9	14	58	10
2.iii.38	9	25	83	11
4.iii.38	9	20	70	12
7.iii.38	9	22	77	13
9.iii.38	9	20	60	14
11.iii.38	9	14	55	15
14.iii.38	9	17	55	16
16.iii.38	9	27	70	17
18.iii.38	9	20	65	18
21.iii.38	9	15	50	19
23.iii.38	9	20	55	20
25.iii.38	9	20	56	21

Following the course he showed no change. During the course he showed surprising vigour of speech and action, in attempting to prove to us that it was harming him; he was frequently confused and restless, and often stated that he was being poisoned. This over-active, paranoid state was in marked contrast to his former apathy, and comparative inaccessibility. At the completion of treatment he quickly relapsed into his former apathetic state, but for a few weeks consented to lay the ward tables, the first work of any kind that he had done since admission.

Reaction to Sodium Amytal.

On 3.vi.38 he received 6 c.c. of 5% sodium amytal intravenously. Before this injection he could not be persuaded to talk, but hung his head in his usual dull manner. During the injection he shivered slightly, and on being questioned replied that he felt cold; the injection was therefore stopped at this point (6 c.c.), though the amount appeared insufficient. Immediately following the injection he spoke spontaneously, and commenced to argue with considerable gusto about the illegality of his detention. He was illogical, and would not agree that his present lethargy would persist if he were discharged. He stated that the patients here " got on his nerves ", and that he would never be fit until he left the hospital. He kept to this topic and would discuss nothing else. Shortly afterwards he became mute and unresponsive.

Reaction to Alcohol.

On 9.vi.38 he received 285 c.c. of 40% brandy at the rate of 15 c.c. per 5 minutes. Until the total amount had been administered he remained practically mute, though he occasionally whispered unintelligibly. A few minutes after receiving the last 15 c.c. he commenced to talk freely, but in his usual uncommunicative manner, chiefly asking for his release, demanding to know the reasons for his detention here, etc. Later, however, he became less paranoid and answered a few questions on other matters. He was fairly orientated for time, stating that he had been here " about two years ". He said that he could not recollect where he had last worked, but thought it was " somewhere near the sea ". This gross amnesia had been hitherto quite unsuspected, it being thought that his refusal to speak of his past life had been due either to his intense apathy or to his paranoid attitude, rather than to any memory defect. There seems little doubt now that he has gross amnesia for events prior to his detention, since dis-inhibition was marked at the moment he made the statement. His speech was slurred, his movements incoordinated, and he laughed uproariously at any joke, however feeble. This was the first time he had laughed since admission. Once he interrupted the conversation and turning to the nurse at the bedside, said " Yes, I should like to be a dance instructor ". When asked what had prompted him to make this remark, he replied that the nurse had just asked the question. This was not so, and thus demonstrated, for the first time, unequivocal evidence of hallucinations. In an attempt to revive his memory I asked him frequently about the science of gemology. He turned at last to me and said in a petulant voice, " What is gemology, anyway ? "

CASE 4.

C. D. G—, single, aged 23 on admission on 27.xii.34.

Heredity: Father doubts his son's paternity.

Father: Social worker describes him as " dissipated, flirtatious type ".

Mother died 10 years ago of " cancer ". Was a sociable stupid woman, who was convicted of keeping a " disorderly house " during the war. Little known of her relatives. Her own paternity is said to be in doubt. One maternal aunt was a mental defective; patient had three siblings all alive and well.

Previous History.

All the children were transferred to the Bisley Homes for Children in 1914, the time of their mother's conviction. Patient was later transferred to the "Arethusa" Training Ship, after which he returned to live with his mother (aged 16). When visited in the Homes he was described as shy, aloof, suspicious, and "not friendly with anyone". No information could be obtained from the period when he went back to his mother and when he was admitted to St. Ebba's Hospital as a certified patient.

Occupation: Barman.

When at St. Ebba's he was described as being "mute, inaccessible, manneristic, incontinent of urine, and frequently attacking other patients". Occasionally he would speak, saying that voices called him a "Nancy boy" and told him that he was incapable of sexual intercourse. He once attempted suicide by strangulation with a belt.

On admission: *Physical state:* Nothing abnormal detected. *Serum Wassermann:* Negative. *Mental state:* He was often mute when questioned, and when he did reply his answers were totally incoherent. He was dull, absorbed in phantasy, and indifferent to his surroundings. He was transferred to an "acute" ward due to frequently smashing windows. He would remain motionless for hours at a stretch, was incontinent, destructive to his clothing, attempted to eat rubbish, picked his skin and rubbed his head repeatedly, producing a bald patch. From 26.vi.37 he was completely mute.

Reaction to Sodium Amytal.

On 7.iv.38, 5 c.c. of 10% sodium amytal was given intravenously. His expression immediately became markedly elated, and mutism gave place to rapid spontaneous disconnected speech (not addressed to anyone present) and meaningless laughter. His speech was a mere word salad, composed principally of nouns. This state persisted for about 2 hours, when he reverted to his former condition.

Reaction to Alcohol.

On 29.x.38 an attempt was made to determine his reaction to alcohol; since July, 1938, he had been mute, stuporous and inaccessible, incontinent and completely out of touch with his environment. 15 c.c. of 40% brandy was administered by mouth every 5 minutes. He showed no obvious change until he had consumed 195 c.c., when his facial expression changed from its usual dull character to one of marked vivacity. He did not at first speak unless addressed, but after a few minutes spoke spontaneously every few seconds in unfinished incoherent sentences. He continued in this manner for over an hour, alternatively laughing uproariously and staring blankly before him.

Questions and answers were as follows:

Q. "What is your name?" *A.* "Napoleon."

Q. Repeated. *A.* "Death."

Q. "What is the name of this place?" *A.* "Brookwood Lunatic Asylum."

Q. "What time is it?" *A.* "Thirteen eggs a dozen."

Q. "What year is it?" *A.* "1930"—"I could do with something to eat though."

Q. "What would you like to eat?" *A.* "A Christmas pudding."

Q. "What time is it?" *A.* "Time to get out."

Q. "What day is it?" *A.* "Well, real thorough—Well, fancy a man doing that!"

A halfpenny was exhibited.

Q. "What is this?" *A.* "How much money is this? Well a penny."

Q. "What day is it?" *A.* "December the fourteenth."

A sample of spontaneous speech was as follows:

" Where were you blown to bits—Where were you sleeping—Precious blood of Christ—There you are—Someone put it into my head to jump off the River Tilbury—I don't want any doctors mucking about with me—meat—we never were—wearing out—No laughing—No laughing—Who do you think will win the Oaks?—aeroplane—Zeppelin—Blown to pieces—I've eaten an apple—Or did the apple eat me?—Had he been hit across the head though—funny—I was eaten—he was eaten—Blood—What is blood?"

He was given in all 270 c.c. of brandy. The state of apparent exhilaration produced took several hours to vanish completely. He was a little ataxic but no slurring of speech was evident. He swept the floor when commanded, but showed a little inco-ordination of movement.

Reaction to Cardiazol.

A course of injections of 10% aqueous solution of cardiazol was given as tabulated below:

Date.	Dose in c.c.	Duration of time in seconds from completion of injection to onset of fit.	Duration of fit in seconds.	No. of fit.
15.iv.38	5	22	74	1
18.iv.38	5	68	118	2
20.iv.38	5	25	28 "*petit mal*"	3
2 mins. later	5	20	60	4
23.iv.38	6	15	62	5
25.iv.38	6	85	147	6
27.iv.38	6	No reaction	..	..
2 mins. later	5	..	Not recorded, major fit	7
	Not recorded			
30.iv.38	7	56	101	8
2.v.38	7	28	66	9
4.v.38	7	18	68	10
7.v.38	7	90	138	11
10.v.38	7	No reaction	..	..
2 mins. later	5	,,	..	..
2 ,, ,,	5	74	109	12
12.v.38	9	25	100	13
14.v.38	9	17	58	14
19.v.38	9	18	72	15
21.v.38	9	25	72	16
23.v.38	9	No reaction	..	..
2 mins. later	5	,,	..	..
2 ,, ,,	3	,,	..	..
2 ,, ,,	3	45	95	17
25.v.38	10	18	Not recorded, "Petit mal"	18
29.v.38	11	18	73	19
2.vi.38	11	18	76	20
4.vi.38	11	No reaction	..	..
6.vi.38	11	10	62	21

During the course of injections and for about 2 weeks after the completion of the course he ceased to be mute, but his speech was totally disconnected and unintelligible. For several weeks afterwards he became over-active, often to an extreme degree, in striking contrast to his former state of inertia. Often he would rush down the ward striking out at other patients and at meal-times he was observed to eat his food ravenously. He later reverted to his mute and stuporous state. During the fits forward dislocation of the jaw occurred and required reduction.

CASE 5.

F. E. B—, married, aged 34 on admission on 2.ii.37.

Occupation: Coal hawker.

Heredity: No history of insanity (or epilepsy) in ascendants, but father is a chronic alcoholic.

Previous History.

Was a sociable boy, keen at games, and reached top standard before leaving school. At 16 he fell 30 ft. from a tree, and was admitted to King's College Hospital suffering from "concussion". The notes on his case were apparently not obtainable, but it was stated that a right sub-temporal decompression operation had been performed and that he had been discharged "recovered"—after 5 weeks. He returned to work 5 months after this accident. He was described by his wife as "the best of husbands and an excellent partner; always easy-going; never took offence, was cheerful and had a keen sense of humour". He was a teetotaler, and though sociable preferred to stay at home with his two children, his wife and domestic pets, of which he was very fond. In January, 1937, he had been working up to the day before his admission to the observation ward, on 26.i.37. He had gone to bed on 25.i.37 and had complained of feeling unwell. He shortly afterwards became confused, and talked incoherently; a doctor was summoned and diagnosed influenza, finding that he had a "high temperature". On admission to the observation ward he was very restless, talked incoherently about "the King and the League of Nations", and made a homicidal attack on the night nurse. His temperature remained elevated for a few days in the observation ward, but the reason for it remained obscure. His physical condition rapidly improved, but mentally he became stuporous, mute, and comprehension appeared defective.

On admission: *Physical state:* Nothing abnormal was detected beyond slight albuminuria. *Serum Wassermann:* Negative. *Nervous system* appeared normal. *Mental state:* "He is stuporous and inaccessible. He lies in bed, staring vacantly at the ceiling, and pays no heed to questions or commands. He is incontinent of urine, and requires persuasion to take his food, having to be hand-fed. Shortly after admission he attacked a nurse without warning. He sometimes adopts an attitude as if listening to something."

The following abstracts of notes indicate his progress in hospital:

23.ii.37: He lounges about, staring vacantly ahead, hands in pockets. When spoken to, he grins foolishly, but does not look at the speaker.

2.vii.37: When questioned to-day, made a few totally irrelevant remarks, such as: "Happy-go-lucky", and "To repeat quicker in a certain species".

2.x.37: Now stands in one position, unless moved. Completely inaccessible and mute.

Reaction to Cardiazol.

A course of injections of 10% cardiazol was given as tabulated below:

Date.	Dose in c.c.	Duration of time in seconds from completion of injection to onset of fit.	Duration of fit in seconds.	No. of fit.
7.xii.37	5	20	65	1, 2
10.xii.37	5	No reaction	..	..
4 hours later	5	13	50	3, 4, 5, 6
13.xii.37	5	No reaction	..	..
2 mins. later	5	30	55	7
16.xii.37	6	No reaction	..	..
2 mins. later	6	27	52	8, 9, 10, 11, 12, 13, 14, 15

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On receiving his first injection of cardiazol he had a major fit, followed, without recovering consciousness, by a second fit 3 minutes later. His third injection (on 10.xii.37) produced 4 fits in successsion. He appeared ill for the remainder of the day and his temperature rose to 101·4° F. at 7 p.m. The following day he had recovered. After the seventh injection he had 8 major fits, spread over 2½ hours. Afterwards on recovering consciousness he became maniacal, and required seclusion in the P.R. over-night, in addition to an injection of morphine gr. ¼, hyoscine gr. $\frac{1}{100}$. On the following morning he had apparently recovered. That is to say he was again mute, stuporous and appeared to be physically well. Immediately after recovering from the fits induced by the first injection he spoke spontaneously, expressing a desire to work; a few minutes later he said that he felt ill. He then relapsed into his former mute state.

On account of this reaction it was considered justifiable to try another injection, commencing with a sub-minimal dose in view of his apparent susceptibility to cardiazol. On 4.v.38, therefore, 4 c.c. of 10% cardiazol was injected intravenously. After an interval of 59 seconds a major fit commenced, lasting 119 seconds. The fit commenced at 12.15 p.m., and was followed without any intervening period of consciousness by 13 major fits. The times of commencement of these fits were as follows: 2nd at 12.22 p.m. 3rd at 12.35 p.m. 4th at 12.42 p.m. 5th at 12.46 p.m. 6th at 12.49 p.m. 7th at 12.52 p.m. 8th at 12.56 p.m. 9th at 1.5 p.m. 10th at 1.15 p.m. 11th at 1.18 p.m. 12th at 1.23 p.m. 13th at 1.29 p.m.

Paraldehyde 4 drm. in 4 oz. olive oil was then administered rectally by funnel and tube at 1.45 p.m. 14th fit occurred at 2.13 p.m. At the commencement of each fit the right angle of the mouth twitched before the tonic spasm commenced; this twitching of the mouth lasted on each occasion about 30 seconds. The tonic spasm which followed was accompanied by conjugate deviation of the head and eyes to the left, and by extension of the arms at the elbows and wrists. The legs were also extended. The characteristic opening of the jaw in cardiazol fits only occurred in this case during the first fit, the jaw subsequently remaining closed. The pupils were moderate in size and immobile. Plantar responses were inactive. The left knee-jerk was noticeably brisker than the right. The patient remained unconscious until 9 p.m., when he could be roused with difficulty. He appeared well on the following morning, and re-examination of the nervous system revealed nothing abnormal. His temperature rose after the fits to 100° F. at 6 p.m., but returned to normal at 6 a.m. on the following morning and did not again rise. On the morning following the injection he spoke spontaneously, and again asked for some work to do, " as I am tired of standing about doing nothing ". His manner was abstracted, but he answered a few simple questions correctly, viz., his name, age, address, former wages, etc. He was given some work (ruling lines in a book), but although he held the pencil, did not attempt it. He spoke up to 48 hours after the injection, but at no time did he show any real interest in his surroundings, and he was completely unaware of time or place. Within 48 hours he had drifted back to complete mutism.

Reaction to Sodium Amytal.

On 7.iv.38, 5 c.c. of 5% sodium amytal was administered intravenously. He spoke a few words spontaneously but more freely when questioned. He yawned and appeared sleepy. He said spontaneously, " I must be doing something. I had better be doing something ". When asked what he wished to do he replied "Anything you want me to ". His reaction time to questions was slow, marked apathy was evident, and though he answered questions correctly about his home life, did so without any sign of interest. His replies were short but usually relevant. His answers gradually became shorter and difficult to elicit, and within three-quarters of an hour of giving the injection he would rarely answer a question. Neither his speech nor his movements gave any evidence of intoxication.

A note made on 2.vi.38 showed his condition to be little changed: " He is still inaccessible and mute. He obeys commands in a hesitant manner and sometimes

does not complete a movement which he initiates. Sometimes his lips will frame a word, but he gets no further than this. He sits or stands in one position all day, his hands always in his pockets, turning his head slowly from side to side and often grinning foolishly. He will now eat without prompting, but is still incontinent of urine."

Reaction to Alcohol.

On 28.vi.38, 300 c.c. of 40% brandy was given orally at the rate of 15 c.c. every 5 minutes. He showed much distaste for it, but drank it each time on command, holding the glass himself. Towards the end of the administration he became ataxic, but he spoke a little, showing much characteristic slurring of speech. He answered a few questions about his past life, correctly, but did not speak spontaneously. He quickly became somnolent, so that his lucid phase lasted only about 7 minutes. He was much less accessible than when under the influence of sodium amytal.

CASE 6.

W. J. R—, single, aged 19 on admission 17.xii.34.

Occupation: G.P.O. storekeeper and sorter. No insanity in ascendants. Two brothers and two sisters alive and well.

Previous History.

Said to have been "dull" at school, and left from standard V at 14. Worked in G.P.O. until 16, when he gave in his notice in order to "go on the stage". He had always wished to be an actor (his two sisters were "on the stage"), and had done a little amateur work in this direction. He failed to realize his ambitions, and did not again find employment. He became depressed at home (he had always been described as being moody, with fits of temper), his temper became worse, and at 17, in an ungovernable fit of rage he cut up his sister's trousseau and smashed furniture. He was admitted to an observation ward, but was discharged within 14 days. After this he steadily deteriorated, did not trouble to look for work, and for long periods at a time would not speak to his family. He did not sleep at night, lay on his bed most of the day, and became increasingly difficult with his food. Eventually he was admitted on 17.xii.34, aged 19, having refused food for the previous 4 days.

On admission: *Physical state:* Nothing abnormal detected, apart from signs of inanition. *Serum Wassermann:* Negative. *Mental state:* "He is lacking in urge and initiative. He never speaks spontaneously, but answers questions when these are constantly repeated. He can give a good account of his past life, but only with much stimulation. When left alone he falls into a stuporous condition. He appears to realize that he is ill, and states that he had a "breakdown" at 17 years of age. He only eats when prompted, and has to be washed and dressed".

From his admission he appeared to become more and more stuporous, and by 17.vi.35 he was completely mute, but had become automatically obedient, so that he would work mechanically with constant prompting, and would dress, wash, etc., as long as each movement required was preceded by an order. He appeared completely disinterested in his surroundings, Flexibilitas cerea was present. By 16.xi.36 he was unemployed, incontinent and required hand-feeding. As regards single commands he was still automatically obedient.

Reaction to Sodium Amytal.

On 2.ix.37, 5 c.c. of 10% sodium amytal was administered intravenously at the rate of 1 c.c. per minute. No mental change was observed except slight drowsiness, and at first, after 2 c.c., a facial expression of anxiety. He remained mute, however, and his "flexibilitas cerea" was unaffected.

Reaction to Alcohol.

On 3.vi.38, 400 c.c. of 40% brandy was administered orally at the rate of 15 c.c. per five minures. He showed no change except increasing drowsiness, and when left alone, fell asleep. Flexibilitas cerea remained present.

Reaction to Cardiazol.

Cardiazol treatment was commenced on 13.vi.38. Previous to this 4 attempts had been made (over a period of two weeks) to X-ray his lungs. On each occasion, however, on seeing the X-ray apparatus, he had struggled violently with his nurses in an attempt to escape. It was therefore impossible to obtain a picture of his lung condition. This had been the only evidence on the patient's part of resistance, and indeed of interest in his environment to date. Physical examination had revealed no abnormality. It was resolved, therefore, to proceed with cardiazol, but to make daily observations of the blood sedimentation-rate. Cardiazol was given as tabulated below:

Date.	Dose in c.c.	Duration of time in seconds from completion of injection to onset of fit.	Duration of fit in seconds.	No. of fit.
13.vi.38	4	Anxiety attack	..	..
14.vi.38	5	18	75	1
16.vi.38	5	32	80	2
18.vi.38	5	No reaction	..	..
2 mins. later	5	,,	..	..

On 20.vi.38 the sedimentation-rate was noted to be above normal (15 mm. per hour, Westergren) and no injection was given. He was kept in bed for observation. On 23.vi.38 his temperature (axillary) rose to 99.4° F. Treatment was discontinued, and sanatorium treatment instituted. In the ensuing months, clinical examination and repeated bacteriological investigation of fæces failed to reveal the evidence of any tuberculosis, though intermittent rises of temperature, never more than 99·6° F., occurred. He is now (6.xi.38) ambulant and practically apyrexial. At first he lost a few pounds in weight, but at no time had he any cough, sputum, night sweats, etc. It was concluded that a tuberculous focus had been reactivated as in case E. B. H—, but that the use of the sedimentometer limited the amount of reactivation in the latter case. Immediately following the first cardiazol injection he became very agitated, and spoke for the first time for three years. He said spontaneously, "Can I go to the lavatory?" When asked how he felt he replied "All right", He then relapsed into his mute stuporous state.

Immediately *before* his second injection of cardiazol he appeared frightened at the sight of the syringe, and again spoke spontaneously, saying. "It's only a prick, isn't it?" but would not answer questions. Immediately after the fit he answered questions, giving the name of the hospital correctly, his home address, and stated that he had been in hospital "a few weeks". He could not give the name of his ward, or of any of the nurses or doctors, and was unable to state the day, month or year. He showed no interest in these questions, but kept gazing at the site of injection on his arm and repeatedly said, "Please treat it with poison, and bandage it". After the arm was bandaged he said, "I want to go to Balham Hippodrome". Asked why, he replied, "My sisters are there". To many questions he gave no answer, and he appeared at all times preoccupied. He became mute within half-an-hour after the fit. Following the second fit he again answered simple questions, but in a few minutes became mute. At no time had he shown disconnection of speech or evidence of irrelevancy or illogicality, though of course he spoke very little.

