

THE INFLUENCE OF PHARMACOLOGICAL SHOCKS  
ON THE PSYCHOSES.\*

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WHEN, a few months ago, your Association honoured me with its invitation, I undertook the task of presenting to you the results of the first 100 cases treated in the Clinic in Vienna. I intended to draw from the individual reactions and the effect of the therapy some conclusions as to its justification. I could also have brought forward conclusions drawn from the records of cases whose treatment has been terminated for a long time and who have remained under continuous observation. These results would have been of some value inasmuch as these would have referred to the cases which I myself treated individually, and in which treatment had been individualized by employing various types of shock.

However, for extraneous reasons, my intentions cannot be carried out, and I have therefore had to change the conception of my paper. Consequently I ask your permission to replace a purely factual lecture and a purely clinical analysis of my material by a more theoretical interpretation of pharmacological shock. I shall also be able to give you statistical material from a large number of patients from the State Hospitals of the State of New York. I shall also take the liberty of subjecting this statistical material to a purposeful analysis.

Even the most exact science cannot do without conceptions and theories. One cannot deny that modern medicine has been richest in achievement since it threw off the narrowness of limited scholastic thinking, and made clinical experiment and bedside observation the starting-points of its knowledge. But one must consider at the same time that factual experiments expressed in figures cannot be constructive without the aid of fertilizing speculative thought. Only the uniting of the results of observation with the facts of an experimental series into a hypothetical entity makes it possible to form a synthesis, and allows of further progress. Man is not a test-tube, and it requires art and even, if I may use the ominous word, "intuition"—to progress from the knowledge of individual points to an understanding of the entity. For the research of individual pathological manifestations the ability to observe facts properly may be enough, but for anyone who is principally a therapist there

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cannot be any doubt that to heal, one needs to possess not only scientific knowledge, but also artistic ability. A medicine which is entirely caught in the net of experiments, and which does not acknowledge individualizing modifications and the variations of the human character, is condemned to become a merely technical medicine, and its practitioners to be, not physicians, but medical technicians.

If the conception outlined above is of importance to the whole field of medicine, it is still more important to psychiatry. For the mind and its special manifestations are, and will probably long remain, unapproachable to strict laboratorial comprehension.

This conception of a synthesis of art and soberly gained clinical facts is also the basis of the origin of insulin therapy. It owes its start to a single clinical observation which in a favourable moment was interpreted correctly. The consequences and further possibilities of my conviction in regard to the curative value of large doses of insulin were not clear to me for a long time, although I never doubted that I was on the right road. The history of the insulin therapy of psychoses could be used as proof of the usefulness of intuition in medicine.

When, as a young physician, I had to treat drug addicts, I noticed that the usual theories did not contribute much to the treatment, and that they also did not do justice to most of the problems raised by this disease. I therefore tried to study the problem anew at the bedside. The clinical manifestations shown by the addicts did not seem to me to be purely psychological, and I therefore endeavoured to overcome them by means of conceptions drawn from physiology and internal medicine.

I endeavoured to find a connecting link between the functions which we recognize as purely somatic and the others which we consider purely psychic—a connecting link which undoubtedly exists. At the bedside, and in this special case, in persons with abstinence symptoms, one could not fail to see that the pathological manifestations, the purely somatic and the purely psychic, mutually influenced each other. The abstinence symptoms seemed to me to consist of a disturbance of the vegetative nervous system. When analysing this disturbance, I found that almost all the symptoms could be accounted for as being due to the dominantly increased activity of one pole of the vegetative nervous system, the sympathetic. In order to obtain a sedative action on the sympathetic and an antagonistic increase in the effect of the parasympathetic, I treated the patient with insulin.

The results seemed to confirm my assumptions. A critical analysis of these and the need for a connecting hypothetical explanation resulted in the scheme (probably known to you) of the effect of insulin on the nerve-cell and in the theory of the dynamic equilibrium of the hormones.

My experiments were not confined exclusively to insulin. I tried to alter the effect of the insulin by adding other drugs, and to influence the hypoglycæmia. I already emphasized in my earlier work that the dosage for addicts

can only be handled individually. Success and failure depend on the precise ascertaining of the individual dosage. This, however, proved to be extremely difficult. Frequently the doses were excessive; these excessive doses led to shock manifestations, which of course at that time were unintentional. They were considered as especially dangerous to life, and I at first looked for means to eliminate these shock-manifestations, especially the convulsions. During many animal experiments I ascertained that the convulsions which usually took place as a consequence of an exactly determined dosage could be completely prevented by derivatives of barbituric acid. It was therefore possible in animals by using a drug of this group to change the convulsive or dry type of shock into the wet or comatose type.

