

# Drug Therapy of Schizophrenias in the Community

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Papers and conferences on treatment usually emphasize the advances and improvements in the development of new methods. At the same time deficiencies in treatment tend to be given insufficient attention. But for clinicians who have to treat and manage both acute and chronic schizophrenic patients such deficiencies are only too obvious (Hamilton, 1975).

This paper reviews some of the problems and prospects of maintenance drug therapy of schizophrenia in the community while emphasizing such deficiencies.

Schizophrenia is a destructive disease affecting young people in the most critical period of their lives. Scrope-Davies once wrote to Thomas Raikes, "Babylon in all its desolation is a sight not so awful as that of the human mind in ruins." The introduction of neuroleptic drugs has created a more hopeful atmosphere in the overall management of the condition.

On May 26, 1952, Delay et al. presented a paper at the Centenary

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Meeting of the Societe' Medico-Psycho-logique in Paris. It was entitled "The Therapeutic Use of a Phenothiazine with Selective Central Action (RP4560)." This began a new era in the treatment of psychiatric disorders. Although J. Hamon and his coworkers at Val de Grace have used chlorpromazine previously in conjunction with barbiturates for manic excitement, their relatively mediocre results did not anticipate the potential of this series of compounds. A short time afterwards, in 1954, Nathan Kline introduced Rauwolfia in North America for the treatment of psychiatric disorders. Since then, the use of pharmacological agents in psychiatry has been the subject of several national and international conferences.

The first article on largactil appeared in *Presse Medicale* on February 13, 1952. In this Laborit et al. described the fundamental observation that "in doses of 50 to 100 mg intravenously, chlorpromazine does not produce loss of consciousness or a change in patients' mentality, but it does produce a slight tendency to sleep and above all an indifference to the surroundings."

Since the introduction of largactil in psychiatry, more than 500 new compounds with psychoactive properties

have been synthesized and tested, and more than 50 of them have been in use in psychiatric patients. It is calculated that over one million people may have received largactil or one of its congeners to date.

Our main concern today is the effect of these drugs on schizophrenias. The question is, do they work in the treatment of schizophrenias? In the 50's and 60's there was great enthusiasm for using this drug not only for schizophrenia, but for all types of clinical psychiatric conditions. Several reports have pointed out that there is a steady decrease in the number of chronic schizophrenic patients residing in mental hospitals since the introduction of this drug. Associated with this remarkable fact was the improvement in the general atmosphere of acute admission wards in mental hospitals. Both of these have been claimed as being due to the introduction of "tranquilizer drugs." But there is good evidence to indicate that the decrease in the number of chronic schizophrenics began to appear before the introduction of these new drugs (Hamilton, 1975). It is possible that the acute admission wards have improved because of the use of these drugs, but the evidence is not at all certain.

An optimistic wave in psychiatry has risen following the introduction of the major tranquilizers for the therapy of schizophrenic patients. We have expected an antipsychotic effect, which was shown directly by a swift amelioration of the acute agitated state (Cole, 1962; Delay and Deniker, 1952; Delay et al., 1952; Gittelman et al., 1964; Goldberg and Mattson, 1968; Keskiner et al., 1968; Laborit et al., 1952; Lehmann and Hanrahan, 1954; NIMH, 1964). This assumption led us to believe that there was a new perspective in therapy, and that by suitable maintenance therapy, as with insulin in diabetes, a lasting compensation would be obtained in schizophrenic patients. In spite of the definite therapeutic success, this optimism has been followed by disappointment; a large percentage of the apparently recovered patients have had

to return to the institutions, though they had been continuously in medical care and receiving maintenance drug therapy. According to recent data, although 65 percent of our patients do some productive work, in many cases the adaptation to society is not satisfactory and stable. Many are working only part time, and for most of them the work is not appropriate to their educational level, that is, it is at a lower level than before the illness. A very good illustration of the unsatisfactory therapeutic effect is that more and more tranquilizers appear on the market. Today we can choose from a large variety of major tranquilizers according to our opinion and the supposed need of the patient. Thus, there are drugs which cause extrapyramidal symptoms and others with little tendency to do so. In general they produce too much drowsiness, and we know that these side effects in particular hinder adaptation back to society, and also impair the working capacity of the patient. During long-term medication we often encounter depersonalization accompanied by drowsiness and weakness. The symptoms together produce a so-called negative placebo effect, characterized by secondary anxiety or excitement which results in some patients rejecting their drugs. This again speeds up the so-called "revolving-door." It is well known that during chronic treatment tolerance may develop to some actions of the most frequently used phenothiazine derivatives, especially to their hypnotic and hypotensive effects (Kornetsky et al., 1959; Mirsky et al., 1959).

### **Schizophrenic Patient and the Social Environment**

Russell Barton in 1959 wrote a book called **Institutional Neurosis**. In this book, he stated that much of the "end state" of patients in mental hospitals is a product of social forces.