Reaction to Sodium Amytal.

A second injection of sodium amytal was given on 3.viii.38, on this occasion 10 c.c. of 5% solution was administered. At 3 c.c. he appeared apprehensive, but

did not move, at 5 c.c. he smiled foolishly for about 30 seconds. He became progressively more sleepy as the injection was continued, and tended to drop off to sleep, but would arouse himself on command, obeying as usual "to the letter", e.g., when commanded, raising his eyes to the ceiling with prodigious effort. He remained mute throughout, and when left alone, immediately fell asleep.

GROUP II.

CASE 7.

V. W. W—, single, aged 26 on admission on 22.ix.36.

History Previous to Admission.

Up to the age of 10 years he was a "spoilt" child, being allowed to do much as he liked by his mother. He found that he could "get what he wanted in order to keep him quiet". Had frequent temper tantrums, and often did not attend school. Debarred from playing games owing to "weak heart". His mother died aged 50—"cancer". Patient's father then married his sister-in-law, who was less sympathetic to the patient and reduced his "pamperings". He did well at school from 10–14. At the latter age he joined a motor engineering firm as apprentice, was ambitious, and studied at night school. He continued to work for this firm until the day of his admission to the observation ward, on 22.viii.36. He had been a reserved type, but with no definite abnormal traits until 3 months before his admission to the observation ward. At this time he had just returned from a short holiday with a girl friend. They had disagreed over expenses, and the girl had thought him miserly. There would appear to have been no sexual misconduct. When he returned he was quiet, depressed, and would not discuss the holiday. A few days later he visited his panel doctor, to whom he stated that he had become sexually excited when on the holiday. He said he had spoilt the girl's holiday, that he had not touched her, but had found it hard to control himself, especially when she was in bathing dress. He was advised to "go and find a woman". (This injunction played a prominent part in his future delusions.) The girl herself said that the patient had been annoyingly protective and brusque when they bathed, mean, and refused to go on expeditions. He returned to work after his holiday, but in his spare time was restless, moody, and frequently declared that he had lost his manhood, and would not get it back until he had "found a woman". A few days before entering the observation ward he stated that people were mocking him in the streets, and spitting at him. On admission to the observation ward, he continually demanded his discharge, in order to tell the girl that he "really loved her". He stated that she was sending him messages, altering the smell of things for him, and had caused his ears to enlarge and his eyes to sink. He stated that if he could not have her, he would have any prostitute. He required sedatives. Serum Wassermann was negative. Serum bromide 10 mgrm.%.

Physical examination revealed nothing abnormal except carious teeth. He became increasingly more resistive to nursing attentions and was transferred to West Park Hospital on 22.ix.36.

On admission he was fairly communicative and still deluded and hallucinated. He said, "I have got large pupils, and get messages through them as a Nancy man". He was extremely violent, resisting every attention, and paid no heed to the voiding of his urine and fæces. He required to be tube-fed from 7.x.36 until 20.xi.36. He was then hand-fed until 12.i.37 when tube-feeding was again necessary until 17.xi.37 (when cardiazol treatment commenced). A few partial remissions occurred during this period, coinciding with the administration of sodium amytal, which will be discussed later. From 13.x.36 he became practically inaccessible, mumbling only a few words in reply to questions, and more often not speaking at all. For example he would say, "Can't I go home?", "My bowels are stopped up", "I want a woman", but never more than a sentence at a time. For weeks at a time he was

completely mute. Left alone he would stand in the farthest corner of the ward, head bowed on chest, arms hanging limply by his side, his face turned to the wall. When attended, he would resist with all his strength, so that it always required two nurses to dress and wash him, or drag him to the lavatory. His expression was " hang-dog ". Sometimes he would smile sheepishly when addressed, but apart from this appeared totally disinterested in events going on around him. At times on account of losing weight he was kept in bed for a week or two, and then he would lie curled up on his side, the sheets pulled completely over his head, and clutched tightly in his hands so that it was difficult to uncover him at meal and toilet hours. On 20.viii.37 I attempted to interrupt his stupor by injecting intravenously 1 minim of 1 : 1000 adrenaline hydrochloride diluted to 10 minims with distilled water. As a result marked facial pallor occurred, with tachycardia and all the outward appearances of fear. The effect lasted two minutes, during which he spontaneously sat up in bed. He remained, however, mute and negativistic.

Reaction to Sodium Amytal.

Later (several hours) on the same day 5 c.c. of 10% sodium amytal in distilled water was administered intravenously, at the rate of 1 c.c. per minute.

Immediately following cessation of the injection a lucid interval occurred, in which he appeared to be abreacting incidents leading up to his certification. He spoke spontaneously and gave the following information without being questioned. Indeed he appeared ready to confide in anybody who was prepared to listen to him. He stated that his girl friend had separated from him, following a proposal on his part of sexual intercourse between them, and that since that time he had suddenly ceased to feel hungry. He said that it was impossible for him to pass fæces. He dwelt at length on the fact that he had always been a hard worker, conscientious, etc., but that he had, in spite of this, not progressed as he would have wished. He wept bitterly, his speech was slurred (though the latter sign disappeared in about half-an-hour). He sought sympathy from those around him, and for over an hour insisted that all should hear the story of his life. One hour and forty minutes from the time when he first spoke he commenced to show signs of his former state, spoke less, eventually became mute and fell asleep. The following morning he allowed himself to be dressed without putting up his usual furious resistance, being in fact quite passive. He remained, however, mute and quite unco-operative. Daily injections each of 5 c.c. 10% sodium amytal were then given intravenously from 26.viii.37 until 30.viii.37–5 injections in all. A period of comparative normality followed each injection, during which he dressed himself, attended to his toilet, insisting quite definitely on doing everything for himself. He ate heartily, went for walks with a nurse in the hospital grounds, and displayed a keen interest in all he saw. During these subsequent periods he never dwelt on his delusional ideas, and scarcely ever mentioned them unless questioned directly. He smoked cigarettes, showed a keen sense of humour, and on one occasion gave me a useful lecture on electric batteries. Psychotic traits were, however, still present. Once he said to me, " You can possibly read my thoughts ", and often he would repeat that his trouble could be cured " by having a woman ". He persisted that if he were allowed home in this phase (of sodium amytal intoxication) he would not relapse into stupor. On each occasion he commenced to withdraw from his environment about 7 hours after the injection, and after this, within half-an-hour, he was again mute, negativistic and inaccessible. During one of these lucid intervals he was visited by his relatives, with whom he conversed for the first time in 11 months, and who thought him to be fully recovered.

On 31.viii.37 the same dose (5 c.c. of 10% solution) of sodium amytal was given intramuscularly. This produced practically no effect except a slight lessening of his negativism ; he remained mute. On no occasion during these injections did he lose consciousness. At first his speech was slurred, but this was the only evidence of intoxication, and always disappeared completely in about half-an-hour. His first words when he spoke on each occasion were profuse apologies to the nursing staff

for the trouble he was causing them. He stated that during his stuporous periods he felt that he wished to speak and to help himself, but could not do so. He gave evidence of being aware of even minor events, which had taken place in the ward, when he had been apparently indifferent to his environment. He complained of having had troublesome dreams in his stuporous periods.

On 16.ix.37 he received another 5 c.c. of sodium amytal, with similar results to those mentioned previously. An injection of 5 c.c. of sterile water given to rule out any element of suggestion was totally ineffective.

On discontinuing injections tube-feeding had to be recommended, and was continued until he had received eight injections of cardiazol as mentioned later.

Reaction to Cardiazol.

Date.	Dose in c.c.	Duration of time in seconds from completion of injection to onset of fit.	Duration of fit in seconds.	No. of fit.
20.x.37	5	Not recorded	148	1
22.x.37	5	,,	68	2
25.x.37	5	Anxiety state	..	..
26.x.37	6	No reaction	..	..
2 min. later	6	Not recorded	150	3
29.x.37	6	,,	62	4
31.x.37	7	,,	55	5
3.xi.37	7	,,	55	6
6.xi.37	7	10	85	7
9.xi.37	7	25	65	8
13.xi.37	7	Not recorded	58	9
17.xi.37	7	No reaction	..	..
2 mins. later	7	6; from this ate with prompting and talked; no longer incontinent	65	10
19.xi.37	8	24	55	11
20.xi.37	8	55	150	12
23.xi.37	8	20; no longer resistive	55	13
25.xi.37	8	25	70	14
28.xi.37	8	15	55	15
1.xii.37	8	No reaction	..	..
2 mins. later	5	Anxiety state	..	..
,, ,,	8	10; takes diet without prompting	60	16
4.xii.37	10	10; working in ward	60	17
7.12.37	10	10	50	18
10.xii.37	10	8	60	19
13.xii.37	10	10	38	20
16.xii.37	9	22	50	21
19.xii.37	9	20	45	22
21.xii.37	9	15	48	23
24.xii.37	9	15	50	24
29.xii.37	9	16	60	25
1.i.38	9	17	49	26
3.i.38	9	12	50	27
7.i.38	9	7	40	28
12.i.38	9	5	62	29
15.i.38	9	17	48	30

On 22.xi.37 he wrote to his former employers asking for work on his discharge, and received a favourable reply. He was discharged recovered on 13.iv.38 and returned to work. Still working in August, 1938.

CASE 8

W. H—, single, aged 23, admitted on 5.xi.24.
Occupation: Theatre hand.
Heredity: Paternal grandfather died in a mental hospital.

Previous History.

He appears to have been an average boy at school, said to have been cheerful and friendly; was always ambitious to become an actor. On leaving school he got work as a theatre hand, and is said to have occasionally played small parts. He showed no abnormality until four weeks before admission. A relative stated "he then commenced saying that people could hear him thinking". "He continually annoyed his mother, stating that she was thinking about him. He said he could hear people shouting in the street."

On admission: *Physical state:* Nothing abnormal detected. *Serum Wassermann:* Negative. *Mental state:* "He lies in bed, his head covered by the sheets; he takes no interest in his surroundings, but is resentful of interference, suspicious and at times truculent. He is correctly orientated. He states with little show of interest that he is heir to the Selby millions, that someone reads his thoughts, and that some man has mysterious powers over him. For the ensuing five years he alternated between confused periods, when he was impulsive, hallucinated, often violent, and given to outbursts of meaningless laughter; and quiet periods, when he was employable at routine tasks, could give a fair account of his past life, but was disorientated in time, and indifferent to the fact that he was in a mental hospital."

From 26.ix.29 onwards the character of his psychosis changed. He still showed phasic alternations, but the two phases consisted of a quiet phase similar to that mentioned and a phase of stupor during which he was completely mute, required hand-feeding, was incontinent and had to be nursed in bed, where he lay immobile for 4 to 7 days at a time. These phases alternated (and still do, 31.x.38) about every week to two weeks. From this time onwards he never showed any tendency towards impulsive behaviour, and in his accessible periods no evidence of his former delusions could be obtained. He was at times resistive during his periods of stupor, but often flexibilitas cerea could be demonstrated. In his accessible periods he was even more detached from his environment than formerly and never spoke unless addressed. He would give a few facts about his past life, but had no idea how long he had been in hospital, and did not know the names of any of his nurses or doctors. He could still work in a mechanical fashion at dusting and rug-making.

Reaction to Cardiazol.

A course of injections of 10% aqueous solution of cardiazol was given as tabulated below:

Date.	Dose in c.c.	Duration of time in seconds from completion of injection to onset of fit.	Duration of fit in seconds.	No. of fit.
4.iii.38	4	25	85	1
7.iii.38	4	21	76	2
9.iii.38	4	No reaction	..	..
2 mins. later	5	,,	..	..
11.iii.38	10	13	48	3
14.iii.38	10	15	65	4
16.iii.38	10	22	78	5
18.iii.38	10	15	60	6
21.iii.38	10	20	60	7

Following on his last injection he was observed to limp when walking. Examination revealed evidence of fracture of the neck of the right femur, which was confirmed by X-ray. Injections were therefore stopped. From the time of his first

fit until a month later he remained stupor-free. I have no accurate record of the exact length of the periods he was stupor-free, during his stay in hospital, but from those available this would appear to be twice as long as at any time previously. As the injections continued it was observed that he was becoming more alert, and showed more interest in his environment. He was at no time restless or impulsive. He quickly reverted to his former condition after cessation of the injections.

Reaction to Sodium Amytal.

On 3.vi.38 he received 8 c.c. of 5% sodium amytal intravenously. He had up to the time of injection been in a state of stupor for 3 days. He lay in bed, his eyes staring fixedly ahead, his limbs retaining attitudes imposed upon them. He was resistive to certain movements, e.g., although one could move his limbs as one wished, one could not, even by exerting force, open his mouth. He was mute, and paid no attention to questions addressed to him. He appeared not to be aware of cutaneous stimuli (pinching the skin of the cheek).

During the course of the injection he at first appeared to become sleepy, closing his eyes repeatedly. Marked blepharospasm was noted. Towards the end of the injection he commenced to answer questions, and then appeared to be in the same mental state as he usually was in his non-stuporous phase. That is to say he would converse fairly freely, but his voice was toneless, and he did not show interest in the conversation; he was correctly orientated in space, but only roughly in time, giving the date as December, 1937. His guess at the date was, however, much better than usual (he was usually many years out of reckoning). He could discuss past events, and mentioned a visit by a relative which had occurred a week before. He observed, for the first time apparently, a rash on the dorsi of his hands, which had been present for a few days (erythema solare), and seemed surprised at it, rubbing his hands together. This incident, and the subsequent avidity with which he ate his next meal, were the only signs he exhibited of interest in his environment. Usually in his stupor-free phase he ate his food mechanically, and with indifference.

CASE 9.

C. F. D—, single, aged 25 on admission on 23.iv.37.
Occupation: Soldier.

History Previous to Admission.

On 17.ii.37 he arrived home from service with his regiment in India. He had been sent home for treatment for detached retina caused by the flick of a mule's tail. At the time of his arrival from India he appeared to be mentally normal, but on 18.ii.37 his relatives noticed a change in his conduct; he became garrulous and over-active. On 23.ii.37 he was admitted to Netley Hospital, where it was noted that his speech was incoherent, and that he was aggressive and over-active. A diagnosis of acute mania was made at that time. He required large doses of sedatives. The ophthalmologist failed to find evidence of a detached retina, but stated that colour-blindness was present, and suggested that there had been a retro-bulbar neuritis. He was transferred to West Park Hospital on 23.iv.37.

Physical state: Nothing abnormal detected. Eyes appeared normal on routine examination. *Serum Wassermann:* Negative. *Mental state:* He was over-active, elated, and replies were given at random, and were of a facetious nature. He said, "I am a king; I can see anything I like. It doesn't matter if I go blind". He attempted to put his feet on the table and was aggressive when prevented. He was noisy, abusive and restless, but attended to his personal needs. He made unprovoked attacks on the nursing staff.

From 29.iv.37 until 20.v.37 he received a course of injections of somnifen sufficient to keep him in a continuous state of semi-narcosis. He showed no improvement following this treatment, and when it was discontinued, reverted to

his previous state, fighting with other patients, breaking windows, etc. His speech, however, was noticed to have changed in that it exhibited the typical irrelevant and disconnected character of schizophrenia, with disharmony of mood. He was accordingly diagnosed as schizophrenia. He became more untidy in appearance, incontinent of urine, and frequently tore his clothing. When his attention could be held he was found to be disorientated in space and time and for person. He stated, for example, that I was his brother, and that he was in Sing-Sing prison. He could not concentrate on any work for more than a few minutes at a time, and connected conversation with him was impossible. He remained in this state until cardiazol treatment was commenced on 4.ii.38.

Reaction to Cardiazol.

A course of injections of a 10% aqueous solution of cardiazol was given as tabulated below:

Date.	Dose in c.c.	Duration of time in seconds from completion of injection to onset of fit.	Duration of fit in seconds.	No. of fit.
4.ii.38	5	Not recorded	23	1
7.ii.38	5	30	50	2
9.ii.38	5	No reaction	..	..
2 mins. later	3	,,	..	..
,,	2	,,	..	..
11.ii.38	6	,,	..	..
2 mins. later	5	,,	..	..
,,	5	,,	..	..
14.ii.38	11	12	50	3
16.ii.38	11	18	13	4
18.ii.38	11	18	75	5
21.ii.38	11	28	38	6
23.ii.38	11	20	6	7
25.ii.38	11	13	53	8
28.ii.38	11	18	50	9
2.iii.38	11	20	72	10
4.iii.38	11	20	60	11
7.iii.38	11	17	56	12
9.iii.38	11	15	45	13
11.iii.38	11	12	48	14
14.iii.38	11	No reaction	..	..
2 mins. later	5	,,	..	..
,,	5	,,	..	..
16.iii.38	12	17	60	15
18.iii.38	12	20	65	16
21.iii.38	12	10	50	17
23.iii.38	12	20	65	18

Following the seventh fit he showed a marked but temporary improvement. He became quiet, well-behaved, and worked on a loom quite efficiently. His manner was natural, his conversation relevant and logical, showing no evidence of disconnection. He showed almost complete amnesia for the period which had elapsed since he left India. He stated that he "could not have been here more than a week or two", and would not accept my statement that he had already been in hospital ten months. For events up to the period since he had left India he appeared to have full recollection. He related the incident of his eye injury, and said that he had not wished to leave India because he had had a sweetheart there. He asked for his immediate discharge, and said that it was absurd that he should be kept in hospital any longer. This improvement lasted but a few days, and during the latter part of his treatment he became progressively more impulsive,

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confused and over-active. For a few weeks after the cessation of treatment it was found impossible to allow him to mix with other patients, and he was confined to bed, and given large doses of sedatives in an attempt to stem his violent behaviour.

Reaction to Sodium Amytal.

By 10.v.38 he had reverted to his former state, in which, though still impulsive, he was to a certain extent amenable to discipline. 8 c.c. of 5% sodium amytal was administered intravenously at the rate of 1 c.c. per minute. He remained quiet during the first half of the injection, but as it was being completed, and afterwards, he became garrulous, and talked and laughed uproariously, describing many sexual exploits perpetrated by himself and a friend in India. This type of conversation and behaviour was quite unusual in my presence, his usual attitude when summoned to the clinical room being to stand stiffly to attention, speaking (though irrelevantly) only when addressed. No physical signs of intoxication were observed. The effect of the drug lasted several hours.

CASE 10.

E. B. H—, single, aged 27 on admission on 3.xi.36.
Occupation before admission: basket maker.

History Previous to Admission.

Nothing obtainable, except that he was admitted to an observation ward on 27.x.36 on a three-day order.

Note on admission: *Physical state:* No gross abnormality found. *Serum Wassermann:* Negative. *Mental state:* "He lies motionless in bed and requires every nursing attention, including hand-feeding. He is incontinent. He resists all attempts to move his limbs, is mute as a rule, but will occasionally answer 'Yes' or 'No' to a question. When addressed he grimaces, breathes heavily and holds himself tense. He does not appear to take interest in his surroundings."

He remained in this state of resistive stupor until 17.xi.36, when although still mute and incontinent, he could be persuaded to sort coloured wools, which he did in a purely mechanical fashion. From 3.ii.37 it was found that he would reply to questions, if these were frequently repeated, though he never spoke spontaneously. It was then noted that he was correctly orientated in time and space, but blocking of thought was so extreme that no connected conversation could be maintained. He had by this time ceased to work, even at wool-sorting, and remained in one position for hours at a stretch, unless moved. By 8.v.37 he was again completely mute.

A note made on 1.x.37 reads as follows: "He is in a state of stupor, mute, inaccessible, inert, showing flexibilitas cerea, and requiring every nursing attention, including washing, dressing and feeding. He is prone to retain his urine for long periods."

Despite the mention of flexibilitas cerea in this note, he was often most resistive when being attended.

Reaction to Sodium Amytal.

When the drug was administered he was in a state of stupor noted above. On 17.xi.37, 5 c.c. of 10% sodium amytal in doubly distilled water was injected intravenously at the rate of 1 c.c. per minute. Immediately following the injection he appeared preternaturally bright, sat up in bed, and talked vivaciously, both spontaneously and in reply to questions. He was found to be correctly orientated, and to have a passing knowledge of current events (gleaned apparently from wireless broadcasts in the ward). He had, however, absolutely no insight into his mental state; expressed no wish to leave the hospital. The following morning he was still bright and accessible, and expressed a wish to watch the football matches

played by other patients. His condition remained thus for several days, during which his time was spent in watching football and reading newspapers. Thereafter his interest dwindled, he became less responsive to questioning, and within a fortnight of the injection had relapsed into his former state of stupor. During this accessible period he had not been incontinent and had taken his meals voluntarily.

On 19.ii.38 he received a second injection of sodium amytal, this time 4 c.c. of 5% aqueous solution. A period of accessibility followed similar to that produced on the first occasion, with the exception that he relapsed into stupor within approximately seven hours of giving the injection.