These experimental results were not confirmed at the bedside. There were constant alternative manifestations of each kind of shock, and it was just these accidental shock-manifestations which furnished the basis for shock therapy.

The material originally at my disposal consisted of drug addicts. As is well known, addicts offer an extremely rich gallery of abnormal characteristics and psychopathic personalities. Among them I had, of course, some with serious asocial, autistic-egocentric characteristics. What I noticed first of all was the following: whenever such a patient had an accidental hypoglycæmic shock, one observed after their awakening that the psychic personality had undergone a considerable change for the better; the individual pathological characteristics disappeared partially or totally, although after the single shock abstinence symptoms were still present. This improved psychic behaviour, the patient's completely changed outlook and improved manner of reaction towards the demands and requirements of their surroundings induced me to employ shock as a therapeutic measure. Consequently, as early as 1928, I started to treat the mentally disturbed by means of excessive doses of vegetative drugs, in the supposition that it should be possible to change the patho-physiological utilization of the irritants in this manner into a normal physiological utilization.

Of course I had immediately to introduce a modification of the original treatment for addicts. In order to give the shock the highest possible intensive effect and possibly to awaken the reserve defensive forces of the cell, I discontinued adding barbituric acid derivatives in these cases. As mentioned above (in contrast to the animal experiment), the wet (comatose), and the dry (epileptic) shocks appeared alternately.

To ascertain the correct shock dosage, and also for the purpose of adapting the circulation of the patient to the shock, I divided the treatment into phases.

In many cases an improvement showed already in phase I—at a time, therefore, when the patient had not yet offered any obvious somatic hypoglycæmic manifestations. These improvements also led to remissions at times—indubitable proof that not only the shock but also insulin by itself is effective.

Nevertheless, in time it became more and more clear that the deep symptoms of the insulin effect which (lacking another expression) I called "shock" had to be evaluated as the most competent factor in the cure.

Three factors are absolutely required to obtain a lasting and satisfactory improvement by pharmacological shock treatment:

(1) The provocation of the proper type of shock for the particular case, *i.e.*, either of a convulsive-epileptic attack or of a comatose state. In the latter case it is particularly necessary to watch the appropriate depth of the coma.

(2) The termination of hypoglycæmia or shock at the most appropriate moment. This interruption time differs with the different clinical pictures of psychoses.

(3) A correspondingly long treatment. The treatment should not only not cease with the disappearance of the secondary psychotic symptoms, but it must be continued until those symptoms disappear which I have called "activated psychotic" symptoms.

The following can be said in regard to the type of shock:

Although, according to Banting, there are always manifestations of convulsions in the case of every insulin shock, it seems that a certain therapeutic importance in some cases must be attributed to the attack-like motor discharges, namely the epileptic and epileptoid fits. As early as 1933 I found it necessary sometimes to provoke such an attack by the addition of convulsant drugs such as camphor and cardiazol. Simultaneously I gained the conviction (by way of practical clinical deliberations) that the important factors of insulin treatment must be looked for in all the very rich and manifold complexes of the patho-physiological changes caused by the insulin effect.

I should like to say at this point that, even if the epileptic attack causes a dramatic change in the picture of the patient's condition, this nevertheless does not represent the only important part of the treatment, although in my publication of the year 1933 I laid more emphasis on the importance of the seizure. Therefore I must utter a warning against being misled—as I was originally—by the sudden improvement in the condition of the patient after an epileptic attack. In this case there is the danger that one may be satisfied with the passing elimination of secondary symptoms, and may miss the opportunity of removing the deeper located processes of the diseases by the complex influences of the entire hypoglycæmic syndrome. The provocation of convulsions by injections of cardiazol alone means an advantage for the physician but a disadvantage to the patient.

The observations arising out of the pharmacological shock treatment seemed to open a new avenue to psychiatry, which makes it possible to regard psychiatric problems from a new point of view. From its results one is justified in viewing psychotic states merely as mental symptoms of patho-physiological or organ-functional disease. From this point of view the old nomenclature

seems to be merely a " formal classification " following its phenomenal and not its nosological character.