These forces led to such features as:

1. loss of contact with the outside world
2. enforced idleness
3. loss of personal friends and possessions

4. loss of prospects outside of the hospital, and
5. poor ward atmosphere

The publication of this book and the description of this syndrome attracted worldwide attention. A large part of the features of the mental hospital patient was thought to be due to his/her staying in the hospital. From this theory arose the corollary that they would be much better off if only some way could be found to accommodate them outside the mental hospital. On this presumption chronic patients, mostly schizophrenics, were discharged in large numbers into the community. It was decided to do a follow-up study on these discharged patients to see if in fact they were doing better than in hospital. From 1968 to 1971 such a follow-up study was carried out in the province of Saskatchewan.

Of the 512 patients discharged in 1963-1965, 343 were followed up between 1968 and 1971. Of these, 270 were schizophrenic patients. As I mentioned earlier there are two primary indicators of the efficacy of any mode of therapy in any illness. One of them is the decline or absence of symptoms, and the other is the performance at work and social activities. Therefore we proceeded to analyze the employment status, social activities, and the relationship of these parameters to drug therapy.

Only 14 of the 270 were considered unemployable at the time of the follow up. Yet only 28 (10 percent) were employed regularly full time for 48 months or more. Another 13 percent had irregular part-time employment during the five years. The remainder (77 percent) were unemployed. At that stage, our thinking was that the unemployed people were probably too sick to be employed. Therefore we proceeded to examine the relationship between the level of psychopathology and employment. It was found that the degree of psychopathology was significantly different between those patients who were employed and those who were unemployed. Next on consideration was whether the patients were on psychotropic medications or not. It was

observed that a very large number of unemployed persons were on "tranquilizers" compared to a small percentage of the employed group of people on "medications."

#### **Social Contact and Activity**

Only 130 out of 270 patients had any type of social contact with friends or relatives living in the area. Of these, 20 patients had contacts once a month or more and the remainder had fewer than one contact per month. Two hundred and fourteen patients had no desire for any type of activity for at least once a week. If we take social contacts, social activities, and employment together, there were only seven patients who had satisfactory levels in all the three, and most surprisingly, they were not among the patients with the least severity of illness.

#### **Other Studies**

What does it all mean? This issue was puzzling to us for some time. So we decided to look at some of the other studies of similar questions. Kun and Pataky (1975) from Budapest have reported on the problems of maintenance therapy in the community adjustment. They analyzed the case histories obtained in a 10-year period and found that the average daily dose and the average total quantity of phenothiazines given during readmissions progressively increased to a significant degree. Thus the average total quantity given during the third admission was more than twice the average amount given during the first admission. They go on to comment that "chronic medication directs the patient into the 'sick role model' which is entirely opposite to the 'problem of living model' " which should be adopted for successful therapy of the schizophrenic patient.

J.P. Leff (1975) from the Institute of Psychiatry in London in an elegant study has attempted to clarify the contribution of drugs in maintaining schizophrenic patients in the community. He did a double-blind study of the efficacy of two drugs, lergactil and stelazine, as opposed to a placebo, in maintaining acute

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patients in the community following discharge after their first hospitalization: Thirty-three percent of the patients maintained on drugs relapsed during the 12 months of follow up whereas 83 percent of the patients on placebo relapsed during this period. Therefore the obvious conclusion would be that maintenance phenothiazine treatment should be recommended for all acute schizophrenic patients. But when they considered the results of the follow up of a group of nontrial controls, they were forced to modify their conclusion.

These nontrial patients were all on maintenance medications except for a "good prognosis group," which was off drugs. The overall relapse rate was 57 percent compared with a relapse rate of 53 percent for the trial group. But when subgroups were analyzed on the basis of prognostic indicators, it was found that 66 percent of the poor prognosis group relapsed and only 27 percent of the good prognosis group did so. The good prognosis group was kept off drugs by their doctors, and the relapse rate is significantly lower ( $P > 0.01$ ) than the relapse rate of the trial patients on placebo. It is clear that in general, neither the good prognosis group nor the poor prognosis group can be said to benefit from maintenance therapy with drugs. The patients with a good prognosis remained well without drugs, and patients with a poor prognosis relapsed despite drugs. He concludes by saying that a significant proportion of patients does not respond to drugs presently available for maintenance therapy.

The effectiveness of drugs in the treatment of chronic schizophrenia is not clear. In long-term trials, the effect of the drugs tends to be obscured by other factors. Much information has been obtained by examining the effects of stopping the use of drugs. Pasama-nick et al. (1967) carried out a controlled trial on the effects of stopping the use of drugs with outpatients. After 30 months they reported that 77 percent of the patients who were receiving drugs had been continuously in the community, but only 34 percent of those patients on

placebo had been able to do so. Prien and Klett (1972) reviewed the literature on the effects of both withdrawal of drugs and intermittent medication. They report that although there is great variation between different investigations, it can be said that about 40 percent of chronic schizophrenic patients who are receiving medication will relapse when it is stopped. If 40 percent relapse in their symptoms, then that means 60 percent do not relapse. This means at least 60 percent of chronic schizophrenics are being given unnecessary medication.