Reaction to Cardiazol.

A course of injections of 10% aqueous solution of cardiazol was given as tabulated below:

Date.	Dose in c.c.	Duration of time in seconds from completion of injection to onset of fit.	Duration of fit in seconds.	No. of fit.
19.xii.37	5	15	47	1
21.xii.37	5	10	47	2
24.xii.37	7	No reaction	..	..
2 mins. later	9	15	45	3
29.xii.37	7	12	50	4
1.i.38	7	18	54	5
3.i.38	7	15	43	6
7.i.38	7	15	55	7
12.i.38	7	7	40	8
15.i.38	7	10	50	9

Following the last injection he ran a slight evening temperature. No definite signs of disease were detected, but treatment was discontinued. On 5.ii.38 tubercle bacilli were detected in his fæces, though he had at that time no cough or other signs of infection beyond a slight evening temperature. He rapidly lost weight, and died on 11.iv.38.

Post-mortem examination revealed widespread tuberculosis of both lungs, and tuberculous ulcers in large and small bowel.

He showed no mental change either during or after his cardiazol injections, remaining in a condition of profound stupor throughout.

CASE II.

H. A. P—. Single, aged 19 on admission on 16.viii.30.
Occupation: Attaché-case maker.
Heredity: Negative.

Personal History.

Birth and development normal. School: Exceptionally good scholar. Reached standard Ex.-7. Work: For some years labourer in timber works; later made attaché-cases, but was unsatisfied with the prospects and was taking lessons in motor-driving at night.

Habits: Teetotaller. Moderate smoker. Health, good. Had no girl friends, and showed no interest in women.

Pre-psychotic Personality.

Liked being alone; could not make friends; was always embarrassed when meeting strangers. Good-natured, but often sulky. Very ambitious. Very particular of personal appearance; almost "foppish".

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History of Personal Illness.

Showed no abnormal traits until three days after falling off a bus. At the time he appeared "only a little shaken up", and was normal in the interval. At breakfast on the third day he "changed a terrible colour" and began to mutter to himself. When urged to go to his shop, he said, "There ain't no shop, and there ain't no work". He began to express delusions concerning his sister and was taken to an observation ward.

On admission: *Physical state:* Nothing abnormal detected. *Serum Wassermann:* Negative. *Mental state:* "He lies in bed, his eyes closed, at times grinning foolishly. He states that he hears voices calling him, 'a dirty maggot', and says that this is because he once made a sexual assault on his sister. He states that his former neighbours threatened to throw him "over the Monument' as a punishment for his act of rape, and that even now he is persecuted by some force which is forever pushing him forward."

Shortly after admission he commenced to work well in the ward. His mental state deteriorated, however, and his delusions became less strongly held, and were only vaguely expressed. On 19.vii.32 he ceased to work and has not done any since. He became more manneristic, impulsive, and foolish in his behaviour, rarely spoke, and for hours sat without moving. On 31.i.37 he attempted to cut his throat with a piece of glass, obtained by smashing a window. He stated that he had heard a command to end his life. By 16.ii.38 it was difficult to converse with him due to marked blocking of thought and irrelevant remarks.

Reaction to Cardiazol.

A course of injections of 10% cardiazol was given as tabulated below:

Date.	Dose in c.c.	Duration of time in seconds from completion of injection to onset of fit.	Duration of fit in seconds.	No. of fit.
15.iv.38	5	44	98	1
18.iv.38	5	28	30	2
20.iv.38	5; no reaction	..	..	..
2 mins. later	5	25	70	3
23.iv.38	6	No reaction	..	..
2 mins. later	5	15	62	4
25.iv.38	7	21	24	5
27.iv.38	7	19	69	6
30.iv.38	7	17	65	7
2.v.38	7	17	70	8
4.v.38	7	No reaction	..	..
2 mins. later	5	10	20	9
7.v.38	8	No reaction	..	..
2 mins. later	5	14	58	10
10.v.38	9	22	Not recorded	11
12.v.38	10	18	68	12
14.v.38	10	13	57	13
19.v.38	9	18	50	14
21.v.38	9	15	65	15
23.v.38	9	17	85	16
25.v.38	8	17	84	17
29.v.38	8	19	67	18
2.vi.38	8	19	61	19
4.vi.38	8	18	58	20

From 19.v.38 until the completion of the course of injections he became restless, agitated, and was more frequently impulsive than heretofore. A few days after the last injection he relapsed into his former state.

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Reaction to Sodium Amytal.

On 13.vi.38 he received 8 c.c. of 5% sodium amytal intravenously. He became somewhat euphoric and garrulous, and insisted on relating many childhood reminiscences. Apart from this his speech was grossly irrational, and displayed a total lack of insight into the nature of his illness. One remark he made was, however, enlightening. He said, "Sometimes my body becomes demented; the nurses punch me on the earhole as they pass by, and that makes me want to break windows and kill myself". He was speaking of his impulsive episodes.

CASE 12.

J. R—, single, aged 26 on admission on 3.xi.36.

Heredity: Father alive and well; 13 years ago was in Claybury Mental Hospital for 1 year. Diagnosis: Neurasthenia. He has been well since.

Paternal grandfather: Dead, aged 50; died suddenly, cause unknown. Had always been healthy.

Paternal grandmother: Dead, aged 69; "gastric disease". Previously healthy.

Paternal siblings: One sister, dead, aged 48, accident. One sister dead, aged 69, old age, healthy. One brother has been in a mental hospital for 20 to 30 years, following "extensive head injuries". Was healthy prior to this. Remaining siblings alive and well.

Mother: Aged 61, second of family of 13. Healthy.

Maternal grandfather: Died bronchitis, aged 50.

Maternal grandmother: Died bronchitis, aged 69.

Eight maternal siblings alive and healthy. No nervous illness.

Patient's siblings: Patient is a twin, and sixth in family of 12. Other twin alive, healthy and at work. Four died, "children's illnesses". Three married with children. Three single, all healthy, and have had no nervous illnesses.

Personal History.

Birth, normal; development, normal; health, good. School: Excellent scholar. Reached standard Ex-7. Work: Skilled worker in brass foundry for 5 years. Keen and conscientious. Was on learner's pay. Other workers induced him to ask for standard pay, and this led to his dismissal. Had only obtained odd jobs since; much unemployment. Sex: Had no girl friends, and showed no interest in this direction. Habits: Moderate drinker and smoker.

Pre-psychotic Personality.

Sociable and friendly. Had a group of constant friends. Keen on camping, football, music halls, and most outside activities. Very independent, thrifty and punctilious about his personal appearance. Conscientious and thorough worker. Not sensitive. After being some time unemployed he became rather sensitive, and tended to keep to himself and make no new friends. His twin is a boisterous, sturdy, "slap-dash" individual.

History of Present Illness.

He gradually became depressed, irritable and sensitive because of unemployment and the attitude of some members of the family to this. For 3 months prior to admission suffered from nocturnal enuresis. Medical advice was sought by his brother-in-law for this latter complaint, and he was then recognized as being "psychotic" and transferred to West Park Hospital via an observation ward.

On admission: *Physical state:* Nothing abnormal detected. *Serum Wassermann:* Negative. *Mental state:* He moved "like an automaton", never spoke spontaneously, but would reply to questions and was found to be correctly orientated. He said that he heard voices crying "Carmichael". He grimaced, exhibited flexibilitas cerea, was incontinent of urine, resistive and required to be

hand-fed. He remained thus until 27.xii.36, when he entered a stage of excitement, during which he repeatedly tore his night-shirts, and attempted to hurl himself against windows. This phase lasted until 7.i.36, when he reverted to his former condition of stupor. This persisted until 4.iii.38, being only occasionally interrupted by short outbursts of violence, when he would attack other patients and steal food from their plates. From time to time loss of weight gave rise to anxiety, and he was often very difficult to feed.

Reaction to Cardiazol.

A course of injections of 10% aqueous solution of cardiazol was given as tabulated below :

Date.	Dose in c.c.	Duration of time in seconds from completion of injection to onset of fit.	Duration of fit in seconds.	No. of fit.
4.iii.38	5	35	90	1
7.iii.38	5	23	83	2
9.iii.38	5	No reaction	..	..
11.iii.38	6	20	50	3
14.iii.38	6	No reaction	..	..
2 mins. later	5	,,	..	..
,,	5	13	75	4
16.iii.38	8	17	58	5
18.iii.38	8	15	75	6
21.iii.38	8	No reaction	..	..
2 mins. later	5	15	55	7
23.iii.38	9	20	55	8
		Very restless and violent; nursed in padded room		
25.iii.38	9	15	65	9
28.iii.38	10	11	44	10
30.iii.38	10	18	65	11

From the time of his first injection he became more violent and impulsive than he had ever been before, attacked the nursing staff with the utmost ferocity, and was restless both day and night. It was found necessary on many occasions to seclude him in the padded room. On this account it was considered inadvisable to continue with the injections. His restlessness did not abate, however, and he still remains restless and confined almost entirely to bed in a single room, to date (18.viii.38). The cardiazol treatment had, however, one striking, though temporary effect. He had been mute since 3.xii.36, but from the third injection of cardiazol he commenced to answer questions. His replies were, however, totally irrelevant. He again became mute a few days after the last injection.

Reaction to Sodium Amytal.

On 15.v.38 he received 8 c.c. of 5% aqueous solution of sodium amytal intravenously. Up to the time of the injection he had been over-active, getting in and out of bed and spitting at the nurses, and while the injection was being given he struggled furiously. When 8 c.c. had been administered he showed every signs of being about to fall asleep. The injection was accordingly stopped at this point. He did not speak spontaneously, but when asked if he wished for anything, he replied that he wanted to go back to his ward. He dressed without assistance and without prompting and went quietly back to his ward.

CASE 13.

T. S—, married, aged 38 on admission on 17.vii.36.
Occupation before admission: Warehouseman.

Reaction to Cardiazol.

A course of injections of 10% aqueous solution of cardiazol was given as tabulated below:

Date.	Dose in c.c.	Duration of time in seconds from completion of injection to onset of fit.	Duration of fit in seconds.	No. of fit.
20.x.37	5	Not recorded. Treatment suspended due to tonsillitis	133	1
3.xi.37	5	Not recorded	60	2
6.xi.37	5	8	65	3
9.xi.37	5	20	70	4
13.xi.37	5	Not recorded	65	5
25.xi.37	5	25	105	6
28.xi.37	5	15	65	7
1.xii.37	5	25	65	8
4.xii.37	5	22	60	9
7.xii.37	5	18	65	10
10.xii.37	5	14	58	11
13.xii.37	5	15	55	12
16.xii.37	5	16	52	13
19.xii.37	5	22	53	14
21.xii.37	5	22	54	15
24.xii.37	5	15	60	16
29.xii.37	5	18	55	17
1.i.38	5	15	65	18
3.i.38	5	10	42	19
7.i.38	5	12	45	20
12.i.38	5	25	60	21
15.i.38	5	15	55	22
17.i.38	5	16	62	23
20.i.38	5	15	45	24
21.i.38	5	15	60	25
24.i.38	5	No reaction	..	..
2 mins. later	5	25	60	26
26.i.38	6	No reaction	..	..
2 mins. later	5	10	60	27
29.i.38	7	15	50	28
31.i.38	7	18	53	29
4.ii.38	7	10	50	30

Progressive improvement occurred. He ate voluntarily from the time of the third injection onwards. Talked freely from the fourth injection onwards and commenced to do ward work. Thereafter he steadily took more and more interest in his surroundings and was discharged "recovered" on 13.iv.38.

History Previous to Admission.

Was at Banstead Mental Hospital from 11.vii.34 until 31.xii.34, where he was certified as "melancholia". During his stay there is said to have had a period of mania. Had been unemployed since discharge from hospital. Usually a contented and happy type, but had worried over his mother's death, which occurred 7 months prior to his admission to West Park Hospital. One month before admission here became very depressed, wept bitterly at times, attempted to "pull himself together" but was unable to do so.

Family history: One brother "insane".

On admission: *Physical state:* Nothing abnormal detected, except chronic bronchitis. *Blood Wassermann:* Negative. *Mental state:* "He is in a state of

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stupor. He looks profoundly miserable, does not speak and lies in bed quietly all day, taking no interest in his surroundings. He understands what is said to him, and is obedient. He will write replies to questions. He is clean and able to attend to himself. Sometimes he heaves a deep sigh and his eyes fill with tears. He smiles occasionally. He takes his food well."

The following abbreviated notes summarize his progress in hospital:

19.viii.36: Has become resistive and requires tube-feeding.

29.viii.36: Suddenly leapt from bed to-day and broke two windows. Is mute, resistive, and now inaccessible.

11.xi.36: Lies in bed in a state of stupor. Is being hand-fed.

17.vii.37: No change. Exhibits flexibilitas cerea.

27.vii.37: 5 c.c. evipan injected intravenously in an attempt to interrupt stupor. No effect.

17.viii.37: After etherization shows some reaction, crying softly and clasping his hands together with an appearance of great misery, but remains mute.

18.viii.37: Again very resistive and requiring tube-feeding.

Reaction to Sodium Amytal.

On 25.viii.37 he received 7 c.c. of 10% aqueous solution of sodium amytal intravenously. Almost immediately after the injection he appeared to become conscious of his surroundings, as if awakening from a sleep, whispered monosyllabic replies to questions, and smiled when asked if he would like some beer, indicating that he would like two pints. He then fell asleep (about 5 minutes after the completion of the injection). About 4 hours later he awoke and asked spontaneously for a "cup of cocoa and a piece of cake", which were given to him. He again fell asleep after finishing these and a few hours later awakened (now in the early morning), got out of bed, and walking up to the night nurse, asked him for some tea, bread and butter. He was provided with this and went back to bed. At rising time he was found to have relapsed into his former inaccessible state of stupor.

CASE 14.

A. M. K—, single (female), aged 35 on admission on 23.iv.26.

Occupation: Domestic servant.

History: Defective. Five years before admission had an illegitimate child. Had never had any previous mental illness. Her normal disposition was described as "brooding". One year previous to admission she began to express ideas that everyone was against her, became depressed and lost her appetite. One month before admission she showed evidence of being hallucinated, and her speech became disconnected. She had expressed suicidal ideas since 2.iv.26. For the past 6 months had been sleepless. Was described as being a keen Salvationist.

Heredity: Maternal grandfather was an epileptic.

On admission: *Physical state:* Nothing abnormal detected. *Serum Wassermann:* Negative. *Mental state:* "She is retarded, appears to find it difficult to collect her thoughts, and is depressed. She insists that she is being too well treated, and that she really deserves to be punished and put into prison. She states that she has visions of Christ being crucified, and she continually refers to Him. She lies quietly in bed, takes no interest in her surroundings, and does not speak spontaneously. Her expression is one of profound misery."

A diagnosis of "melancholia" was then made, but this was altered to "schizophrenia" on 18.iii.33. The following abstracts of notes indicate her progress in hospital:

7.v.26: She is still hallucinated and expresses ideas of unworthiness, but now smiles occasionally and works at light tasks in the ward. She states that it is due to herself that there is a general strike in the country at present, and expresses a hope that no one else will be blamed for it.

23.vi.26: She states that she hears her (illegitimate) son's voice, and that he is needing her.

25.ii.27: She is dull and depressed, still expresses delusional ideas, but these are now vague in nature.

30.iii.28: She remains very depressed and sometimes refuses food.

19.iii.30: It is now difficult to encourage her to speak. She appears disinterested in her surroundings, can give no idea how long she has been here and states that she hears voices "saying unpleasant things". She is now doing a little work in the ward, but her powers of concentration are poor. She is disorientated in time and place.

18.iii.33: Her conversation has become disconnected so that she is now almost incoherent. She appears to be actively hallucinated, and pays no heed to her environment.

19.iii.33: She now frequently attempts to smash windows.

21.iii.33: Has sudden outbursts, when she will attempt to destroy any article at hand.

23.i.34: She is becoming very difficult with her food.

16.iii.34: She is now very stuporous and is being tube-fed. Saliva dribbles from her mouth unheeded, her face is usually expressionless and sometimes shows "Schnauzkrampf", and this latter expression is becoming more noticeable. She is mute, inaccessible and resistive.

2.vi.34: Tube-feeding discontinued. Is a little less stuporous and eating voluntarily. Still mute and resistive.

30.xii.35: She had a fit to-day, which had all the characteristics of a "grand mal" attack.

23.vii.36: Mute, resistive and at times impulsive. Cannot be employed.

7.vii.36 until 14.iii.38: Required tube-feeding during this period and lay in bed withdrawn from her environment, resistive to attention, mute and incontinent of urine. Saliva continually dribbled from her mouth which remained in the typical "schnauzkrampf" expression.

Reaction to Sodium Amytal.

On 18.xi.37, 7 c.c. of 5% sodium amytal was injected intravenously. Five minutes after the injection she commenced to talk spontaneously, and was no longer resistive, appeared interested to a slight extent in her environment and at times smiled. Her spontaneous speech was, however, totally disconnected and irrelevant. On being questioned she was found to be aware of the name of her ward and of the hospital, to know the names of several nurses who had attended her and the name of the Superintendent. She was, however, completely disorientated in time, and had no idea how long she had been here. She asked if it would be possible for a man named E— A— to visit her in hospital, and stated that he lived "somewhere in Chiswick". This was the only comprehensible remark that she made spontaneously. She did not appear depressed. A few hours later she reverted to her state of negativistic stupor.

Reaction to Cardiazol.

From 2.iii.38 until 22.iv.38 she received injections of 10% cardiazol thrice weekly. In all she received 24 injections and had 23 fits. The reaction times were not recorded in this case. The commencing dose was 4 c.c., the final dose 9 c.c. Following the eighth fit she commenced to talk disconnectedly, but answered a few questions correctly. From this time she ate voluntarily, attended to her toilet and dressing and did a little dusting in the ward. She has maintained this state to date. She is orientated, but her conversation is irrelevant and foolish, and she takes little interest in her surroundings, spending the day between sitting in the day-room, dusting in a mechanical fashion, dressing and eating. She has many mannerisms and still gives evidence of being hallucinated, e.g., she will

frequently rise from her chair at table, stating that someone is pushing her from behind.

CASE 15.

S. J—, single, aged 23 on admission on 14.xi.34.

Family history: Father aged 62, alive and well; no illness. Four siblings; three alive and well. One sister aged 31 has been in a mental hospital since aged 21.

Personal History.

Patient was a "dull scholar" and went to a special school from 7–16. He worked in a wood merchants' as "handyman" from 16–17. Since that time until aged 19 had only had odd jobs. Had been unemployed for 4 years prior to admission. Personality described as gloomy, reserved and timid. On 17.vii.34 he complained of headache, and talked incoherently about something he had seen at the pictures. He became very excited, and was admitted that day to an observation ward. He was discharged after 3 weeks. On his return home he at first appeared normal, but after a few days became neglectful of his personal appearance and acted strangely, stating that he saw people in his bedroom and threatening to "cut them to pieces". He stated that he had been accused of murdering a child, hid knives in armchairs, and frequently repeated, "I didn't do the murder".

He was again admitted to an observation ward on 6.xi.34, and was transferred to West Park Hospital on 14.xi.34.

On admission: *Physical state:* Nothing abnormal detected. *Serum Wassermann:* Negative. *Mental state:* "He appears simple and childish, is garrulous and talks in an indistinct fashion. His remarks are rambling and irrelevant. He is disorientated in time and space. He boasts childishly of his exploits: 'I have great strength, and used to catch people down my street, by the legs, and swing them around my head on to their backs.' He states that he can hear his father speaking to him."

The following abstract of notes indicate his progress in hospital:

14.iv.35: He has become dull and unemployable, sits nodding his head and muttering to himself, but does not reply to questions. He requires to be prompted to dress and wash.

11.v.35: For two days he has been very excited and has repeatedly shouted "Jesus Christ". He required injections of hyoscine. Apart from this, has been mute and apathetic.

15.vi.35: He is mute, unemployable, incontinent of urine and fæces and shows no interest in his surroundings. He acts as if listening to voices.

16.i.36: He sits with his eyes closed, and remains in one position unless moved. He is automatically obedient. Completely mute.

Reaction to Sodium Amytal.