As a consequence of this treatment, a conception (which should be a matter of course) has come to the fore, namely, that one can only speak of disease of an organ, but not of the disease of something abstract, such as " the mind ". A mental disease represents the expression of the dysfunction of an injured organism, and not an injury of something not concrete. One should also not speak of a specific treatment of individual " mental diseases ", but of biochemical and patho-physiological changes, expressed by abnormal mental manifestations and behaviour. According to my opinion, there can therefore be no contrast between epilepsy and schizophrenia, since both are nothing but symptom-complexes, nothing but manifestations of unknown pathological origin and not " diseases " by themselves. The effect of the pharmacological shock on that dysfunction of the organism which we call a " mental disease " seems to be manifold. Insulin not only influences sugar metabolism, water and calcium-potassium metabolism, it changes also the equilibrium of the ions and oxygen consumption, and it also influences by way of the vegetative centres of the hypothalamus all functions of the living cell. If we now see that a dysfunction of short duration, for instance a short psychosis, can easily and quickly be removed by an insulin treatment, then we must not be surprised if a dysfunction of long duration can smooth the way to such an extent that the disturbance gradually becomes a lasting habit. These, then, are the chronic psychoses. The attempt to treat this condition by prolonged and deeper " condensed " shocks is still in an experimental stage, and therefore not yet ripe for publication.

#### STATISTICS FROM THE NEW YORK STATE HOSPITALS.

With your permission I will now descend out of the blue haze of theory to sober figures and facts in order to make the effect of this treatment more acceptable to you. The statistics come from the Statistical Bureau of the Health Department of the State of New York. In 1936 I was invited by the Commission of Mental Hygiene to give courses on the pharmacological shock treatment at the Harlem Valley State Hospital, these courses to be for the physicians of the 28 psychiatric hospitals of the State of New York. Each hospital of the New York State Hospital System assigned a physician to these courses. Consequently all cases mentioned in these statistics have been treated by physicians who completed my course. Because of the distance between the various hospitals and the sometimes impersonal attitude, it was impossible for me always to keep to a uniform line in my treatment in the various State hospitals. Expert reports on the success or failure of the treatment were left to the various hospital superintendents, and they in turn transmitted them to the Statistical Bureau of the State of New York. Obviously these statistics cannot lay claim

to unanimity of manner of diagnosis or of manner of reviewing the success. But they give us the great advantage of an impersonal cross-section. Dr. J. R. Ross was appointed by the Commissioner of Mental Hygiene to analyse the results of pharmacological shock treatment and of its modifications from the various State Hospitals, to classify them objectively and to draw his conclusions.

Dr. Ross's reports are as follows :

" A total of 1,356 patients with dementia præcox received insulin treatment. Table No. 1 shows these patients classified according to duration of illness before treatment, and the outcome of treatment. Of this number, 192, or 14.2%, were reported as recovered after such treatment, 280, or 20.6%, were much improved, and 357, or 26.3%, showed improvement. A total of 829, or 61.1%, thus showed some degree of improvement. Only 527, or 38.9%, failed to respond to insulin treatment. These statistics may be compared with those for a group of 1,039 first admissions with dementia præcox to the Civil State Hospitals of New York, none of whom were treated with insulin. Of this control series, 36, or 3.5%, were described as recovered, 116, or 11.2%, as much improved, and 77, or 7.4%, as improved. The recovery-rate of the insulin-treated group exceeded that of the controls by 283%. The rates of much improvement and of improvement were similarly in excess by 84 and 255% respectively. Considering all degrees of improvement as a unit, we find the rate of improvement of the insulin-treated group to exceed that of the control group by 173%. The same standards for the estimation of results were observed in both groups.

" Table No. 1 shows recoveries and improvements occurring, no matter how long the duration of the illness before treatment. It will be seen that in the group of 195 patients with a duration of 6 years or more, 9 recovered after treatment with insulin, 22 were much improved and 50 were improved. This is important to note, since a long-existing chronic state of the disease is often held to offer no hope of successful treatment.

" It is evident, however, that the rate of recovery and of improvement depends upon the duration of the illness before treatment. The rates were highest among those who have been ill less than 6 months, and gradually decreased as the duration of the illness increased. Contrariwise, the percentage showing no improvement increased as the duration of the illness before treatment increased.