Other studies have also indicated that a large proportion of schizophrenic patients can be maintained in the community on placebo. Englehardt and Freedman (1969) found that two-thirds of their patients remained out of hospital for periods of one to five years on placebo, and that the risk of admission for this group of patients after six months was no greater than for those on active medication. The success rate with placebo is notable in other studies also. It has already been mentioned that one-fifth of Leff's patients remained out of hospital for a year on placebo alone. Olson and Peterson (1960) found that in a group of patients where nothing replaced the discontinued drug the relapse rate was 85 percent, whereas when a placebo was given it was only 29 percent.

Recently Hogarty et al. (1974) studied the effects of drugs and sociotherapeutic intervention on the performance and adjustment of patients who survive in the community. They concluded that "the medication clinic that simply offers 'pills' would do little to improve the adjustment of patients beyond forestalling relapse." Those that offer psychosocial treatments exclusively neither prevent relapse to any extent nor improve adjustment. These findings are in agreement with the results of earlier studies (Greenblatt et al., 1965).

So far in our discussion we have found that there is a group of acute patients who do not require drug treatment in the community. We have also found that a substantial proportion of chronic schizo-

phrenic patients do not require maintenance drug treatment either. Moreover the proportion of patients who could be maintained in the community increases substantially whenever a placebo is used. All these go to point out that a large number of patients are receiving drug therapy unnecessarily. The question may be asked, why not? Is it not better to prevent the possibility of a relapse in 40 percent, of patients, even if you have to give medications? The answer is yes it would be better to do that, if the drugs do not produce any undesirable effects: But unfortunately that is not the case. Textbooks of medicine are full of lists of complications produced by these drugs. I would mention one of the most incapacitating side effects of the drugs. It is called persistent dyskinesia. Forty percent of all patients receiving neuroleptics develop neurological side effects like Parkinsonism, motor restlessness (akathisia), and other abnormal movements (dyskinesia). The most disabling and irreversible side effect is the persistent dyskinesia, which is characterized by abnormal involuntary movements of the mouth, tongue, and face. The muscles of the trunk and limbs may also be affected. This syndrome occurs after prolonged treatment with neuroleptics. There is no totally effective treatment for this condition.

The commonest side effect is akinesia. It is characterized by weakness and muscular fatigue. It causes the patient to be almost constantly aware of fatigue in a limb used for ordinary repetitive motor tasks such as walking or writing. In advanced form the patient complains of aches and pains in the musculature of the affected limb. This may be associated with joint pains, most often in the shoulder, with limitation of motion. Patients with akinesia seem apathetic. They are disinclined to initiate or to expend energy to complete a task. Hence there is a reduction in their voluntary activity.

Apart from these and other side effects, there is the possibility that drug administration may actually inhibit the therapeutic process in the chronic

patient (Hamilton et al., 1963). Earlier in this paper I referred to the possibility of the side effects of drugs hindering the social adaptation of patients. Paul et al., following a drug withdrawal study, have commented as follows (Paul et al., 1972). "Presence of maintenance drugs not only failed to contribute positively to patients' responsiveness to active treatment programs, but tended to produce a temporary decrement in response to such programs in comparison to patients placed on placebo, adding support to previous findings of impaired performance on learning tasks under drug states vs. nondrug states (Hartledge, 1965; Kamano, 1966; Otis, 1964; Vestre, 1965; Vestre, 1966)."

The introduction of longer acting drugs was greeted by another wave of enthusiasm. The first of these compounds was moditen (fluphenazine enanthate) which can be administered intramuscularly and which has therapeutic activity lasting two weeks or more. Subsequently fluphenazine decanoate was introduced, which has an even longer duration of action. More recently, penfluridol, an orally administered butyrophenone derivative, which has a duration of action of one week, has been tested in patients. These long acting preparations have solved the problem of the so-called "drug defaulters" to some extent, but much less than was anticipated (Johnson, 1976). But they have not affected the core problem of nonresponse to drugs. Nor have they improved the situation regarding the side effects which were mentioned before. On the contrary, the situation has become even more complicated in the area of side effects. Akinesia has become more of a problem, and the incidence of irreversible dyskinesias is on the increase. Depression as a complication of drug therapy has also shown a higher incidence.

### Summary

The usefulness of maintenance medication in schizophrenic patients in the community is a controversial subject. For acute patients, the need for such medication has been demonstrated, even

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though it has also been shown that a low-risk group (good prognosis group) in this population may need no maintenance medication at all. In the majority of chronic schizophrenic patients in the community, maintenance medication may be unnecessary. This is especially so for those patients who are on a low-dosage maintenance. It may even inhibit the reintegration of these patients into the community.

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