On 13.vi.38, 9½ c.c. of 5% sodium amytal was injected intravenously. When 6 c.c. had been injected he appeared sleepy, closed his eyes occasionally, and his neck (held characteristically off the pillow) tended to fall back. He would not answer questions, but as usual exhibited flexibilitas cerea and was automatically obedient. An opportunity was taken of the latter phenomenon to attempt to make him speak, first by ordering him to open his mouth and say "Ah!" and then by working him up through letters to words and sentences (similar to the persuasive method of treating hysterical aphonia). Automatic speech was then followed by short replies to questions, in a low toneless voice. (This experiment was repeated later when not under the influence of sodium amytal, but he remained mute.) He was disorientated in space, and apart from stating that it was "early summer", was disorientated in time. His speech when replying to questions was neither disconnected nor irrelevant, and he gave correctly the names of relatives who had recently paid him a visit, his mother's address, names of siblings, etc., though

questions sometimes had to be repeated in order to gain his attention. Later he occasionally spoke spontaneously, and on these occasions he was found to be soliloquising on his sister's insanity. His remarks were then rambling, though with obvious meaning, e.g., " They are all insanity—it is they who are all mad—they drove her mad—it's like an actor, you think he is mad, but he is sane all the time ". When questioned on these remarks he would not reply. Apart from the marked apathy present there were remarkably few signs of the gross intellectual deterioration one might have suspected from his conduct in the ward, and his speech was always relevant when replying to questions. It was, however, very difficult to coax answers from him, and where he could nod his head or use his fingers to indicate numbers he always did so. He appeared sleepy throughout, yawned prodigiously, but denied that he felt tired. When asked what had become of his sister Jessie, he replied, " She is in an insanity house at Epsom " (correct). He remained in this condition for several hours before he went to sleep. On the following morning he again replied to questions, but was less in contact and usually replied irrelevantly ; within a few hours he became mute and inaccessible.

Reaction to Cardiazol.

A course of injections of 10% cardiazol was given as tabulated below :

Date.	Dose in c.c.	Duration of time in seconds from completion of injection to onset of fit.	Duration of fit in seconds.	No. of fit.
7.ii.38	5	28	52	1
9.ii.38	5	No reaction	..	..
2 mins. later	3	30	56	2
11.ii.38	8	14	56	3
14.ii.38	8	12	52	4
16.ii.38	8	19	69	5
18.ii.38	8	25	75	6
21.ii.38	8	20	73	7
23.ii.38	8	17	72	8
25.ii.38	8	16	55	9
28.ii.38	8	14	60	10
2.iii.38	8	17	68	11
4.iii.38	8	20	65	12
7.iii.38	8	16	61	13
9.iii.38	8	20	55	14
11.iii.38	8	No reaction	..	..
2 mins. later	5	15	54	15
14.iii.38	9	14	58	16
16.iii.38	9	16	75	17
18.iii.38	9	15	50	18
21.iii.38	10	Not recorded	..	19
23.iii.38	10	,,	..	20
26.iii.38	10	,,	..	21
28.iii.38	10	,,	..	22
30.iii.38	10	,,	..	23
2.iv.38	10	,,	..	24
4.iv.38	10	,,	..	25

Following the course of injections his habits became even more depraved than formerly. He was frequently incontinent of urine and fæces and usually required assistance in washing. He remained inaccessible during and after treatment and was stuporous except immediately following each fit, when for a few moments he became confused and restless, shouting out incoherently.

CASE 16.

A. W—, single, aged 25 on admission on 27.xi.35.
Occupation: Plumber's mate.

Reaction to Cardiazol.

Date.	Dose in c.c.	Duration of time in seconds from completion of injection to onset of fit.	Duration of fit in seconds.	No. of fit.
4.iii.38	5	20	95	1
7.iii.38	5	21	74	2
9.iii.38	5; anxiety attack	..	..	..
11.iii.38	6	No reaction	..	..
2 mins. later	3	13	62	3
14.iii.38	7	No reaction	..	..
2 mins. later	5	14	62	4
16.iii.38	8	15	64	5
18.iii.38	8	15	60	6
21.iii.38	8	18	52	7
23.iii.38	8	20	55	8
25.iii.38	8	15	55	9
28.iii.38	8	13	56	10
30.iii.38	8	15	68	11
1.iv.38	6	14	40	12
4.iv.38	6	44	87	13
6.iv.38	6	20	26	14
9.iv.38	7	No reaction	..	..
2 mins. later	5	22	76	15
11.iv.38	8	17	52	16
13.iv.38	8	14	58	17
15.iv.38	8	24	29	18
18.iv.38	8	24	74	19
20.iv.38	8	15	60	20
23.iv.38	8	23	28	21
25.iv.38	9	16	70	22
27.iv.38	9	16	79	23
30.iv.38	9	11	68	24
2.v.38	9	21	67	25
4.v.38	9	15	80	26
7.v.38	9	25	Not recorded	27
10.v.38	9	13	84	28
12.v.38	9	17	72	29

During and after this course of cardiazol injections he became less stuporous, but over-active and more impulsive than formerly. Whereas before treatment he was only rarely "booked-up" as impulsive, now the casualty book recorded his name as having struck other patients several times a week. It was necessary to transfer him to a ward for violent patients (the first time he had ever been there). On being questioned he would reply quickly, but in monosyllables and in an irritable manner, and often appeared ready to attack the questioner. He showed no intellectual defect *per se*, but would often reply irrelevantly. He rarely spoke spontaneously. Once he said, "Why do you keep repeating, 'yes, yes, yes', at me?" whereas I had not done so. He complained that other patients would persist in making a noise "like barbed wire" at him and stated that that was why he attacked them. His behaviour was still uncertain though less impulsive in August, 1938, but he showed signs of reverting to his former stuporous state.

Previous History.

No previous illness. Was said to have been clever at school, but proved unsuccessful in work after leaving school and went from one job to another, his chief fault being "slovenliness". A stay-at-home type, reserved and with few friends. A few months before admission he became "sulky", untidy in dress; went to his family doctor complaining that he felt ill, and that "his nose was too long". He then accused others of talking about him and said he would kill anyone he heard doing so. This latter statement led to his certification.

One brother suffers from post-encephalitis lethargica.

On admission: *Mental state:* When received from the observation ward he was found to be in a condition of stupor and exhibited flexibilitas cerea. He was practically mute, but would answer "Yes" or "No" to questions occasionally, and in this way by a process of elimination he was found to be correctly orientated. He was incontinent, but would eat and dress with prompting. On 27.ii.36 he commenced to work at routine simple tasks under supervision. Otherwise he showed no change, except that he would occasionally attack those around him without warning. He remained thus until cardiazol treatment was commenced on 4.iii.38.

Reaction to Sodium Amytal.

On 30.v.38 he was given 10 c.c. of 5% sodium amytal intravenously at the rate of 1 c.c. per minute. He showed no change until 9 c.c. had been injected, when he commenced to answer questions more freely, his usual replies at this time being monosyllabic. He showed none of his usual irritability at being questioned and frequently spoke spontaneously. He was found to be correctly orientated in space and fairly well in time, knowing the year and month, though not the exact date. He did not know the names of doctors or nurses. Remote memory was good. His speech became slightly slurred about 5 minutes after the injection and remained so for half-an-hour. When he spoke spontaneously his speech showed the dilapidation and illogicality typical of the schizophrenic. He commenced to air certain opinions which had apparently occupied his thoughts. He said that he would prefer individuals to help each other in an economic crisis, rather than that there should have to be a "dole". On being asked why he spoke of such matters, he replied that he had been on the "dole" himself. He was for a short period a little maudlin, but did not cry. He could not give any coherent account of what the other patients said to him which caused him to strike them. He would only say that they "spoke of barbed wire and death". These words, he said, meant nothing to him, but irritated him. When I again mentioned "barbed wire" he shouted out, "Can't you say any other word but that?"

GROUP III.

Case 17.

G. F—, single, aged 20 on admission on 4.ix.30.

History defective.

Heredity: Father dead; rheumatic fever. Said to have been "mental"; died in a public institution.

Paternal grandfather: A barrister. Led a dissolute life and died "young".

Paternal grandmother: Chronic alcoholic. Died suddenly—"internal hæmorrhage".

Siblings: Not known.

Mother alive, aged 65. An epileptic in Long Grove Mental Hospital for past twenty-two years. Chronic alcoholic.

Maternal grandparents: Nothing definite known. Said to have been "heavy drinkers".

Mother's siblings: Nothing known.

Patient eldest of four children. One sister in Long Grove Mental Hospital. One brother married, two children; healthy. One sister married, said to be " mental but harmless "; looked after by husband; has two children.

Personal History.

Mother said to have been ill-fed and " drinking heavily " during pregnancy. Development: Brought up in a public institution.

Pre-psychotic personality. Description inadequate. " Inoffensive, quiet, obedient, willing "; " very honest principles ".

At 14 patient was sent to a training ship. Said to have been " driven away " from the ship in America by his comrades, who bullied him, to have been certified in America, and later discharged and sent home. In England was found wandering and admitted to observation ward in London. (Veracity of history, given by foster-mother, doubtful.)

On admission: *Physical state:* Nothing abnormal detected. *Serum Wassermann:* Negative. *Mental state:* " He appears dull and disinterested in his surroundings. He smiles fatuously at times. He states that before coming into hospital his foster-mother had poisoned his food, a gang of men in the public-house had ' drugged ' his beer, and that a snake-charmer had tried to influence him by music in order that he might ' pick his pockets '. He relates these incidents in a disinterested manner."

The following abstracts of notes indicate his progress in hospital:

25.ix.30: Dull and unoccupied. When questioned, still relates vague delusions of persecution.

14.iv.31 until 13.v.31: Underwent a course of pyreto-therapy by intramuscular injections of sulfosin (see " Sulfosin Therapy of Schizophrenia ", W. McCartan (1)). No change was observed following this treatment.

6.vi.31: Appears to be aurally hallucinated and still expresses persecutory delusions.

6.iii.33: Is at times mute. To-day he said, " Two men robbed a child of a large sum of money—I was that child ". He then became mute, but continued to grin in a fatuous manner. Is unemployed and disinterested in his environment.

1.v.33: Impulsively smashed a window.

7.viii.34: Frequently shouts out " Radio Paris " but is now completely mute when questioned. Manneristic and at times impulsive. Cannot be persuaded to work.

9.viii.37: He is now incontinent of urine and fæces and will stand in one position for hours at a time if allowed. He always obeys commands automatically. At times is still impulsive.

Reaction to Sodium Amytal.

On 27.vi.38 he received 6 c.c. of 5% sodium amytal intravenously. Shortly after the injection had been completed he commenced to answer questions (he had been mute for about four years, except for his intermittent shouting of " Radio Paris "). He evinced no interest in the questions, but his answers were relevant and prompt, though short or even monosyllabic. He could give no guess as to his length of time in hospital, the date, or the name of the hospital. He gave his birth place and the date of his birth, his former address in London, the number of siblings, etc., correctly. He stated in answer to questions that he would like his foster-mother, Mrs. Lloyd, to visit him, and when asked to write a letter to her, commenced to do so, but got no further than writing her name and address on the notepaper. He said that he would like her to bring him some " cigarettes—Woodbines ". He always addressed me as " Sir " during the interview, but could not state my name or occupation, nor the names of anyone else in hospital. He gave his age as 20 (his age on admission). He could add single numbers correctly, but failed at 20 plus 10. The majority of these answers were obtained after he

had slept for one hour, as, after answering a few questions at the completion of the injection, he fell asleep. About half-an-hour after awakening he ate a good meal, after which he again fell asleep. He slept throughout the night, and on the following morning was found to have reverted to his former state. At no time had he spoken spontaneously.

Reaction to Alcohol.

On 19.x.38 he received 400 c.c. of 40% brandy orally at the rate of 15 c.c. per 5 minutes. After 30 c.c. he gave his name correctly, but thereafter remained mute. When he had consumed the total amount he became very drowsy, though only slightly ataxic. He was put to bed (he undressed as usual on command) and fell asleep almost immediately.

CASE 18.

G. W. B—, single, aged 17 on admission on 28.i.27.
Occupation: Office-boy.

Previous History.

The second child of four, the other three siblings being alive and well. No history of insanity in ascendants. Did well at school and reached standard Ex-7 at 13½. He showed no abnormality of conduct until aged 16¾ years. He had worked as an office-boy in a shipping office since aged 14½, and it was not until he had been there 21 months that the first signs of his psychosis became manifest. He became depressed at that time, and complained that people were talking about him and nagging him. He left his employment 3 months later for this reason. He remained unemployed for 6 months and was then certified insane; gross deterioration had occurred by this time.

On admission: *Physical state:* Nothing abnormal detected. *Serum Wassermann:* Negative. *Mental state:* "He can only give a disconnected account of himself and talks in an off-hand manner. He states that his father has been very irritable with him since he became unemployed. He says: "I hear people nagging me—I went out to stop them—I heard Mrs. Angus's voice here last night—people talk about me when I go out'. He takes little interest in his surroundings, but is sullen and irritable when disturbed for nursing attention."

The following abstracts of notes indicate his progress in hospital:

11.ii.27: He is now working in the ward in a mechanical fashion, but is listless and indifferent. He shows no interest when questioned about his delusions, and says, "It remains to be seen why they did, and if they will continue it".

28.vi.27: He cannot now be persuaded to work.

28.ix.27: He is occasionally incontinent of urine, and on several occasions has attacked other patients in an impulsive manner.

29.xii.27: Flexibilitas cerea can now be elicited. He is dull, manneristic, unemployable and never speaks spontaneously.

28.vii.28: He remains mute for long periods. When he does speak it is only in monosyllables. Remains in fixed attitudes, usually with bowed head and "stooping" shoulders.

29.vii.37: Completely mute and inaccessible, unemployable and faulty in habits. Occasionally he makes impulsive attacks on other patients. He will obey simple commands automatically.

Reaction to Sodium Amytal.

On 10.ix.38, 10 c.c. of 5% sodium amytal was injected intravenously. He remained mute and inaccessible. A few minutes after the injection he fell asleep. When aroused shortly afterwards he was still mute. His facial expression remained dull and apathetic.

On 11.xi.38, 10 c.c. of 5% sodium amytal was again administered. No change whatever occurred. He remained automatically obedient until the full amount

had been given, when he became so drowsy that he was unable to rouse himself in bed and could not fully elevate his upper eyelids. Even at this stage when he tended to fall asleep if left alone, flexibilitas cerea could still be demonstrated in his upper limbs.

Reaction to Alcohol.

On 21.xi.38 he received 315 c.c. of 40% brandy orally at the rate of 15 c.c. per 5 minutes. He remained mute and expressionless throughout the administration. He remained automatically obedient, and once when given a pencil and told to write his name he wrote "Bat", but did not cross the "t", and could proceed no further despite much persuasion. When he had consumed the amount stated he fell asleep in his chair. He was put to bed, and on being awakened an hour later was still mute and inaccessible.

CASE 19.

G. G—, single, aged 27 on admission on 5.xii.30.
Occupation: Porter.
No history obtainable.
On admission: *Physical state:* Nothing abnormal detected. *Serum Wassermann:* Negative. *Mental state:* "He is dull and disinterested in his surroundings, requiring every personal attention. He states the year is 1926, but gives the month (December) correctly. He is disorientated in space. He states that there are twenty pennies in a shilling, and that Henry V is now King of England. He is unable to give any account of the events that led to his detention."
The following abstracts of notes indicate his progress in hospital:
5.x.31: He now works in a mechanical manner at dusting, etc., but is still apathetic and asocial.
3.xi.32: The intense apathy persists. He is unable to carry on a sustained conversation, and his brief answers to questions, though relevant, display a complete lack of interest. He states that he is happy here and has no wish to leave. Has no recognition of the flight of time.
9.vi.33: Is now completely mute; he will obey simple commands and still works mechanically in the ward. Is never impulsive.
5.vi.36: Has not been heard to speak for years, but still obeys orders, and works at simple tasks.
5.xi.37: He cannot now be persuaded to work and is mute and inaccessible, but will obey simple orders automatically. He will only wash, eat and dress to the accompaniment of repeated commands.
8.i.38: Is now incontinent of urine and fæces.

Reaction to Sodium Amytal.

On 19.xi.37, 5 c.c. of 10% sodium amytal was injected intravenously. He showed no change throughout the period of injection, and when it had been completed, fell asleep. On awakening he was found to be still mute and inaccessible.
On 10.ix.38 he received 10 c.c. of 5% sodium amytal intravenously. He again showed no change, went to sleep, but could easily be aroused. When awakened he was found to be completely inaccessible.

Reaction to Alcohol.

On 27.x.38, 360 c.c. of 40% brandy was administered orally at the rate of 15 c.c. per 5 minutes. No reaction was observed beyond increasing torpor and ataxia. When he had consumed the total amount he appeared as if about to sleep. He was markedly ataxic, but could stand without support. When put to bed he immediately fell asleep. He remained mute and inaccessible throughout, but continued to obey simple commands automatically up to the moment of falling asleep. His facial expression did not alter.

CASE 20.

W. C—, single, aged 18 on admission on 25.iii.25.

Occupation: Clerk.

No history of insanity in ascendants or siblings (brother and sister). All the children were sent to Norwood Homes for Children when father deserted the family. Patient was then aged 3. Father is described as being "fidgety and with a vicious temper".

Mother: Nervous and often depressed, but never stopped her work.

Previous History.

At Norwood Homes he is described as having been "studious and above the average". Left the Homes at 14 and worked as messenger at War Office. He was ambitious and studied at night-schools. Shy and reserved type, but had "charming manners". Left War Office due to curtailment of staff and got a "City job". A few months later (aged 15) he became restless, bad tempered and often violent; gave up his job and "terrorized the family". If annoyed would throw crockery about in the house and often wandered for hours on his own. He could give no explanation for his conduct. He was repeatedly brought home by the police, having wandered, sometimes in private premises. Eventually, 18 months after he had left his work, he was arrested on a charge of "loitering with intent to commit a felony" and sent to Feltham Borstal Institution. From there he was certified and sent to West Park Hospital.

On admission: *Physical state:* Nothing abnormal detected. *Serum Wassermann:* Negative. *Mental state:* "He lies quietly in bed, smiling and talking disconnectedly in reply to auditory hallucinations. His conversation appears to be chiefly concerned with railway strikes. Emotional dilapidation is evident and he exhibits many mannerisms. At times when his attention can be held he replies relevantly to questions."

The following abstracts of notes indicate his progress in hospital:

15.xi.26: He is dull, slovenly and apathetic, stands aimlessly about when unoccupied, but works in a mechanical fashion on the farm under supervision. His conversation is grossly irrational, he is manneristic, and has frequent outbursts of meaningless laughter. He is disorientated in time and place and under-estimates his age.

28.iii.29: He is now incapable of working and rarely speaks.

13.ix.30: He is solitary, disinterested, often mute for long periods. Rational conversation with him is impossible. He states that he hears someone say, "Your body is down there". When asked his name, he replies, "Portugal". He is incontinent, but is automatically obedient and will wash and dress when ordered.

24.ix.31: He is now completely mute and inaccessible. Flexibilitas cerea is present.

26.ix.32: Sits about all day. Impossible to occupy, as he will only obey one order at a time and becomes motionless when left alone.

Further notes indicate no change from the above, and he was mute, inaccessible, but automatically obedient when attempts were made to determine his reaction to sodium amytal and to alcohol in 1938.

Reaction to Sodium Amytal.

On 2.vii.38, 8 c.c. of 5% sodium amytal was administered intravenously. His eyes closed, but he was not asleep, and flexibilitas cerea was present throughout. At no time could he be induced to speak, but continued to obey commands automatically, though slowly and in an ataxic manner.

On 3.viii.38 he received 6½ c.c. of 5% sodium amytal. Although this dose was smaller than the previous one (which had not produced sleep) he rapidly lost consciousness. His pupils became pin-point, but reacted to light. Pallor of the

face and cyanosis of the lips was evident, the jaw tended to fall back, the pulse was feeble and respiration shallow. It was interesting to note, therefore, that in spite of the apparent depth of anæsthesia, a slight degree of flexibilitas cerea appeared to persist. This was apparent from the fact that when an arm was lifted up in a vertical position it remained in that position for a fraction of a second longer than the action of gravity itself would have allowed. 4 c.c. of coramine was given intramuscularly. He awakened 2½ hours later and was found to be still mute and inaccessible.

Reaction to Alcohol.

On 10.x.38 he received 300 c.c. of 40% brandy orally at the rate of 15 c.c. per 5 minutes. No mental change was observed beyond progressively deepening somnolence. He vomited a small amount of the liquid when he had consumed 300 c.c. He was put to bed and fell into a deep sleep. It was then found that his limbs retained positions imposed upon them, for about a minute, while the patient still slept.

CASE 21.

E. M. B—, single (female) admitted on 9.vi.25.

No insanity in ascendants.

Father and mother alive and well. No history of nervous illness. Both appear to be stable and well adapted. Patient is the third of 9 children. Her twin died at birth and she herself was premature. Eldest daughter died of heart disease, aged 24. Another of cerebro-spinal meningitis, aged 7. Of the 5 remaining siblings, 4 are married and one brother lives at home. All healthy with no nervous illness. Economic position of family good.

Personal History.

Patient had rickets and did not walk until aged 3. Fits from before 12 months until aged 3. Talked at 12 months. School: Said to have been "very dull" and only reached standard IV, aged 14. First worked as factory-hand in biscuit factory, then in domestic service. In 1925 she complained of lethargy and depression and felt unable to work. She quickly became intensely depressed and preoccupied and within 3 weeks was admitted to hospital.