" Of the 1,356 patients who received insulin therapy, 578, or 42.6%, were 'on parole'.\* Table No. 2 shows the number paroled after treatment and the duration of the parole. Of this total, 328 had been on parole for 6 months or less, 68 had been on parole for 7 months, 37 for 8 months, 34 for 9 months, 51 for 10 months, 36 for 11 months and 16 for 12 months. Eight had been on parole for over a year. The number paroled varies inversely with the duration of illness before treatment. Of those ill less than 6 months, 66.7% were on

\* Corresponding to 'on trial' in this country.

TABLE 1.—Patients with Dementia Præcox receiving Insulin Treatment in the New York Civil State Hospitals, Classified according to Duration of Illness Before Treatment and Outcome of Treatment.

Duration of illness before treatment.	Number.				Per cent.			
	Total.	Recovered.	Much improved.	Unimproved.	Total.	Recovered.	Much improved.	Unimproved.
Less than 6 months	192	56	58	37	100.0	29.2	30.2	21.4
6 to 12 months	195	45	55	55	100.0	23.1	28.2	20.5
1 year	306	45	72	99	100.0	14.7	23.5	29.4
2 years	198	20	36	87	100.0	10.1	18.2	27.8
3 "	114	9	22	50	100.0	7.9	19.3	28.9
4 "	77	4	7	38	100.0	5.2	9.1	36.4
5 "	79	4	8	47	100.0	5.1	10.1	25.3
6 " and over	195	9	22	114	100.0	4.6	11.3	25.6
Totals	1,356	192	280	527	100.0	14.2	20.6	26.3

TABLE 2.—Number of Patients with Dementia Præcox Paroled after Treatment with Insulin, and Duration of Parole.

Duration of illness before treatment.	Number under treatment.		Duration of parole.									
	Total.	Per cent.	Under 6 months.	7 months.	8 months.	9 months.	10 months.	11 months.	12 months.	1 year and over.		
Less than 6 months	192	66.7	71	19	7	11	10	6	2	2		
6 to 12 months	195	55.4	62	13	10	6	11	3	3	..		
1 year	306	50.7	80	13	11	9	15	18	5	4		
2 years	198	35.9	48	6	2	2	9	2	2	..		
3 "	114	31.6	17	5	2	3	4	3	1	1		
4 "	77	32.5	16	3	2	2	1	..	..	1		
5 "	79	21.5	10	..	2	1	..	3	1	..		
6 " and over	195	19.5	24	9	1	..	1	1	2	..		
Totals	1,356	42.6	328	68	37	34	51	36	16	8		

parole; those with a duration of 6–12 months had 55.4% on parole; those with a duration of 1 year had 50.7% on parole. The percentage declined rapidly after the first year, and reached a minimum of 19.5% among those who had been ill for 6 years and more before the beginning of insulin treatment. The preceding statistics do not include 62 who had been discharged from parole, nor 42 who had been awaiting parole. A total of 126 had been returned from parole.

“There were 599 patients paroled and 62 were discharged from parole, making a total of 661 patients with dementia præcox who were presumably on parole after treatment with insulin. Of this total, 126, or 19.7%, were returned from parole. These may be considered as ‘failures’. The question, therefore, arises as to how the degree of failure compares with that among all patients paroled from the New York Civil State Hospitals. In a paper by Dr. Horatio M. Pollack, which appeared in the *Psychiatric Quarterly* for April, 1938, it is shown that 9,563 patients were placed on parole during 1937 and 3,894 were returned from parole during the year. The latter represents 40.7%, which is slightly more than twice that found among the groups of insulin-treated patients who were returned from parole.”

*Patients treated with cardiazol (metrazol) alone.*

“A total of 523 patients received treatment with cardiazol. Table No. 3 shows these patients classified according to duration of illness before treatment and the outcome of the treatment. Of this total, 23, or 4.4%, recovered after the treatment, 51, or 9.8%, showed much improvement, and 168, or 32.1%, were improved. The rates of recovery and much improvement do not differ significantly from those of the control series. It may be noted that the rate of much improvement is even slightly greater in the control group. The improvement-rate, however, is more than 4 times that of the control group. The cardiazol results are not as good in view of recovery as those from insulin therapy. Thus the recovery-rates in insulin and cardiazol were 14.2% and 4.4% respectively. The percentages of much improvement were 20.6% and 9.8% for the insulin and cardiazol groups respectively. The rate of improvement was slightly higher in the cardiazol group, though the difference in percentage is not significant. Combining all degrees of improvement, we find that the insulin-treated group showed a rate of 61.1%, compared with 46.3% for the cardiazol group. As in the case of insulin, the rate of recovery and improvement after treatment with cardiazol decreased as the duration of the illness before treatment increased.