On admission: *Physical state:* Nothing abnormal except tachycardia (P.R. 116). No cardiac abnormality detected. *Serum Wassermann:* Negative. *Mental state:* "She is depressed, dull and retarded, poorly orientated and hallucinated visually and aurally. She states that she has killed people and is afraid she may kill more, and that she is responsible for the sufferings of those around her. She resists nursing attention, is incontinent of urine and requires hand-feeding."

Her mental state at this time suggested a diagnosis of "depressive state", but by 9.xi.25 she had not improved, and now frequently smiled in a fatuous manner and exhibited echolalia. From 19.xii.25 until 17.ii.26 she became noisy, restless and impulsive, interfered with other patients and required to be transferred to an acute ward. She was eventually taken home by her relatives on 28.vii.26 on their own responsibility. She had at that time reverted to a mute, dull and depressive state.

She apparently had recovered after some time at home, and had entered domestic service, until 1933, when she again became depressed. This time she remained at home and apparently recovered partially, but did not return to work. Since a child she had been the most spoilt of her family. She had always been obstinate and quick-tempered, and as she grew older the other members of her family had found it difficult to humour her. Her main interest in life had always been religion and she attended regularly at the local Baptist Church. At home she was tidy and methodical and hoarded all manner of things in boxes.

In January, 1938, she again became depressed; was at first inclined to stay

later in bed than usual in the morning; then she was noticed to be more silent than usual, did not want to go to church, became sleepless and ate poorly. At first she would give no reason for her conduct, but later admitted that she was worried because she could hear herself swearing. She became fearful, and stood in dark corners of the house where she could not be seen.

She was readmitted to West Park on 29.iii.38.

On admission: *Physical state:* Nothing abnormal detected. *Serum Wassermann*: Negative. *Serum bromide:* <25 mgrm.%. *Mental state:* "She appeared dull, confused and retarded. Her expression was heavy and bemused, as if she had been drugged, her speech was indistinct, and it was only with difficulty that she could be persuaded to answer questions. She was disorientated in space and time, and did not recognize the hospital. She resisted attention blindly, was incontinent and required hand-feeding."

Shortly after admission she ran an irregular temperature (about 100° F.) and cystitis was recognized. This condition did not clear up until 12.v.38, otherwise she showed little change, except that she became mute.

Reaction to Alcohol.

On 10.vi.38 she received 12 doses of 40% brandy orally at the rate of 15 c.c. per 5 minutes. Before the administration of alcohol she sat in a chair staring blankly ahead, was mute when questioned and did not obey simple commands. Occasionally when pressed for an answer she would give an interrogative grunt. When 105 c.c. of brandy had been consumed (that is, at the end of half-an-hour) she appeared a little flushed but could scarcely be persuaded to talk at all. However, she was persuaded to give her name and address (correctly) in a low voice. Twenty-five minutes later, that is, 55 minutes from commencing administration of the brandy, her attitude and expression suddenly changed. She appeared bright, self-assertive, and assumed a mildly antagonistic attitude. She now spoke in a loud voice to all questions. Her replies were mostly a repetition of questions asked, e.g.:

Q. "What age are you?" *A.* "What age am I—oh you are a silly!"

She would frequently repeat "You want to know that, do you?" and "Why are you asking me these questions?" Her own replies appeared to afford her much satisfaction. Once she turned suddenly to another doctor and nurse standing beside her and said, pointing to them in turn, "I know who you are; you're the doctor, and you're the nurse!" She gave her father's occupation correctly and knew important dates (beginning of Great War, etc.), but though she stated she was not at home, could not say where she was, nor give even the approximate date. When shown another ward, from the window, she said, "That's an aeroplane—now what do you want to know?" Her articulation remained unaffected, but she became slightly ataxic when walking. She had in all 180 c.c. of brandy. When put to bed she immediately fell asleep. When awakened one hour later she had reverted to her former mute and resistive state.

Reaction to Sodium Amytal.

On 19.ix.38, 3½ c.c. of 5% sodium amytal was given intravenously. When the amount had been injected she appeared very sleepy, made a few spontaneous but irrelevant remarks and exhibited some slurring of speech. She answered questions more freely than she had done when under the influence of alcohol, but was at no time easily accessible. Perseveration and echolalia were again in evidence. She was disorientated in time, but gave the name of the hospital correctly. When asked what ward she was in, she mentioned a ward she had never been in, neither on this occasion nor during her previous stay in hospital. She recognized that she had been in this hospital before, knew the name of the nurse who attended her, the nickname of a patient who was pointed out to her, the name of her last employers, etc. She gave details about the Baptist religion and her part in it,

but showed little interest in these questions, and appeared apathetic throughout most of the interview. At first she smiled foolishly at times, but later she appeared to become depressed, tears filled her eyes and the corners of her mouth drooped. She could volunteer no reason for this.

Case 22.

A. E. B—, single, aged 24 on admission on 12.viii.31.

Family history: Father committed suicide when patient was 3 months old. Had had a head injury at work, 9 months before his death. Apart from a hasty temper he was said (by his wife) to have been a good husband. Habits moderate. He had not appeared depressed after the head injury.

Mother: Alive and well. No nervous or mental illness.

Paternal aunt died in Banstead Mental Hospital.

Siblings: Two sisters insane and in mental hospitals. One brother died at birth.

Personal History.

Normal birth and development. School: Reached top standard at 14. A good scholar, but mischievous. Worked as motor-body builder from 14 until 21, when he joined the army. Was engaged to a professional dance-partner, who jilted him, and this was the reason for his joining the army. Personality was described as often jolly, lively, had lots of friends, was ambitious and daring. He was an amateur exhibition dancer and a crack billiard player. Never stayed at home except to eat and sleep. He had a quick temper, but was neither vicious nor sulky. Nine months after joining the army his mother was notified that he had been transferred to a military hospital and was suffering from encephalitis lethargica. He was sent home 1 month later. He lived at home for 2½ years. From the first he was dull, "sleepy", but flew into violent tempers at times, in which he lost all control of himself. He was sullen, brooding, felt inferior and shunned his former friends. He took long solitary walks, never asked for food, but ate whatever was given him. When not in a rage he was "extremely suggestible". He was eventually admitted to Winchmore Hill Colony (for chronic encephalitics) but was found too difficult to control, and was sent to an observation ward and thence to West Park Hospital. At Winchmore Hill no signs of encephalitis lethargica could be found. We also found no evidence of this disease or its sequelæ.

On admission: *Physical state:* Nothing abnormal detected except evidence of rheumatic carditis. *Serum Wassermann:* Negative. *Mental state:* "He is dull and apathetic, shows no interest in his surroundings and is disorientated in time and space. He states that he can hear his father telling him not to steal. He is at times incontinent of urine, cannot be employed, and requires prompting to wash and dress. His conversation is irrelevant and accompanied by foolish smiling."

The following abstracts of notes indicate his progress in hospital:

12.xii.31: He has had a course of injections of sulfosin given intramuscularly, commencing at 1 c.c. and increasing to 7 c.c.; these were given every fourth day for a total of 8 injections (see McCartan (1), already quoted). No change in his mental state was observed. He remains dull and disinterested. He states that he has been here 3 weeks.

12.iv.32: He is incontinent of urine and fæces, detached from his environment, and appears to be actively hallucinated aurally. His conversation is totally irrelevant. He states that he is in Japan, and gives the date as April, 1911.

1.vii.33: He shows no change except that he is almost mute. Occasionally he repeats, "I am dead".

16.ii.34: No change except that he has been taught to work in a mechanical manner on the farm.

12.viii.36: He is now completely mute.

Reaction to Sodium Amytal.

He had to date been practically mute since 1.vii.33, and completely mute for over a year when the injection was given. On 17.xi.37 he received 7 c.c. of 5% sodium amytal intravenously. He remained apathetic and disinterested and did not speak spontaneously. On being questioned he answered disinterestedly in a low voice. He was correctly orientated in space and for person, could give the name of his ward and the names of his nurses correctly, and knew the doctor. His replies were monosyllabic, and he relapsed into mutism within an hour.

Reaction to Alcohol.

On 21.xi.38 he received 255 c.c. of 40% brandy orally at the rate of 15 c.c. per 5 minutes. He vomited once after this amount had been given, and administration was therefore discontinued. He remained automatically obedient throughout, but did not speak. When given a pencil and paper he wrote in reply to questions. He did so slowly and without interest, and after writing a few replies ceased to do so on command, instead staring blankly at the questioner. Occasionally he gave a sudden short laugh for no apparent reason. He was a little ataxic when walking. The following written answers were elicited :

Q. " What is your name ? " *A.* "A. E. B—."
Q. " What is your home address ? " *A.* " 7 . . . ." (Correct.)
Q. " Do you feel sick ? " (He had just vomited.) *A.* " No."
Q. " What is the name of your ward ? " *A.* " J. Ward." (Correct.)
Q. " What is the name of this building ? " *A.* " Donans Slacle." (Unintelligible ; he would not repeat this.)
Q. " What is the date of your birthday ? " *A.* " 1st December." (Unconfirmed.)

GROUP IV.

Case 23.

R. M—. Single, aged 39, admitted on 14.ix.36.
Heredity : Father, aged 66, healthy until war. Served in army and was treated for " neurasthenia ". Has a war pension on this account.
Symptoms : Depression and outbursts of temper.
Paternal grandparents : Dead. Nothing known.
Paternal siblings : All alive (5) and healthy. Most of them abroad.
Mother : Aged 65. Very healthy.
Maternal grandparents : Dead. Healthy.
Maternal sibling : One brother alive, and has always been healthy.
Patient's siblings : Patient is second child of ten. Two died of tuberculosis in their 'teens ; four married with children ; healthy ; three single ; living at home ; healthy.

Personal History.

Apparently a normal boy. Left school at 14 from top form. Worked as van guard on Southern Railway until 18. Joined army at 18 and fought in the Great War. Went to Australia for 2 years (Government emigration scheme), and then went to Canada after the war (labourer). Returned from Canada in December, 1933, and it was then remarked by his family that he " appeared very quiet and had peculiar ideas on religious matters ". Quarrelled with father and left the home a few weeks after arrival. Shortly before admission he was arrested for " wandering at night with intent to commit a felony ", and was then found to be psychotic.

Reaction to Cardiazol.

A course of injections of a 10% aqueous solution of cardiazol was given as tabulated below :

Date.	Dose in c.c.	Duration of time in seconds from completion of injection to onset of fit.	Duration of fit in seconds.	No. of fit.
21.ii.38	4	No reaction	..	..
2 mins. later	4	,,	..	..
,, ,,	5	33	81	1
23.ii.38	7	17	75	2
25.ii.38	7	18	58	3
28.ii.38	7	13	63	4
2.iii.38	9	19	70	5
4.iii.38	9	15	80	6
7.iii.38	9	17	69	7
9.iii.38	9	25	60	8
11.iii.38	9	15	58	9
14.iii.38	9	18	65	10
16.iii.38	9	19	58	11
18.iii.38	9	20	60	12
21.iii.38	9	20	50	13
23.iii.38	9	15	65	14
25.iii.38	9	20	75	15
28.iii.38	9	15	58	16
30.iii.38	9	23	72	17
1.iv.38	9	No reaction	..	..
2 mins. later	5	,,	..	..
,, ,,	5	19	55	18
4.iv.38	10	18	67	19
6.iv.38	10	15	55	20
9.iv.38	10	18	71	21
11.iv.38	10	12	60	22
13.iv.38	10	10	63	23
15.iv.38	10	28	78	24
18.iv.38	10	20	70	25
20.iv.38	10	15	55	26
23.iv.38	10	No reaction	..	..
2 mins. later	5	,,	..	..
,, ,,	5	14	75	27
25.iv.38	11	18	58	28

After he had had 10 injections he showed a remarkable improvement and at that period I made the following note :

> " He shows a definite improvement. Orientation is correct, conversation is rational, and there appears to be no amnesia either for remote or recent events. He has not been impulsive or manneristic since commencing cardiazol treatment and is now working well and very willingly in the ward. He is no longer sullen, smiles readily, and though still lacking in insight, appears to realize that the injections, against which he at first rebelled vigorously, are part of his treatment."

Unfortunately this improvement lasted but a few weeks, and after completion of the injections he became very impulsive and reverted to the sullen, uncommunicative attitude previously noted. His violent attacks on other patients became more pronounced, and on one occasion he fractured his 5th right metacarpal bone when striking another patient. He ceased to work, and had frequently to be confined to bed as a result of his restlessness.

Pre-psychotic Personality.

Quiet, reserved, suspicious. Did not make friends. Apt to sulk and given to violent flares of temper.

On admission: *Physical state:* Nothing abnormal detected. *Serum Wassermann:* Negative. *Mental state:* "He was dull, appeared absorbed in phantasy, and would occasionally turn his head as if listening to voices. On occasions he was hostile, suspicious and aggressive. He was corectly orientated, but could give no connected account of himself. He answered simple questions correctly, but volunteered no remarks. He was frequently noticed to grimace and mutter to himself."

The following abstracts from notes indicate his progress:

6.xii.36: Abstracted, untidy in dress. Actively hallucinated. Fights with other patients.

15.ii.37: Is sullen and rarely replies to questions. During the interview he suddenly replied to hallucinations. Cannot be persuaded to occupy himself in any work. Has thrice attempted his escape.

15.v.37: Is now doing a little routine work in the dormitory, but otherwise shows no change.

14.vi.37: Impulsively attacked a nurse.

15.x.37: Frequently smashes windows, attacks others, destroys his clothing. Replies in monosyllables when questioned and appears sullen and suspicious.

Case 24.

A. F. G—, aged 24, single, admitted on 3.ii.33.

Heredity: Father, aged 55. Healthy.

Paternal grandfather: Nothing known.

Paternal grandmother: Died aged 81; always healthy.

Paternal siblings: One brother died in Colney Hatch over 20 years ago. Two brothers, both alive, aged 69 and 70; very healthy.

Mother: Aged 62, alive, suffers from asthma; otherwise healthy.

Maternal grandfather: Died of bronchitis and asthma; otherwise healthy.

Maternal grandmother: died of bronchitis and asthma; otherwise healthy.

Maternal siblings: Two brothers, one sister, all dead. One brother stillborn. One brother died, aged 13—"cerebral abscess". Sister, aged 3 weeks, killed by accident.

Patient's siblings: Sister dead, aged 14—rheumatic fever.

Personal History.

Birth, labour prolonged and difficult. Development: Normal except speech, delayed to 3 years. Taught in special school; very mischievous. On leaving school became an hotel porter.

Pre-psychotic personality: Obstinate, impulsive and erratic. Did not make friends, and was aggressive when meeting strangers. He never in his life had a boy friend. He was fond of cinemas and watching football matches.

History of Present Illness.

One week before admission to observation ward he developed "a bad attack of influenza", during which he became violent and excited. No symptoms had been noticed before.

On admission: *Physical state:* Nothing abnormal detected. *Serum Wassermann:* Negative. *Mental state:* "He weeps at times, appears disinterested in his surroundings and requires prompting to eat. His speech is rambling and irrelevant. He states that he has 'blood-pressure due to rushing to work', and that this has resulted in 'fracturing the brain'. He states that his fellow employees were Greeks and that he has contracted 'their disease'. He says 'it is in my mind that I have murdered a Mr. Carr', but cannot explain this statement. He is afraid that he is killing his fellow patients with his breath."

The following abstracts of notes indicate his progress in hospital :

6.iii.33 : He is tearful, agitated and confused. He addresses the nurse as " chef ", and he states that over-work has affected his brain. He is restless, and continually attempts to get out of bed. He says, " I am not educated enough ; it is my father's fault ; he made me eat too much ".

5.xi.33 : He is now dull and uncommunicative. It is difficult to elicit an answer from him, and when one does succeed, his replies are irrelevant. He is at times impulsive. He cannot be persuaded to occupy himself in any way.

31.xii.34 : He is incontinent of urine and fæces, practically unemployable, dull and apathetic.

3.vii.36 : He never speaks spontaneously, and will only reply in monosyllables. He is at times impulsive. Unemployed and untidy.

3.ii.38 : Still at times incontinent. He cannot be employed.

Reaction to Cardiazol.

A course of intravenous injections of 10% cardiazol was given, as tabulated below :

Date.	Dose in c.c.	Duration of time in seconds from completion of injection to onset of fit.	Duration of fit in seconds.	No. of fit.
4.iii.38	5	25	75	1
7.iii.38	5	22	82	2
9.iii.38	5	15	40	3
11.iii.38	5	15	46	4
14.iii.38	6	15	64	5
16.iii.38	6	18	55	6
18.iii.38	6	15	50	7
21.iii.38	6	20	24	8
23.iii.38	6	10	75	9
25.iii.38	6	30	70	10
28.iii.38	6	14	55	11
30.iii.38	6	20	70	12
1.iv.38	6	17	64	13
4.iv.38	6	19	78	14
6.iv.38	6	10	65	15
9.iv.38	6	15	74	16
11.iv.38	6	No reaction	..	..
2 mins. later	6	,,	..	..
13.iv.38	7	12	60	17
15.iv.38	7	27	81	18
18.iv.38	7	20	40	19
20.iv.38	7	15	55	20
23.iv.38	7	17	58	21
25.iv.38	7	No reaction	..	..
2 mins. later	5	,,	..	..
27.iv.38	8	12	78	22
30.iv.38	8	No reaction	..	..
2 mins. later	5	,,	..	..
,, ,,	5	23	60	23
2.v.38	5	No reaction	..	..
2 mins. later	5	,,	..	..
,, ,,	5	18	58	24
4.v.38	8	15	75	25
7.v.38	9	14	53	26
10.v.38	9	No reaction	..	..
2 mins. later	5	20	63	27
12.v.38	10	15	64	28

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For about two months following cardiazol his conduct and appearance changed. He became curiously restless and fidgety, but this activity could be utilized to the extent of getting him to sweep the floor. His facial expression became bright and alert, and if called from one end of the ward he would run up to one quickly and wait in an attentive manner. He spoke freely, but his answers were as irrelevant as they had formerly been, and he was completely disorientated. For example, he stated that he had been here 24 years, and gave the present date as 1908. His habits became cleaner, but he required to be ordered to dress, and to wash. Within two months of cessation of treatment he was observed to be more stuporous, and within three months of the last injection he was again untidy, dull and unemployed.

CASE 25.

F. F— [1], single, aged 22 on admission on 3.xii.29.

History defective. Mother alive. Said to have suffered from (? hysterical) aphasia for 13 years.

Father alive and well.

Paternal grandmother died of " brain trouble ".

Personal History.

Patient reached standard VII at school and worked for 4 years, first as a tailors' porter and then as a grocers' assistant. Since 18 he had had only odd jobs. Personality described as " unfriendly, irritable and obstinate ; sleepy and brooding ". Since March, 1928, had complained of violent headaches and insomnia. He was brought by his sister to the Maudsley Hospital Out-Patients' Department on 6.xi.29. The history given by his sister suggested that he was suffering from schizophrenia, which had been developing for 3 to 4 years. She described his conduct as erratic ; that he had a vague feeling that people were against him. She said that he slept late, and walked the streets by day.

On admission : *Physical state :* Nothing abnormal detected. *Serum Wassermann :* Negative. *Mental state :* " He lies in bed alternately smiling and frowning, and answers questions in an off-hand manner, often irrelevantly. When questioned on the subject of his conduct outside, he said, ' It is quite fashionable for people to walk in the West End of London at night in 1929 ! ' He boasts in a childish manner of his gambling habits, and his success at ' rummy ' (a card game). He appears to lack any insight into the nature of his illness, and shows no interest in his surroundings or associates."

He was at first dull, slovenly and unemployable, but gradually commenced to take a little more interest, and by 1.vii.30 had been put on parole and was doing a little work. He still smiled inappropriately, was rather dull, and did his work in a slipshod fashion. However, on 8.x.30 he was allowed to go home, his parents having applied for him under Section 79 of the Lunacy Act. On 20.viii.31 he was again brought to the Maudsley Out-Patient Department. His relatives stated that since returning home he had resumed his nocturnal wanderings and had become increasingly careless in washing and dressing. He had never troubled even to go to the Labour Exchange to find work. When seen at the Out-Patients' Department he stated ' that he felt at a loose end ', and then bent forward, picking his nails and laughing quietly. He was admitted to West Park Hospital on 1.ix.31.

On admission : *Physical state :* Nothing abnormal detected. *Serum Wassermann :* Negative. *Mental state :* On admission he was able immediately to work in the upholsterer's shop, and played football. He was, however, very apathetic and disorientated, careless of his dress, and would not wash unless told to do so. By 7.i.32 he was " not working so well, becoming more unsociable, untidy and

listless. States his plans for the future are very indefinite". By 1.iii.34 he was "no longer fit for work in the upholsterer's shop, and does little work in the ward. When interviewed he sits with bowed head, fidgeting with his hands. Replies to questions are elicited with difficulty, and he mumbles his words in a low voice. He states that he wishes to remain here, but cannot carry on a connected conversation". He says "this is a nice place, a home from home". And on 1.ix.34 a note states "he now never speaks spontaneously, is slovenly, cannot be employed in any way and is almost inaccessible, replying in monosyllables".

Reaction to Cardiazol.

A course of injections of 10% cardiazol was given as tabulated below:

Date.	Dose in c.c.	Duration of time in seconds from completion of injection to onset of fit.	Duration of fit in seconds.	No. of fit.
9.ii.38	5	15	60	1
11.ii.38	5	No reaction	..	..
2 mins. later	5	,,	..	..
,, ,,	5	20	54	2
14.ii.38	7	15	55	3
16.ii.38	7	No reaction	..	..
2 mins. later	5	,,	..	..
,, ,,	5	13	66	4
18.ii.38	9	23	76	5
21.ii.38	9	17	67	6
23.ii.38	9	20	75	7
25.ii.38	9	12	62	8
28.ii.38	9	16	57	9
2.iii.38	9	14	72	10
4.iii.38	9	20	70	11
7.iii.38	9	15	73	12
9.iii.38	9	10	45	13
11.iii.38	9	No reaction	..	..
14.iii.38	10	13	74	14
16.iii.38	10	No reaction	..	..
2 mins. later	6	,,	..	..
,, ,,	5	15	56	15
18.iii.38	12	13	70	16
21.iii.38	8	No reaction	..	..
2 mins. later	8	Not recorded	..	17
23.iii.38	10	,,	..	18
26.iii.38	10	,,	..	19
28.iii.38	10	,,	..	20
30.iii.38	10	,,	..	21
1.iv.38	10	,,	..	22
4.iv.38	10	,,	..	23

After his ninth fit his mental state showed some improvement, which was maintained for 10 days. During this time he worked in the dormitory, and attended to his personal needs. He also answered questions, but was dull and abstracted. He could hazard no reason why he was receiving injections. After the subsequent injections he became excitable and over-active. He talked freely but incoherently. After each injection he became confused for about half an hour. After the completion of the course he gradually reverted to his former mute and stuporous condition, but for about a month aimless, unproductive over-activity persisted.

CASE 26.

J. E. F—, married, aged 32 on admission on 17.ix.30.

Heredity: Father died aged 71—" cancer ", otherwise healthy.

Paternal grandparents: Nothing known beyond the fact that they were " healthy Irish peasantry ".

Paternal siblings: Three brothers and one sister all alive and healthy.

Mother: Alive and well, aged 73. No illness except arthritis during the past year.

Maternal grandparents: Healthy; died of " old age ".

Maternal siblings: Two sisters and two brothers, married and healthy, with families.

Patient's siblings: One sister, married, healthy, no illnesses.

Personal History.

Birth and development normal. Rather nervous as a child. A very good scholar and reached standard VII easily. Was a dispatch clerk in P.O. until he joined Army at 17¼ years. Taken prisoner in Germany. Had shrapnel wounds of thorax necessitating many operations. Transferred to Du Cane Road Hospital after the war, and was discharged from there in 1923. Married in 1924. The girl's parents insisted on this, stating that she was pregnant by him. When married he discovered she already had two children. She left him after one year and he returned to his mother.

Pre-psychotic Personality.

A great reader—" travel, biography, science ". Sociable, good-natured, never moody. The " sort to turn to in an emergency ".

History of Present Illness.

At 26 he returned from the war and after numerous operations " a nervous wreck ", apparently aurally hallucinated about religion. Never found work and was supported by his mother. Eventually he became more excitable, caused a disturbance in a neighbour's house and was removed by the police.

On admission: *Physical state:* Nothing abnormal detected. *Serum Wassermann:* Negative. *Mental state:* "He is quiet and well behaved; appears mildly depressed. He gives the following evidence of delusions and hallucinations. He states that he is responsible for the Wall Street crash, and that people coughed at him in the street and tried to play on his imagination, because they thought he was a 'Hell Genius'. He says that if he mentions anyone's name they are 'done to death' on the following day by some evil influence. He states that the patients here call him 'Jesus'; that he has a dictaphone which carries messages to him and conveys his thoughts to other people; tunes are whispered to him and 'he whispers tunes back. He states that he has spoken to the Chancellor of the Exchequer on this dictaphone, warning him of the danger of increasing the bank rate."

The following abstracts of notes indicate his progress in hospital:

1.x.30: He is solitary, unsociable and depressed.

17.i.31: He is dull and apathetic, takes no interest in his personal appearance or in the social life of the ward, but does a little work.

19.v.31: His speech is irrelevant and he appears depressed. When asked what he will do when he gets better he replies, " Get into my coffin, I suppose ". He relates an involved story of how he " made tunes for His Master's Voice Gramophone Company ". He is correctly orientated in time and place.

24.vi.31: To-day he attempted to swallow some ground-up china. He did not at the moment appear depressed, and the act had the aimless character of the schizophrenic.

4.vii.31: Impulsively threw a commode across the dormitory.

18.viii.31: He is inconsistent in his emotional responses; for example, he states that he "is rotten right through", yet laughs foolishly as he makes the remark.

18.viii.32: He appears foolishly self-satisfied, yet makes such remarks as "I would like to jump under a car", "I hear voices coming from London", etc.

17.iii.36: Dull, irrational individual, continually hallucinated. He states: 'Voices tell me to get rid of my syphilis and used to tell me to commit suicide; my head is full of syph."

17.iii.37: He is apathetic, poorly orientated, and his conversation is irrational and disconnected. As a rule he is unemployable. He says: "They cover me with syph—that is the second song—the voices tell me to do myself in, to get rid of it—I want an application for Jesus."

Reaction of Cardiazol.

Date.	Dose in c.c.	Duration of time in seconds from completion of injection to onset of fit.	Duration of fit in seconds.	No. of fit.
15.iv.38	5	21	75	1
18.iv.38	5	27	65	2
20.iv.38	4	25	65	3
23.iv.38	4	50	55	4
25.iv.38	5	32	63	5
27.iv.38	5	25	75	6
30.iv.38	5	28	52	7
2.v.38	5	20	62	8
4.v.38	5	15	78	9
7.v.38	5	18	Not recorded	10
10.v.38	5	No reaction	..	..
2 mins. later	5	25	Not recorded	11
12.v.38	6	No reaction	..	..
2 mins. later	5	12	75	12
14.v.38	7	13	57	13
19.v.38	7	15	60	14
21.v.38	7	17	76	15
23.v.38	7	19	74	16
25.v.38	7	19	61	17
29.v.38	7	No reaction	..	..
2 mins. later	5	,,	..	..
,, ,,	3	20	63	18
2.vi.38	9	18	74	19
4.vi.38	9	19	62	20

During treatment and for about a fortnight after cessation of treatment he became hostile, garrulous and over-active. His activity, however, could not be utilized in any productive way. He frequently demanded his discharge, and became threatening when this was refused.

CASE 27.

A. F. B—, single, aged 29 on admission on 22.xi.34.

Occupation: Motor upholsterer.

Heredity: Father dead, aged 68, pneumonia; no mental illness or psychopathic traits.

Paternal grandparents: Healthy; both died "over 80".

Father's two brothers, when last heard of, some years ago, were healthy and well adapted to life.

Mother: Died at Banstead Mental Hospital after 10 years' residence—"melancholia". Onset had been gradual for 6 years before entering hospital.

Maternal grandparents: Healthy; both died "over 80". One maternal sister alive: no mental illness.

Patient has three brothers, all alive and well, with no psycopathic traits.

Personal History.

Defective. Birth and development normal. A healthy child. At 10 years of age he went to live with his maternal aunt. On leaving school he became a motor unholsterer. At 23 years of age was admitted to Bodmin Mental Hospital. He spent two years in hospital, was one year at home and then returned to Bodmin, whence he was transferred to West Park on 22.xi.34.

Pre-Psychotic Personality.

Was said to have been reserved and moody, good natured, but inclined to sulk. Was said to have "become gradually depressed".

On admission: *Physical state:* Nothing abnormal detected. *Serum Wassermann:* Negative. *Mental state:* "He appears dull and stares around in an uncomprehending fashion; he is incontinent of urine, and is resistive to every attention, requiring to be dressed, washed and hand-fed. His resistance is of a mild and aimless character, he rarely speaks, and when he does, perseverates, 'I must apologize—I must apologize' again and again, until his voice trails off into a whisper."

The following abstracts of notes indicate his progress in hospital:

22.i.35: He alternates between a phase of stupor—when he is mute, inaccessible and mildly resistive, appearing apprehensive and confused when questioned—and a phase when he will answer questions (usually irrelevantly), shows marked disconnection of thought, with blocking, but has been found to be correctly orientated.

30.vii.35: Is now almost totally inaccessible, perseverating all questions addressed to him.

24.x.35: Is now working in a mechanical fashion on the farm. He lacks any insight into the nature of his illness, and states that he came here because his employer's brother lives here (untrue). Still exhibits marked perseveration and blocking of thought.

22.xi.35: He is completely disinterested in his environment, rambles incoherently about events connected with his mother's death, smiling frequently as he does so, and perseverating. He states that he has met me somewhere before.

23.xii.35: He is in a restless phase and appears mildly confused. It is almost impossible to gain his attention. When one succeeds in doing so he answers simple questions relevantly, but to most he replies with the same remark, viz., "I didn't sleep well last night; I can't shave myself". He perseverates this remark, scratches his head, rubs his face, and presents a general appearance of bewilderment. He is at present unemployable.

29.xi.36: Even in his "lucid phases" he is now not properly in touch with his environment. In his confused, stuporous phases he does not appear to comprehend speech. He will now always obey simple commands, and even in his most stuporous phases takes his food without prompting. Still unemployable.

22.v.37: Still alternately stuporous and relatively accessible. These alternations occur about once a fortnight. Often in his stuporous phases flexibilitas cerea can be demonstrated.

Reaction to Cardiazol.

Date.	Dose in c.c.	Duration of time in seconds from completion of injection to onset of fit.	Duration of fit in seconds.	No. of fit.
21.ii.38	4	16	79	1
23.ii.38	4	23	80	2
25.ii.38	4	No reaction	..	..
2 mins. later	5	13	65	3
28.ii.38	9	14	62	4
2.iii.38	9	8	61	5
4.iii.38	9	15	65	6
7.iii.38	9	14	71	7
9.iii.38	9	20	45	8
11.iii.38	9	No reaction	..	..
14.iii.38	9	13	64	9
16.iii.38	9	18	55	10
18.iii.38	9	15	60	11
21.iii.38	9	15	60	12
25.iii.38	6	Anxiety state	..	..
28.iii.38	6	13	48	13
30.iii.38	6	17	22	14
1.iv.38	6	No reaction	..	..
2 mins. later	5	16	52	15
4.iv.38	7	No reaction	..	..
2 mins. later	5	22	28	16
6.iv.38	8	15	55	17
9.iv.38	8	18	77	18
11.iv.38	8	14	59	19
13.iv.38	8	14	55	20
15.iv.38	8	17	69	21
18.iv.38	8	22	74	22
20.iv.38	8	20	70	23
23.iv.38	8	12	65	24
25.iv.38	8	No reaction	..	..

During the first part of the course he showed a marked improvement, worked well in the ward, and was more rational and relevant in his conversation than he had been since his admission. He showed a marked press of activity and a desire to converse with the nursing staff, who were much impressed with this desire to co-operate and with his conversation. During the latter part of the course he became confused, mute, and was quite unable to concentrate on the simplest tasks. After the course was completed he reverted to his former stuporous, phasic state.

CASE 28.

W. R—, single, aged 23, admitted on 27.iii.28.
Occupation: Fitter in engineering trade.

Previous History.

Was intelligent at school, reaching 7th standard at 12. Temperament was described as "excitable, brooding, sullen and obstinate". Worked up to 1926. Since that time had been unable to obtain work. After being unemployed for six months he became suspicious of others, depressed, and stated that "everyone was against him". Five months before admission he became very unsettled and threatened violence to his parents.

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On admission: *Physical state:* Nothing abnormal detected. *Serum Wassermann:* Negative. *Mental state:* On admission he was in a state of confusion, with marked clouding of consciousness and disorientation. He misidentified those around him, was aurally hallucinated, grinned and grimaced and spoke irrelevantly.

He commenced to work well in the ward under supervision, but remained hallucinated, was very manneristic, and though he became less confused, and correctly orientated in place and time, was always uncertain to whom he was speaking. He was occasionally impulsive, fighting with other patients, would at times stand for long periods with his eyes shut, and was never able to hold a conversation without showing blocking of thought and interjecting irrelevancies. His facial expression was always one of bewilderment, and when addressed he would start in a frightened manner and stammer out an answer. This fearful, perplexed attitude has not diminished to date (1938).

Reaction to Cardiazol.

Date.	Dose in c.c.	Duration of time in seconds from completion of injection to onset of fit.	Duration of fit in seconds.	No. of fit.
15.iv.38	5	26	73	1
18.iv.38	5	No reaction	..	..
2 mins. later	5	24	26	2
20.iv.38	6	30	65	3
23.iv.38	6	No reaction	..	..
2 mins. later	5	,,	..	..
,, ,,	5	40	56	4
25.iv.38	7	No reaction	..	..
2 mins. later	5	,,	..	..
,, ,,	5	35	56	5
27.iv.38	8	23	79	6
30.iv.38	8	14	72	7
2.v.38	8	19	78	8
4.v.38	8	No reaction	..	..
2 mins. later	5	16	40	9
7.v.38	9	12	43	10
10.v.38	9	15	65	11
12.v.38	9	35	87	12
14.v.38	9	11	35	13
19.v.38	9	15	42	14
21.v.38	9	18	68	15
23.v.38	9	No reaction	..	..
2 mins. later	5	,,	..	..
,, ,,	5	24	Not recorded	16
25.v.38	9	20	72	17
29.v.38	9	20	65	18
2.vi.38	9	20	Not recorded	19
4.vi.38	9	20	70	20

During the period in which cardiazol was being administered he became more acutely confused, restless and unable to work. He was observed for the first time in hospital to give expression to delusional ideas, and for a short time insisted that he was pregnant.

CASE 29.

T. E. G—, single, aged 25 on admission on 7.ii.27.

History defective. Was clever at school and reached ex-VIIth at 13. As a boy suffered from periodic violent headaches. His father described his disposition as

"restless, brooding, indifferent and sleepy". He never kept a job for any length of time, and had had 30 jobs up to date of admission—railway porter, barman, builder's labourer, etc. For one year before admission he had been depressed and had expressed thoughts of suicide.

On admission: *Physical state:* Nothing abnormal detected. *Serum Wassermann:* Negative. *Mental state:* "He was dull and apathetic, but did not appear to be depressed. He spoke freely, but was unable to separate fact from phantasy, and related absurd stories, e.g., that he was an important personage who had been changed at birth."

Reaction to Cardiazol.

A course of injections of a 10% aqueous solution of cardiazol was given as tabulated below:

Date.	Dose in c.c.	Duration of time in seconds from completion of injection to onset of fit.	Duration of fit in seconds.	No. of fit.
15.iv.38	5	23	71	1
18.iv.38	5	30	72	2
20.iv.38	5	No reaction	..	..
2 mins. later	5	25	60	3
23.iv.38	6	No reaction	..	..
2 mins. later	5	,,	..	..
,, ,,	5	45	65	4
25.iv.38	7	No reaction	..	..
2 mins. later	5	,,	..	..
,, ,,	5	55	87	5
27.iv.38	8	24	72	6
30.iv.38	8	No reaction	..	..
2 mins. later	6	,,	..	..
,, ,,	5	Not recorded	Not recorded; "petit mal"	7
2.v.38	8	14	63	8
4.v.38	8	No reaction	..	..
2 mins. later	5	25	53	9
7.v.38	9	13	49	10
10.v.38	9	26	67	11
12.v.38	9	23	65	12
14.v.38	9	No reaction	..	..
19.v.38	9	25	55	13
21.v.38	9	22	73	14
23.v.38	9	25	85	15
25.v.38	9	24	76	16
29.v.38	9	16	62	17
2.vi.38	9	21	66	18
6.vi.38	9	18	65	19

During treatment apathy gave place to restlessness. For example, on getting up in the morning he would rush past other patients from the dormitory into the day-room, whereas before he was most lethargic on rising. In spite of this constant press of activity he could do little work although willing; he apparently found it impossible to concentrate. He was impulsive and irritable, frequently being involved in fights with other patients. A few days after cessation of treatment he relapsed into his former stuporous state. Dislocation of the jaw occurred on three occasions during fits.

His stay in hospital was short, and the following abstracts show his progress:

28.ii.27: Has improved, is working well and on "ground parole".

7.v.27: Sociable, but still dull. Regards his delusions in a detached manner and appears unconcerned as to whether they are true or not.

20.vii.27: Discharged "without insight", but expresses no delusions.

He was readmitted on 3.vii.30. Note on admission: "He is now mildly depressed and anxious. He states that persons in his neighbourhood were passing remarks about him, and that he heard them say, 'He is a mandarin, and an Indian prince'. He still regards himself as an adopted child and has of late been antagonistic towards his father. He relates his delusions in an indifferent manner."

The following abstracts of notes show his progress:

18.xi.30: Is now working in the ward and correctly orientated, but still deluded.

2.ii.31: He now states that other patients make unpleasant remarks about him, e.g., "See how he works when the woman is in him". He smiles vaguely. Dull, but working well.

24.iii.31: Delusions persist, but he only expresses them when closely questioned.

27.v.32: States that his former workmates conspired to make him miserable. He is dull, but works well. Complains that "voices" persecute him at night.

5.xi.34: Impulsively attacked a nurse. His first impulsive outburst.

27.v.37: Leads an automatic existence. He never speaks spontaneously, but when questioned talks incoherently of "television", "elastic knives", and "secret service". He is disorientated in time.

3.i.38: Very dull and disinterested; requires much persuasion to work. Does not speak spontaneously, and when questioned, only in monosyllables.

Case 30.

J. S. G—, single, aged 20 on admission on 11.xi.32.

Occupation: Carpenter's improver. No history of insanity in ascendants.

History defective. Said to have been an "average boy" at school and left from VIth standard, aged 14. No previous illness. Was a "reserved" type with "steady" habits of life, and ambitious. For a year previous to admission had frequently been unemployed and had worried greatly. He ceased to interest himself in every-day affairs and became more untidy in his habits.

On admission: *Physical state:* Nothing abnormal detected. *Serum Wassermann:* Negative. *Mental state:* "Conversation with him is almost impossible. He sits about all day in a state of gross self-absorption, and questioning elicits no more than a halting and listless, partial repetition of the questions asked. Hand-feeding is necessary, but he is not incontinent.

The following abstracts of notes indicate his progress:

11.i.33: Mute and inaccessible, but will now work in the ward under supervision.

11.vii.33: Still mute, but is working well in a mechanical fashion. Not impulsive.

10.x.33: Occasionally he smiles foolishly, but remains mute. Working well, but sits about disinterestedly when not employed.

11.i.34: Will now talk at times, and then answers simple questions relevantly, but without evincing any interest. At other times no amount of effort will make him speak. He is prone to impulsive behaviour, occasionally striking other patients.

10.x.36: Will now always answer simple questions; is correctly orientated in space, but disorientated in time, without insight into the nature of his illness, and is unconcerned as to whether he remains in, or is discharged from hospital. He works well in an automatic fashion; states he is contented, but appears to have auditory hallucinations, as he will occasionally swear profanely at invisible enemies.

Obeys every command promptly and automatically. If stopped working will stand in one position for long periods.

He showed no further change until cardiazol was commenced on 21.iii.38.

Reaction to Cardiazol.

Date.	Dose in c.c.	Duration of time in seconds from completion of injection to onset of fit.	Duration of fit in seconds.	No. of fit.
21.iii.38	5	18	78	1
23.iii.38	5	25	75	2
25.iii.38	5	No reaction	..	..
2 mins. later	5	15	50	3
28.iii.38	6	No reaction	..	..
2 mins. later	7	12	53	4
30.iii.38	7	No reaction	..	..
2 mins. later	5	,,	..	..
,, ,,	5	15	65	5
14.iii.38	9	17	50	6
4.iv.38	9	17	69	7
6.iv.38	9	15	69	8
9.iv.38	9	18	75	9
11.iv.38	9	14	56	10
13.iv.38	9	18	25	11
15.iv.38	9	25	82	12
18.iv.38	9	21	72	13
20.iv.38	9	20	25	14
23.iv.38	9	17	82	15
25.iv.38	9	No reaction	..	..
2 mins. later	5	24	28	16
27.iv.38	10	22	73	17
30.iv.38	10	15	67	18
2.v.38	10	25	35	19
4.v.38	10	15	25	20
7.v.38	10	11	61	21
10.v.38	10	20	87	22

During the interval between his injections he showed a remarkable press of activity, worked furiously at jobs in the ward where previously he had worked at a moderate pace. Otherwise showed no change. From 19.v.38 until 29.v.38 however he again became very over-active and, in addition, was very difficult to manage. He broke furniture, threatened and struck other patients. On the latter date he settled down and has since been quiet.

Case 31.