“Seventy-two of the cardiazol group were on parole—all of them for 6 months or less. Eight patients were returned from parole and 6 discharged. Forty-five were awaiting parole.”

As regards insulin treatment, Dr. Ross includes the opinion verbally expressed by the superintendents that “results in cases of dementia præcox, where the



TABLE 3.—*Patients with Dementia Præcox receiving Cardiazol (Metrazol) Treatment in the New York Civil State Hospitals, Classified according to Duration of Illness Before Treatment and Outcome of Treatment.*

Duration of illness before treatment.	Number.			Per cent.		
	Total.	Recovered.	Much improved.	Total.	Recovered.	Much improved.
Less than 6 months . . . . .	44	5	17	100.0	11.4	38.6
6 to 12 months . . . . .	36	6	16	100.0	16.7	44.4
1 year . . . . .	104	7	13	100.0	6.7	12.5
2 years . . . . .	74	1	4	100.0	1.4	5.4
3 " . . . . .	56	2	4	100.0	3.6	7.1
4 " . . . . .	37	..	3	100.0	..	8.1
5 " . . . . .	50	1	2	100.0	2.0	4.0
6 " . . . . .	122	1	3	100.0	0.8	2.5
Totals . . . . .	523	23	51	100.0	4.4	9.8
			281		32.1	53.7

duration of the illness was over two years, do not justify the time or expense necessary to carry on such treatment". But he thinks that this judgment will hardly stand in the light of the statistics compiled from the entire State. This first opinion is based on the limited experience of each institution with a small number of such cases. When the figures for all the institutions are combined the picture is quite different. Three hundred and thirty patients, or 24% of the total number treated with insulin, showed either recovery, much improvement or improvement, where the duration of psychosis was over two years. The actual figures are :

Recovered . . . . .	46
Much improved . . . . .	98
Improved . . . . .	186

About the old cases Dr. Ross concluded that "Table No. 1 bears out this contention. While the number that responds grows definitely less with the duration of the disease, nevertheless cases in which the illness has lasted six years or more show 9 recovered, 22 much improved and 50 improved, 81 cases in all affected in this group alone".

"We believe," continued Dr. Ross, "that this treatment has passed its trial period and that it should be used in all hospitals for mental disease. We believe that the best results will only be obtained where Sakel's treatment is followed without deviation, and that before attempting to treat, a physician should have, as a minimum, six weeks of intensive instruction. There is no question that the greater the experience of the physician, the better the results will be. There are hospitals in various parts of the country competent to give instruction, and it is hoped that they will be made available to anyone who wishes to have it free of charge. Some difference in results will undoubtedly occur and these, in my opinion, are to be expected. One should not look for the same degree of skill in all physicians employing this treatment, any more than in any other procedure requiring experience and special aptitude or ability. Better and more uniform results will be a natural consequence of longer experience and greater familiarity with Sakel's technique. A complete record with a close follow-up of all cases paroled or discharged should be kept for at least two years." These were the statements of Superintendent Dr. Ross, and these are his conclusions.

"1. Beneficial results from treatment of all cases of dementia præcox of no matter what duration with insulin are much greater than the results of the untreated group.

"2. The results of treatment with insulin are much better than the results obtained from cardiazol alone.

"3. Combination of cardiazol with insulin apparently assists the action of insulin in selected cases.

“ 4. Treatment with camphor is not recommended by those who have used it in New York State Hospitals.

“ 5. The results obtained in cases where the duration is over two years not only justified the expense and time, but shows it would be an error to neglect such cases.

“ 6. The recovery and improvement rates are progressively less according to the duration of the illness.

“ 7. The dangers of insulin therapy in the hands of experienced and trained physicians are almost negligible.

“ 8. An active educational campaign should be carried on, so that an early diagnosis of dementia præcox can be made and treatment instituted at the earliest possible date.”

I wish to express my gratitude to Drs. J. R. Ross, Tiffany and Parsons for their permission to use this material in this paper.