H. F—, single, aged 30 on admission 27.xi.36.

Occupation: Marine engineer.

Heredity: Father in mental hospital in Scotland. Diagnosis, "schizophrenia". Six siblings all alive and without physical or mental disease.

Previous History.

A quiet reserved boy, methodical and clever at school, taking many first prizes. Trained at engineering and spent 6½ years in the British India Steam Navigation Company as fifth engineer. Supported his mother financially and took his responsibilities very seriously. Was a serious reader, especially interested in works of evolution. Seven months before admission he left his ship and settled down in lodgings in Glasgow, where he commenced to study for his "master's ticket". He was considered to have been under age for the examination. He failed three times

and was very disappointed. One month before admission he rejoined his ship to rebuild his dwindling savings. Towards the end of the month his captain reported that he had become "queer", and had refused to shave. He was sent to the Seamen's Hospital.

On admission: *Physical state:* Nothing abnormal detected. *Serum Wassermann:* Negative. *Mental state:* He showed no intellectual defect, was correctly orientated, and could converse rationally on impersonal topics. He expressed fantastic delusional ideas, however. He said, "If we are descended from apes it should be possible to cross them with Man. At the beginning of time men and women had wings, but lost them when Adam lusted for Eve. When Eve's child was born she could not feed him, because she had no breasts." He therefore sat with his thumb in his mouth and on it became imprinted the mark of the hoof! (At this juncture he exhibited his right thumb and said there was such a mark on it. No mark, however, was visible.) This, he said, proved that he (the patient) must be Cain. He exhibited many mannerisms and frequently grimaced, laughed foolishly and appeared quite unconcerned about having been brought to hospital.

He remained quiet until 8.i.37, when he suddenly became restless and impulsive, attempting to attack other patients. Prolonged baths were necessary, and occasionally he had to be secluded in the padded room for his own safety. Chemical sedation was also necessary. He became actively hallucinated, and this was obviously the reason for his behaviour, though he would not divulge what he heard. On 27.iii.37 he became incontinent of both fæces and urine, and his speech was observed to be less connected, though he retained the same delusional system of ideas. He said, "H. G. Wells got the idea from his mother that Cain was an ape". He could do little work owing to lack of concentration, due to auditory hallucinations.

On 22.x.37 his speech was extremely disconnected, but the old ideas were still present, e.g., "I am Cain", "I am 5,000 years old", etc. He was now very impulsive, attacking other patients without warning, and was completely unemployable.

Reaction to Cardiazol.

A course of injections of a 10% aqueous solution of cardiazol was given as tabulated below:

Date.	Dose in c.c.	Duration of time in seconds from completion of injection to onset of fit.	Duration of fit in seconds.	No. of fit.
16.ii.38	5	17	57	1
18.ii.38	5	20	67	2
21.ii.38	5	No reaction	..	..
2 mins. later	5	34	82	3
23.ii.38	7	20	73	4
25.ii.38	7	16	57	5
28.ii.38	7	15	56	6
2.iii.38	7	24	29	7
4.iii.38	7	15	85	8
7.iii.38	7	15	60	9
9.iii.38	7	No reaction	..	..
2 mins. later	7	20	65	10
11.iii.38	8	No reaction	..	..
2 mins. later	3	,,	..	..
14.iii.38	9	18	52	11
16.iii.38	9	18	60	12
18.iii.38	9	30	33	13
21.iii.38	10	20	48	14
23.iii.38	10	20	75	15
25.iii.38	10	No reaction	..	..
2 mins. later	3	,,	..	..
28.iii.38	10	10	52	16
30.iii.38	10	25	69	17

During the time of the first eleven injections of cardiazol he became much more quiet and improved greatly. His speech became more rational and he ceased to be impulsive, becoming instead peculiarly docile. He held his delusions, however, though he did not discuss them unless questioned. He stated that he had recently been much upset over an affair with his landlady in his lodgings in Glasgow; this lady he thought wished him to marry her. It could not be determined whether or not this was phantasy on his part. After this period he became more restless and impulsive than hitherto, and the injections were stopped for this reason. For a month after the last injection he remained very unsettled, and on one occasion suddenly stripped off his clothes and charged at one of the nursing staff in "berserk" fury.

CASE 32.

F. L. P—, single, aged 21. Admitted on 3.viii.36.

Family history: Father alive, aged 68. An obstinate, bad-tempered man, once a wheelwright, but has been unemployed and supported by his family for the past 20 years. Mother dead, pneumonia, when patient was aged 2. Said to have been "queer", and would not speak for long periods.

Maternal aunt suffered from "nervous debility".

Siblings: Two brothers and two sisters. Eldest brother was in an observation ward for 3 months, "talking nonsense" and resistive, but normal for the past 20 years. Remained normal and married.

Personal History.

Early development normal. Was first a page-boy in an hotel, but for 2 years prior to his admission had worked in a biscuit factory.

Personality.—Always inclined to be sleepy and off-handed. Was secretive, unsociable and fond of reading.

Had lived with his aunt until a year before admission, when he changed to lodgings. His landlady stated that he was very quiet, and spent most of his time when at home in tinkering with his wireless set. At times he appeared "a bit excitable" and occasionally "wet his bed". (He had had nocturnal enuresis since a child.) Just before Christmas, 1935, she observed that he was not cleaning his boots and that his trousers required repairing. At Christmas he stayed with a married sister. On Boxing Day his sister states that he was restless, "queer", and appeared delirious. A doctor was consulted and administered a sleeping-draught. He appeared normal on the following day until the evening, when he commenced to cry, apparently without reason. He was admitted to an observation ward on the following day. He was admitted to the Maudsley Hospital on 8.i.36. Here he was difficult to feed, cried continually, but would not speak. He was certified on 3.viii.36 and sent to West Park Hospital.

On admission: *Physical state:* Nothing abnormal detected. *Serum Wassermann:* Negative. *Mental state:* He is unsociable, does not speak spontaneously and appears disinterested in his surroundings. In reply to questions he frequently repeats, "I don't know". He is, however, correctly orientated and can give a few details about his past life. He states that he has had "a nervous breakdown". He does a little work in the ward. He grins to himself for no apparent reason.

Until 28.i.37 he was still apathetic and apparently not impulsive, but on that day he suddenly attempted to strangle himself with his necktie.

3.ii.37: He was described as being "almost inaccessible; he sits in a bowed attitude and grins mischievously when raised up. He still works mechanically in the ward, and attends to his personal needs".

3.v.37: "He is much worse; he is at present almost inaccessible, gives only monosyllabic replies to questions and volunteers no remarks. He requires stimulation to occupy himself and to attend to his personal needs. He appears absorbed in phantasy and to be aurally hallucinated."

2.xi.37: "He is now restless, talks incoherently, is manneristic, untidy and totally unable to concentrate on any work."

18.i.38: Impulsively attempted to strangle another patient.

3.iii.38: He appears nervous and fidgety, talks disconnectedly and irrelevantly, with many facial mannerisms. When asked why he does not look at me as I question him, he states that he is afraid I will hypnotize him.

He received a course of intravenous injections of cardiazol as tabulated below.

Reaction to Cardiazol.

Date.	Dose in c.c.	Duration of time in seconds from completion of injection to onset of fit.	Duration of fit in seconds.	No. of fit.
23.ii.38	4	No reaction	..	..
2 mins. later	5	15	62	1
28.ii.38	9	11	68	2
2.iii.38	9	19	68	3
4.iii.38	9	25	70	4
7.iii.38	9	12	72	5
9.iii.38	9	25	50	6
11.iii.38	9	11	56	7
14.iii.38	9	12	62	8
16.iii.38	9	18	52	9
18.iii.38	9	15	65	10
21.iii.38	9	15	65	11
23.iii.38	6	15	75	12
25.iii.38	6	20	25	13
28.iii.38	6	12	65	14

During the course he became extremely overactive and unsettled; it seemed impossible for him to keep still during his waking hours, and he spent the day aimlessly pacing up and down the ward, talking incoherently, and finding it impossible to concentrate on any form of work. He became progressively more confused, and treatment had to be abandoned for this reason. On discontinuing the injections he relapsed, after a few weeks, into a dull stuporous state, but was able to look after himself and do a little work.

GROUP V.

Case 33.

J. C—, single, aged 24. Admitted on 15.ii.37.

Occupation: Dentist's assistant.

Previous History.

No history of insanity in ascendants. Had been a delicate child since an attack of pneumonia, aged 2½ years, and attended only intermittently at school. Sensitive, reserved and nervous with strangers. Left school at 14, and worked as a dentist's assistant until aged 16. He then had an attack of hæmoptysis and was advised to give up his work. He remained at home from that date and never again found employment. His mother noticed a change in him from the age of 22. He no longer read books, was much more quiet than formerly and would sit for hours at a time unoccupied. He was admitted to an observation ward in 1935, "because he had commenced to think that people were talking about him and accusing him of being 'tuberculous'". He remained there for one month and was discharged on his mother's responsibility. He had shown no improvement since that time.

On admission: *Physical state:* Kypho-scoliosis of the thoracic region was present. He ran a slight evening temperature, and coughed up sputum of a foul odour in

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the mornings. Signs of cavitation were present at the base of the right lung. Diagnosis: Bronchiectasis; repeated tests showed no evidence of tubercle infection. *Serum Wassermann:* Negative. *Mental state:* "He stares vacantly ahead, takes no interest in his surroundings and is incontinent of urine. He does not eat food put before him unless prompted. He gives a few vague answers to questions at first and then becomes mute and inaccessible. He states that at home he heard 'wireless coming from all quarters', and had experimented with his own wireless set in an effort to control it. He appears to be completely disorientated."

He remained in the above state, every effort to stimulate him being unsuccessful. He would always answer the first question asked him, usually in a vague manner, and sometimes he would reply to the second, but after that he became mute, invariably for the duration of the interview. His replies were monosyllabic, and gave little guide to his mental state.

Reaction to Sodium Amytal.

On 29.viii.38 he received 5 c.c. of 5% sodium amytal intravenously. When 4 c.c. had been injected his expression changed and he appeared more alert than usual. He commenced to answer questions freely, laughed at times (he had never done so before) and appeared mildly elated. Asked where he was he replied that he was in "a V.D. ward in a Poor Law Institution". He could not give the name of the hospital, nor the date. Asked who was responsible for keeping him in hospital he replied indifferently, "Charity, I suppose". He was totally lacking in insight into the nature of his illness, stated that he liked living here and wished to remain "as long as I am no encumbrance". His spontaneous speech was disconnected and irrelevant. He misidentified those around him; thus, seeing me with a notebook in my hand, he concluded that I was "the Editor of the *Illustrated News*". Later he turned to me and said, "And how is Mrs. Older?" Asked who "Mrs. Older" was he replied, "Your wife, of course". The following is a sample of his spontaneous speech: "I saw J. McGiskey—I saw him go down two stairs—a fellow next door is a decent fellow—I'd like a spot of tea if I could—as for that beautiful violin of yours, it's far-reaching." As the nurse left the bedside for a moment he looked after him and said, "He's a curious fellow that, generous, well-meaning, but has got a false arm" (untrue). Asked if there was anything the matter with himself, he replied, "Yes, I am narrow-minded and lackadaisical". He was out of touch with current events, and was positive that George the Fifth was still alive. Asked if there were any wars in the world at present he replied, "The Uruguayians are fighting the Chinese". Though he still had a distressing cough he strenuously denied this when questioned, and appeared embarrassed when pressed for an answer. He also denied that he had once heard people accusing him of being tuberculous, but his expression belied his words. It was evident that this question about tuberculosis still called forth an affective response. He ate his tea with relish (which was unusual), and remarked how good the eggs were in this institution. About an hour and a half after the injection he drifted into stupor.

CASE 34.

F. F— [2], single, aged 21 on admission 7.vi.33.

History.

He was found wandering in a confused state. When admitted to Constance Road Institution on 31.v.33 he entered into a condition of catatonic stupor, with flexibilitas cerea. This condition changed on the following day to a semi-stuporous state, with disorientation for time and place, and amnesia for events prior to his admission.

On admission to West Park Hospital: *Physical state:* Nothing abnormal detected. *Serum Wassermann:* Negative. *Mental state:* "He is listless and abstracted, and not in any way distressed; takes but little interest in his surroundings, and is indifferent to his welfare. He gives no evidence of delusional ideas,

nor hallucinatory experiences. He states that he cannot remember well what has recently happened to himself, but gives a fair account of more remote events in a flat, colourless voice. He states that he is an orphan and has no knowledge of his parentage; that he was educated and brought up at the Camberwell Poor Law Home for Orphans. From there he was sent to the Exmouth Training Ship for 18 months, and from there he obtained work as a ship's steward in the Nelson Line. He found the heat in the tropics too much for his health, and gave up the job for this reason. While unemployed in England he had an epileptic fit, was taken to New End Hospital and from there to Edmonton Epileptic Colony, where he spent 18 months. After leaving Edmonton he joined the Army. After 6 months' service he had another epileptic fit and was discharged unfit. He travelled to London to look for work and stayed at a Salvation Army Hostel. He states that he has been there since, but admits that his memory for this time is vague. He states that his fits occur about once a year.

During his stay in hospital to date, 29.viii.38, he has had no fits. The following abstracts of notes indicate his progress in hospital:

7.vii.33: He is still dull and slow, but works well, and is excellently behaved. He has still amnesia for the period of five days between leaving the Salvation Army Hostel and entering hospital.

14.vii.33: Complained of abdominal pain yesterday. Stated he had swallowed stones and buttons and wished to die. On examination nothing definite found except slight tenderness in right iliac region.

16.vii.33: Passed *per rectum* 39 cherry-stones, 39 small pebbles, 2 bone buttons, 3 metal shirt buttons and 2 small pieces of twig.

7.viii.33: He is depressed and obsessed with ideas of unworthiness. States that he has been "doing wrong", and has not been eating his food properly, that in the past he has merely pretended to have fits, and that he is not entitled to the usual allowance of tobacco.

14.viii.33: He has suddenly become mute, resistive and inaccessible. Has to be hand-fed.

29.xi.33: Still mute and resistive. Is now incontinent of urine.

8.iii.34: Will now answer a few questions, but is totally disinterested and appears to have little appreciation of time or place. Still incontinent.

5.v.34: For the past 2 months he has done a little raffia work in a mechanical manner, but now has relapsed into stupor. He gazes ahead fixedly and pays no heed to questions. Still incontinent.

8.xii.34: Acts like an automaton, will obey commands, but is mute and requires every attention.

5.v.37: Still mute, gazes steadily ahead, and now takes no notice of commands or questions. He requires to be hand-fed. Is incontinent. Occasionally he will pick up rubbish and eat it.

Reaction to Sodium Amytal.

He was in the condition indicated by the above notes, and had been mute for over 4 years when the first injection of sodium amytal was given on 2.vii.38. 5 c.c. of 5% sodium amytal was injected intravenously. As the last cubic centimetre was being injected, his limbs, which had for many months been perfectly rigid, became quite flaccid and could be moved without encountering any resistance. He commenced to weep softly and looked profoundly miserable. At first he did not reply to questions, but at the end of an hour commenced to mutter indistinctly.

He answered a few simple questions, but for practical purposes was inaccessible. For several hours afterwards he sat up in bed moaning. He ate a full meal voluntarily (the first occasion for years). In a few hours he was again mute, negativistic and inaccessible.

It was considered that insufficient sodium amytal had been given in this case, and accordingly, on 29.viii.38, 7 c.c. of 5% solution was injected. He appeared

sleepy when 6 c.c. had been injected, and his eyes closed when 7 c.c. had been administered. He slept for 10 minutes. He was then awakened by a gentle shake, and was found to answer questions freely in a low, toneless voice. His face remained expressionless, his speech clear, and there was no evidence of slurring, nor any other evidence of intoxication. He was incorrectly orientated in time, stating that it was 1939, but was well orientated in space, knew the various wards he had been in since coming to hospital and approximate times of transference from ward to ward. He stated that he had once had fits. His speech was relevant, connected and showed no dilapidation, though some blocking of thought (about one minute) was evident. Questioned on this he said, "My wits leave me sometimes"; "I can't remember very well; I had a nervous breakdown". When questioned about his stupor, negativism, etc., he said, "I haven't got that here" (he had been transferred to another ward for the purpose of the injection); "they mesmerized me over there" (in his own ward), "a gang of fifteen of them" (he apparently referred to the nursing staff in his ward, of whom there are five). "They bullied me, and took the sight from my eyes." He stated that the injection he had just received had undone the mesmeric process, with the result that he could now see and speak. When questioned about his life he at first said that he was born in Camberwell Grove, and spoke of his parents and of a brother John, but when asked if he was certain of the truth of his statements he admitted that he had been brought up in an orphanage and that he had no knowledge of his parents; except, he added (with little show of conviction), that he "had heard that they had gone to New Zealand". Asked what he had meant by "brother John" he replied, "There is a patient in the Sanatorium (his ward) who I think is my brother; he is called Francis" (there is no such patient). He related a considerable number of facts about his life, many of which could be compared with his statements made on admission in 1933. These included accounts of his life on board training-ship and as a ship's steward, an account of a shipwreck off the coast of Spain, his period in the Army, etc. He stated that he remembers leaving the Salvation Army Hostel voluntarily, but can remember nothing between that time and his admission to hospital. He again ate a good meal voluntarily. After a few hours he gradually became mute and negativistic, his limbs again assuming their board-like rigidity.

Discussion and Conclusions.

Sodium Amytal.

Twenty-four cases of schizophrenia have received intravenous injections of sodium amytal. In the majority of cases, mutism and negativism were temporarily diminished or abolished, co-operation of varying degree was established, and the nature and extent of underlying deterioration (if any) was ascertained.

Twelve of these cases also received alcohol in varying amounts by mouth, with similar, though less marked and less enduring results than those produced by sodium amytal.

The mode of action of alcohol on the nervous system has already been shown to have been proven, and it is suggested that sodium amytal exerts its peculiar effect on catatonic stupor by virtue of a similar depressant action on the highest inhibitory (cortical) centres. Further support is given to this hypothesis by the work of Lindeman (67), who claimed that "3 to 4½ gr. of sodium amytal removed the mental tension in normal individuals, and rendered them more communicative", to such an extent that they would divulge material

which they would not willingly have done in their normal state; and by Masserman and Carmichael (68), who found that the intravenous administration of from 1 to 3 c.c. of a 10% solution of sodium amytal elicited a more complete history from uncommunicative psychotic and psychoneurotic individuals.

It will have been observed that 4 cases (W. J. R—, W. C—, G. W. B—, G. G—) responded neither to sodium amytal nor to alcohol. Bleckwenn (44) reported 4 cases out of 15 who failed to talk after the injection of sodium amytal, and Thorner (18) reports 4 cases out of 18 who failed to react to this drug. As far as I am aware, no attempt has been made to study those cases of stupor that do not react to sodium amytal. This phenomenon would appear to be very important, because if the evidence given here that sodium amytal produces its effect in catatonic stupor by virtue of its depressant action on the highest inhibitory functions is accepted, then we must assume that this type of stupor is in reality a state of excessive cortical inhibition. But if it has been observed that a small proportion of a group of stuporous patients do not react at all to this drug, the inference must be that there are at least two types of catatonic stupor. On examining these two groups of patients, one is at once impressed by the fact that the 4 non-reacting cases exhibited to a much greater extent than the remainder the phenomena of automatic obedience, and of flexibilitas cerea—in fact one might almost say in contradistinction to the remainder.

It is therefore tentatively suggested that in the former type of stupor we are dealing with cases where the functional derangement is cortical and manifests itself by overaction, or disordered action of the normal processes of cortical inhibition, and that in the latter type of case the stupor is dependent upon impoverishment or dysfunction of the central affective regions of the psyche (? diencephalic-mesencephalic regions) (69, 70, 71, 72).

Studies of the pre-psychotic personality of catatonic dementia præcox appear to support the hypothesis of excessive inhibition as the *modus operandi* of one type of catatonic stupor. Thus Blalock (73) made a study of the personality characteristics in 22 patients of the catatonic form of dementia præcox. Keeping this hypothesis of excessive inhibition in mind his remarks are, I think, revealing. He states that—"In their relations to the environment, the majority were quiet, aloof, stubborn, easily offended and had a limited range of interest . . . almost invariably they were reticent, non-self-revealing, over-conscientious and had few or no friends".

Faver (74) reported on 154 unselected cases, and stated that "Seclusiveness and seclusiveness with other traits, considering seclusiveness the predominating characteristic, forms the bulk of cases, numbering 86, or 55·9% of the total." L. E. Hinsie (75) states: "Irritability, stubbornness and seclusiveness are frequently reported to be outstanding character traits in about two-thirds of the patients."

This type of personality would appear to be one in which the normal process

of inhibition is already excessive (reticent, non-self-revealing, over-conscientious), and suggests that it may represent a biological mechanism of defence, against an environment in which the individual has met with rebuffs when he has attempted to adapt to it by outward expression. The outcome in such a constitutionally predisposed individual when the environment became intolerable would be a further increase of these inhibitory processes, resulting in abolition of psychomotor, and severe depression of sensory and vegetative functions—that is to say, a state of catatonic stupor.

The more favourable prognosis of the catatonic type of dementia præcox (76) may even be to some extent due to this process of inhibition, for it has frequently surprised workers using sodium amytal and carbon dioxide-oxygen anæsthesia in catatonic stupor to find remarkably little underlying deterioration, even after long periods of stupor.

With regard to the second type of stupor differentiated by its non-reaction to sodium amytal, it is noteworthy that the phenomenon of flexibilitas cerea could be elicited in undiminished degree up to the point of unconsciousness, and that in one case where it was particularly marked (case A. C—) it appeared to be present to a slight extent, even after the onset of unconsciousness.

This suggests that it is dependent upon infra-cortical mechanisms, and this is supported by the evidence of Ferraro (77), who has demonstrated that flexibilitas cerea produced in cats and monkeys by the injection of bulbocapnine persists in spite of the removal of the whole of the cerebral cortex and the neostriatum. He concludes by stating: "We are therefore justified in stating that experimental motor catatonia induced in animals by bulbocapnine is the result of the toxic action of the drug over areas of the central nervous system, which are not, however, either the cerebral cortex or the striatum. It is possible that the areas may be represented by some of the diencephalic or mesencephalic centres."

The suggestion is here re-stated that the stupor reaction exhibited by this group of catatonics may also depend upon dysfunction of these areas. It is probable, however, that in many of these catatonic schizophrenics there exists both a cortical and an infra-cortical dysfunction. This would account for the fact that in many cases, although some degree of accessibility was produced by sodium amytal, the underlying mental state was one of marked apathy. It is important to note in this connection that Bleuler (78) divides the phenomena of schizophrenia into physiogenic and psychogenic reactions. He states that the symptomatology can be divided into primary (physiogenic) and secondary (psychogenic) signs. Under the secondary signs he includes "autism, delusions, illusions of memory, a part of the hallucinations, negativism, stereotypies, mannerisms and most of the catatonic signs", and "as the main primary signs, both certain disorders of affectivity, and of association". The primary signs he attributes to pathological changes in the basal ganglia. Certain pathological findings and comparison with the mental picture in chronic encephalitis

support this latter view, and are well summed up by Jelliffe (79), who quotes Josephy's and Buscaino's pathological findings.

Finally, in connection with the action of sodium amytal, it is suggested that, inasmuch as this drug uncovers the underlying psychic state and extent of deterioration in cases of catatonic stupor, it may prove useful as a guide to determining whether or not treatment with cardiazol will prove effective in promoting recovery (compare cases V. W. W— and T. S— with case A. M. K—). The experience gained here is not sufficiently comprehensive to elucidate this point.

Mode of Action of Cardiazol in the Treatment of Schizophrenic Stupor.

It must be admitted that at present the cardiazol treatment of schizophrenia is purely empirical. Since we know little of the nature of epileptic convulsions, and still less about the nature of schizophrenia, it may seem rash indeed to speculate on the possible mechanism of a drug which produces marked changes in the latter disease. But if we are to advance we must form hypotheses, and above all, we must stop at times, and take stock; we must consider how much we know about the tools we are using. I stress this, because some workers in the early part of 1938, four years after the treatment had been instituted, were considering the possibility of using vasodilator drugs in conjunction with cardiazol in order to shorten the latent period before the fit. As will be seen later, cerebral vasoconstriction produced by cardiazol is probably one factor, if not the most important one, in precipitating the convulsion, and a closely related substance, camphor monobromide, had, some years before, been shown also to produce cerebral vaso-constriction when used as a convulsant drug (97).

Theories as to the Mechanism of Improvement.

As these theories have little reference to the hypothesis presented here, they will be but briefly described, full references being given. Meduna (80) instituted this treatment because he had postulated that "between schizophrenia and epilepsy there exists a sort of biological antagonism which must be expressed in the pathological course of the two diseases. Without being able to characterize the pathological actions, I feel justified in asserting, *a priori*, that these courses are either mutually exclusive, or they do at least to a degree weaken each other in their mutual effects" (81). He bases this hypothesis mainly on two facts:

First that there is a difference in somatic constitution in the two types, the epileptic being of Kretschmer's athletic type, the schizophrenic having a leptosomatic constitution; and secondly, that epileptiform convulsions are

rare in schizophrenia. Obviously this hypothesis does not lead us far in understanding the mechanism of cardiazol therapy. It has, moreover, been severely criticized by Harris (7), who cites many cases in the literature of combined epilepsy and schizophrenia, and who quotes Kretschmer as stating that the athletic type is susceptible to schizophrenia.

Stief (82) believes that the drug acts by vaso-spasm on the cerebral circulation, thereby eliminating diseased nerve-cells, and that cortical activities are restored to normal, by virtue of functioning through normal cells.

Pfister (83) regards schizophrenia as a disease of the autonomic nervous system, and states that "cardiazol whips the autonomic system to epileptiform attacks, and for this reason, can restore to fertility the fallow field of vegetative function". He does not, however, bring forward any evidence to show that cardiazol affects the autonomic nervous system, and all we know of epileptiform attacks leads us to suppose that the cerebral cortex is the essential and the first portion of the cerebrospinal axis to be affected.

Wilmanns (84) states that "one of the most puzzling brain changes in schizophrenia is cerebral œdema. . . I consider it possible that the organic processes which take place in the brain during an epileptic seizure produce an alteration in the water balance of the brain, and thus decrease the oedema. . . . If this assumption is correct one may perhaps place the effects on schizophrenia, produced by . . . the epileptic attacks in Meduna's cardiazol therapy, on the basis of a change in the water economy of the brain, brought about by . . . epileptic seizures".

Gillies (85) supposes that cardiazol may act by stimulating nerve-cells which have become inactive.

Rees Thomas and I. G. H. Wilson (86) suggest "that the fact that cells are deprived of oxygen, either by lessening the amount supplied in the circulating blood, or by some other means, is somehow directly or indirectly therapeutic". They do not suggest how anoxia may effect improvement. It is the aim of the present article to elaborate on this suggestion to attempt to show how anoxia may occur in the cardiazol convulsion, and to indicate possible neurological mechanisms which are thereby set in action, and which, it will be suggested, effect the changes seen in the cardiazol therapy of schizophrenia.

It is suggested by Humbert and Friedemann (87) that the effective element in producing the remissions in cardiazol treatment is the sense of dread induced—"the life and death struggle". If this is so it would appear that the more terrifying anxiety states produced by sub-convulsive doses of cardiazol would be more effective in producing improvement than the convulsions themselves. Walk and Mayer-Gross (89, and personal communication) have attempted, on other grounds, to produce remissions by means of sub-convulsant doses of a related drug (triazol 156). It is still, however, generally accepted that the production of actual convulsions is necessary to effect remissions (88).

Great stress has been laid on psychotherapy during cardiazol treatment

(87, 90, 91), but though one must agree with the importance of psychological factors, in adapting the patient once more to his environment, they do not explain the mode of action of the drug which makes psychological approach possible.

The Similarity of Induced (Cardiazol) and Spontaneous Epileptic Convulsions.

The similarity between convulsions produced by cardiazol and those of epilepsy itself is so great that most observers are convinced that they are physiologically identical. In cardiazol convulsions the classical sequence of the cry, the tonic and clonic spasms may be seen as in the spontaneous epileptic fit, though it must be admitted that the cardiazol fits are more uniform in appearance, and the initial opening of the mouth at the commencement of the tonic spasm is not so commonly seen in true epileptic fits. It has, however, been described by Gowers (92) as a regular occurrence in an individual epileptic with dislocation of the mandible on almost every occasion. In addition, the biochemical changes found by Frisch and Fried (93) after the fits of idiopathic epilepsy (reduction of chlorides in the urine, with increase of acidity and of ammonia and phosphorus content) have also been found by Meduna (94) after fits induced by cardiazol. Gibbs *et al.* have shown the similarity between electro-encephalographic records in idiopathic and in induced epileptic fits (126), while Cook and Grey Walter (127) observed a focal discharge, coincident with the onset of the tonic spasm, localized in the region of the superior frontal gyrus.

Finally Wichmann (95) finds that when cardiazol is given to epileptics, fits are induced which are exactly like the spontaneous ones, and when given in the symptomatic epilepsies the fits show focal signs. In addition he induced fits in 76 out of 99 epileptics, using a dose of cardiazol so small as only to induce fits in one out of 42 normal individuals. It must therefore be admitted as very probable that cardiazol convulsions, and those of true epilepsy are subserved by the same neurological mechanisms. If it be admitted as probable that the convulsion in cardiazol treatment is the essential factor determining its efficacy as a therapeutic agent, and that cardiazol and epileptic fits are physiologically identical, it would seem profitable to inquire into—

(1) The mechanism of the convulsant action of cardiazol.

(2) The mechanism of epileptic fits, and most important—

(3) The changes known to be produced in epileptics as a direct result of the fits.

In other words the crux of the problem would appear to be: What changes in the schizophrenic patient are brought about by the convulsions, and can we infer what they may be from a study of epilepsy, and especially of the post-convulsive stage of this disease?

The Mechanism of the Convulsant Action of Cardiazol on the Nervous System.

Cardiazol has the same pharmacological effects as camphor except that it is very soluble in water (96).

Harris (7) reviews the literature on the action of cardiazol on the nervous system, and concludes that there is a general agreement that "cardiazol has a profound and widespread action on the central nervous system, excitability and conductivity being greatly increased. The result is first a stimulation and restoration of depressed functions, rapidly passing to unco-ordinated activity and convulsions."

It would appear from his review of the literature that convulsions may be produced by the action of cardiazol on any isolated part of the cerebrospinal axis. As students of epilepsy will realize, this does not necessarily mean that cardiazol induces convulsions in the intact animal by a simultaneous action on all parts of the central nervous system.

In 1931 Foster Kennedy (97) quotes Bernard Wortis as having "observed the blanching of the mucous membranes and the cerebral cortex in cats during the moment preceding convulsions produced by the injection of camphor monobromide".

In 1932 Cobb (98) stated: "The convulsive drugs caffeine, ergot, nicotine and camphor and lead poisoning have all been observed to cause vasoconstriction (cerebral)."

Köst (99) has shown that inhalation of large doses of amyl nitrite prevents convulsions from following the injection of cardiazol in man, and Denyssen and Watterson (100) demonstrated that amyl nitrite when inhaled, and histamine when injected intravenously, prevent the occurrence of the cardiazol convulsion. They refer to Hildebrandt's (101) collected evidence, and conclude that cardiazol stimulates the vasomotor centre, causing vasoconstriction, and that "vasodilatation, under appropriate conditions, prevents the occurrence of the convulsion". They state, however, on the evidence of Blume (102), who found that convulsions could be produced by cardiazol in decapitated cats, that "the evidence . . . suggests that in animals at least the cerebral hemispheres play no part in the convulsion".

It is necessary to point out here the important experiments of Pike, Elsberg, McCullough and Chappell (103), who, producing convulsions in cats by intravenous injections of absinthe, show that on removal of the hemispheres, and by cutting off the cerebral circulation, the clonic element of the convulsion disappears, tonic convulsions only being then elicited by the injection of absinthe. This proves conclusively that the cerebral cortex does play a part in the convulsion, for the clonic element is a typical component of the true epileptiform fit.

The Evidence for Cerebral Vasoconstriction, as one of the Causes, Concomitants, or Sequelæ of Epileptic Fits.

Evidence will be referred to here concerning the probability that cerebral vasoconstriction may be the cause (the precipitating, not the ultimate cause) of a type of epilepsy—that is to say, of one of the " idiopathic " epilepsies. It will be seen that the evidence is not conclusive that vasoconstriction occurs before the fit, but that it is certain that cerebral vasoconstriction occurs coincidently with epileptic fits, or as a sequela to epileptic fits. The theory that vasomotor spasm of the cerebral arteries causes the epileptic fit, by producing cerebral anæmia, is an old one which was held by many in the middle of the last century, but was discarded for a time, because, according to Lennox and Cobb (104), of experimental work by Leonard Hill in 1896 and by Bayliss in 1923, which seemed to indicate the improbability of the existence of cerebral vasomotor nerves.

In 1928 Forbes and Wolff (105) demonstrated constriction of pial vessels, seen through a skull window, on stimulation of the cervical sympathetic nerve, and dilatation after stimulation of the central end of the cut vagus. This was confirmed in 1938 by Forbes and Cobb (106), who also showed that a larger part was played by chemical agents in producing vasoconstriction than by direct vasomotor control. Histological studies have also demonstrated the presence of nerve-fibres on the pial vessels (107, 108, 109), and Penfield (110) has shown that the blood-vessels within the brain bear perivascular nerves. Hughlings Jackson (111) in 1863 first reported vasoconstriction in the retinal vessels during an epileptic seizure, and since that date several observers, including Foster Kennedy (112), Foerster (113), Dandy (114) and Leriche (115), have been able to observe vasoconstriction of the exposed cortex, when spontaneous fits occurred in epileptics on the operating table.

Some assert that the vasoconstriction occurred before the fit, some that it was coincident with the fit. In fits induced by faradic stimulation of the exposed cortex, Penfield (116) has observed cessation of arterial pulsation during the epileptic seizure, with the appearance of focal areas of cortical anæmia, immediately after the convulsion in 29 out of 30 cases. In the remaining case blanching of the cortex commenced coincidently with the convulsion. The arrest of cerebral circulation with blanching of the cortex is described by all observers of spontaneous fits as intense.

Spielmeyer (117) has shown that the sclerosis of Ammon's horn, reported since the time of Meynert (Gowers, 118) as a frequent pathological finding in epilepsy, is the end-result of frequently recurring vasospasm in the epileptic brain. It is not, of course, thought here that vasoconstriction may be the only precipitating cause of convulsions.

Cobb (119) cites 56 clinical causes of fits, but says that " the mechanism of anoxæmia appears to be numerically the most frequent precipitating cause

of clinical convulsions", and that "cerebral anæmia can, and does, cause epileptiform seizures". From the point of view of this article, the important fact is that the most frequent sequel to convulsion is, as Penfield (116) states, "the appearance of focal areas of cortical anæmia". In the same article he states that "the post-epileptic paralysis is doubtless to be explained by these associated vasomotor changes, and certainly not on the basis of simple fatigue". This, and the following quotations by the same author (120, 121), are of the utmost importance for an understanding of the hypothesis expressed here to explain the action of cardiazol in schizophrenia. He states: "A unilateral epileptic seizure is, on some occasions, followed by unilateral paralysis, which usually affects the part that was earliest and most severely involved in the seizure. This post-seizure paralysis may consist in monoplegia, hemiplegia, aphasia, or mental stupor, or even complete coma, or diplegia. The cause of post-seizure paralysis was thought by Jackson to be fatigue of the discharging cells. It was suggested by Kinnier Wilson that it was a phenomenon of after-discharge inhibition. The present evidence suggests that these paralyses are due to post-convulsive spasm of the cerebral arteries, or at least to the focal cerebral anæmia, which frequently follows epileptic seizures, of whatever variety" (p. 430).

"Jackson expressed the belief that post-epileptic automatism is invariably due to post-epileptic paralysis—paralysis of the highest level of neural activity, the substratum of consciousness. He therefore concluded that the state is a phenomenon of release from higher control. If it is in truth post-convulsive paralysis, I suggest, on the basis of what is now known, that effective anæmia remains in the region in which consciousness is represented".

"Post-epileptic automatic states *and post-epileptic psychoses . . . are negative states due to temporary paralysis of the highest cerebral centres.*"

The Neurological Mechanism of Post-Convulsive Phenomena.

It is not the purpose of this article to discuss the neurological mechanism of the epileptic convulsion itself. The four main theories are fully discussed in Lennox and Cobb's monograph (104).

Penfield, who, like many workers at present, favours the irritation theory, has given his views, already quoted here, regarding the mechanism of post-epileptic phenomena. That is to say, he considers them as due to areas of effective anæmia, remaining in the cortex, as a result of cerebral vasospasm occurring during or after the convulsion. He has not, I think, attempted to elaborate on this theory, but one mechanism which would account for this sequence of events producing post-epileptic automatism, impulsive conduct, etc., is Southard's (122) theory of "short-circuiting". He pointed out that "the cerebral arcs normally escape automatism through a multitude of synaptic connections", and that destruction of these arcs by gliosis "procures new reflex arcs with fresh

surfaces of separation which are perhaps even simpler and more automatic than the spinal arcs and synapses". In other words, the multiplicity of cerebral association paths allows of delay in response, co-ordination of present stimulus with past memories, and higher integration—in short, prevents impulsive activity.

It is obvious that focal cerebral anæmia, while present, would act in a similar manner to lesions such as gliosis. Supporters of the release theory, such as Foster Kennedy (112) and Hartenberg (123), who suppose a massive temporary cutting out of cerebral activity with sudden release of lower centres as the cause of the convulsion, explain post-epileptic phenomena as due to an imperfect recovery from cortical inhibition, the motor functions having recovered, and the psychic (more recently developed and therefore less stable) functions being still partially in abeyance. It will be seen that Penfield's theory of focal cerebral anæmia would also explain the "release mechanism", and in fact, there is no reason to suppose that both "short-circuiting" and "release mechanisms" might not occur coincidently. Either or both would, according to Hughlings Jackson's theory of cerebral dissolution, explain the post-convulsive phenomena of epilepsy. Thus Jackson (124) states, speaking of the post-epileptic state: "There is a duplex condition, a negative state with each positive state . . . the positive element is physically activity of lower nervous arrangements, which are, except for overactivity, healthy, . . . they are healthy, except figuratively speaking for 'insubordination from loss of control'; then the positive condition is hyperpositive, . . . they are no more diseased than the heart, and the rest of its nervous system is, when it goes faster on cutting the pneumogastric nerve."

This quotation will have more significance in the final argument.

The Post-Convulsive Phenomena in Epileptiform Fits Induced by Cardiazol.

It will have been observed that in the majority of the cases cited in this paper who received cardiazol treatment, post-convulsive phenomena occurred, which varied from temporary excitement and confusion to long periods, often many weeks, of overactive, impulsive and violent behaviour. As has already been stated, other observers also mention the occurrence of this phenomenon in cases of schizophrenia who received cardiazol treatment. The similarity of this phenomenon with that occurring after spontaneous epileptic fits is too obvious to require stressing.

Evidence has been adduced here to show the similarity in the mechanisms of spontaneous epileptic and of cardiazol, epileptiform convulsions. It is suggested here that in the present state of knowledge it would seem probable that repeated convulsions induced by cardiazol in schizophrenic patients produce focal areas of anæmia in the higher psychic areas of the cerebral cortex, resulting

in a temporary loss of function in these areas, with " short-circuiting " or " release " of lower nervous arrangements, and consequent impulsive conduct.

If, as we have assumed in this article, deterioration in schizophrenia is associated with functional disturbance in diencephalic-mesencephalic regions, we might suppose that these regions, when released from control, exhibit to an even greater extent than normally their pathological condition. In early cases of schizophrenia, on the other hand, where underlying deterioration is minimal, release of higher (inhibitory) centres may allow the patient more energy to adjust to his environment, and by cutting out for a time higher cerebral arcs, may perhaps stop, at least temporarily, pathological trains of thought and conduct. In this connection I quote the remarks of a schizophrenic patient who had received cardiazol treatment, and had recovered (Starks) (125): " As to the effects of the treatment he spoke as follows: ' I believe there is a general toning up of life all around. I have a wonderful appetite. I'm more alive, more active. . . . The reason I haven't objected to the needle is that it has practically stopped my mental processes. Under the influence I find I'm not a thinking animal.' Asked why he thought this a good effect he replied: ' That's an individual opinion. . . . I anticipated that these treatments would rile the processes up, and start a train of thought. Instead I found myself held back from going in that direction. Instead of stimulating my thought processes it stimulates my appetite, my physical condition, ease of doing things, emotional ease, no concentration of effort. It has held my imagination in curb. . . . There is nothing I'm hunting for. . . .' "

Such an attitude of not wishing to " mentally explore " has been noted by many observers in cardiazol-treated schizophrenics, and supports the hypothesis advanced here.

In conclusion I would point out that it would appear from the evidence cited here that all three drugs, cardiazol, sodium amytal and alcohol, produce their effects in at least the catatonic type of schizophrenic by virtue of a depressant action on higher cerebral activities; though it would seem that in the case of cardiazol this depressant action is more radical, and relatively more permanent, than in the case of the other two drugs. We might, in the sense of the term used here, regard the cardiazol treatment of schizophrenia as a method of therapeutic cerebral dissolution—a somewhat disquieting title! For it is possible that the persistent production of areas of cerebral anæmia might result in permanent damage to cortical neurones.

It must be emphasised that the hypothesis expressed here, to explain the mode of action of cardiazol, is based on incomplete evidence, and appears possible only on the basis of what is at present known concerning the pathology of schizophrenia and of epilepsy.

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