Early Intervention, Time-Limited, Targeted Pharmacotherapy of Schizophrenia

by William T. Carpenter, Jr., and Douglas W. Heinrichs

Abstract

A growing appreciation of the risks of long-term, continuous neuroleptic use in the aftercare of schizophrenic patients has led to a search for alternative strategies. The authors report their experiences with the clinical strategy of “targeted” medication, in which patients are followed drug free until prodromal signs of impending relapse appear. Medication is then initiated to abort the impending episode and discontinued when patients restabilize clinically. Preliminary experience suggests that control of schizophrenic symptomatology comparable to that obtained with maintenance drugs can be achieved with a marked reduction in medication use when the targeted strategy is applied in the context of a broad-based program of psychosocial intervention based on a comprehensive medical model.

Continuous use of antipsychotic medication during aftercare is virtually ubiquitous for patients with schizophrenia. In most settings clinicians recommend indefinite medication for their patients. Indeed, anyone conducting followup assessments or attempting to recruit off-drug patients for special study can attest to the extent that these drugs are used. This widespread practice draws support from numerous controlled studies demonstrating the superiority of continuous medication over placebo in reducing relapse rates in schizophrenics (Davis 1975). The exceptions to continuous drug use are found predominately among dropouts from the mental health care system and medication noncompliers who either refuse drugs or fail to follow treatment because of apathy, demoralization, or the like. Despite increased risk for relapse off medication, there is evidence that a number of such patients do well, and others with an unfavorable course of the illness would probably not do substantially better on drugs (Gardos and Cole 1976). We have suggested guidelines for identifying such patients elsewhere (Carpenter and Heinrichs 1981). However, determining the proportion of patients who can do well off drugs and the extent to which the increased risk of relapse can be countered by alternative pharmacotherapeutic strategies requires systematic evaluation.

Interest in such alternative approaches has grown with recognition of actual and potential risks associated with continuous medication. Prominent among these is the risk for tardive dyskinesia (Crane 1973; Gardos and Cole 1976; Jus et al. 1976; Carpenter and Rudo 1979; Task Force on Late Neurological Effects of Antipsychotic Drugs, Tardive Dyskinesia 1980; Jeste and Wyatt 1982). Other worrisome possibilities include an exacerbation of the deficit syndrome (Hartledge 1965; Vestre 1965, 1966; Paul, Tobias, and Holly 1972; Simpson 1975; McGlashan and Carpenter 1976) and the development of a "tardive psychosis" (Davis 1975; Gardos and Cole 1976).

Continuous use of antipsychotic medication during posthospital treatment has proved superior to placebo, especially as assessed by readmission rates (Davis 1975). However, a controlled study of the comparative effectiveness of continuous and noncontinuous pharmacotherapy has yet to be reported, except in preliminary communication (Carpenter et al. 1982). It is important to note that

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the intermittent drug approach, while involving periods during which the patient is drug free, is nevertheless a drug strategy and as such should not be prejudged on the basis of the placebo literature in early studies of maintenance neuroleptics. Furthermore, most clinicians' experience with drug-free patients involves those who refuse medicine, often avoid treatment, and are not likely to cooperate with clinicians to avert relapse with medication. Such experience is not an adequate basis for judging the feasibility of a carefully monitored strategy of medication discontinuation when patients are stable and readministration when relapse threatens.

Hogarty et al. (1976) reported experience with 41 patients who were discontinued from neuroleptics in a nonblind manner following 2 to 3 years of stable, nonrelapsed status on continuous drugs as part of an earlier study. Patients judged by clinicians to be "too ill" for drug withdrawal were not included. There was no control group, but the relapse rate for the year following drug withdrawal was 65.8 percent—almost identical to the 67.4 percent relapse rate for the first year after discharge following placebo substitution in the earlier controlled study by this group (Hogarty et al. 1973). A somewhat different definition of relapse was used in the open study, i.e., "unequivocal exacerbation of symptoms" instead of "clinical deterioration of such magnitude that rehospitalization seemed imminent." In fact in the open study hospitalization was avoided, presumably by reestablishing medication, in 23 of 27 relapses. At first glance these results may appear discouraging to a strategy of noncontinuous drug use. Indeed the authors of that report conclude that indefinite maintenance medication is required for most schizophrenic patients and that there is no basis for identifying cases which may be exceptions. Even in stable, cooperative patients judged not "too ill" to try discontinuation, a relapse rate comparable to the placebo condition of earlier studies occurs. However, it is critical to note that noncontinuous strategies do not promise to reduce relapse rates in the absence of drugs. The data on this point are clear and abundant. Rather such strategies argue that the relapses that inevitably occur can be detected in the prodromal phase and, with prompt pharmacologic intervention, aborted before the disruptive effects of a florid psychosis occur. Indeed if just moving the timing of intervention forward to the point of unequivocal relapse can reduce the hospitalization rate among relapsed patients from nearly 100 percent (Hogarty et al. 1973) to 15 percent (4 of 27 in drug discontinuation), is it not reasonable that intervening even sooner—at the first appearance of prodromal changes suggestive of impending relapse—might allow a restabilization of the patient with little consequence for clinical deterioration or role dysfunction?

The utility of noncontinuous pharmacotherapy has been demonstrated in the practice of a number of experienced clinicians with the special vantage of long-term involvement with schizophrenic patients (Bleuler 1978; Huber, Gross, and Schüttler 1979; Ciompi 1980). Furthermore, an open study reported by Herz, Szymanski, and Simon (1982) demonstrated feasibility in 19 carefully selected patients. Together these descriptions suggest that, in the context of an ongoing relationship between clinician and patient, an extended period without drugs when patients are stable is a workable strategy. In fact, some patients show improvement: greater energy, emotional expressiveness, motivation, and interest in the environment. Such a relationship allows the detailed knowledge of the patient and the careful monitoring of clinical state needed to recognize and treat promptly the early, perhaps subtle, changes suggestive of impending relapse.

Further support for the feasibility of an intermittent drug strategy comes from hints in the literature that patients decompensating off medication are more responsive to treatment and/or have more benign decompensations than patients who experience relapse on medication (Gardos and Cole 1976). This may be because both mild and severe relapses occur with the unmedicated group, while for the medicated group only severe relapses break through the barrier provided by medication; any comparison of severity of relapse and treatment resistance is biased in favor of the unmedicated group. An additional possibility is that prolonged use of antipsychotic drugs diminishes their effect, resulting in a more robust therapeutic response in the unmedicated patient. It is also a plausible assumption that patients responsive to continuous medication would be quite responsive to the initiation of medication during subsequent drug-free intervals. For such patients, responsiveness to continued medication offers an a priori basis for assuming that relapse off medication can be effectively controlled by the prompt resumption of medication. The key unknown issue here is whether such intervention can come quickly enough to avoid the risks and discomfort associated with the emergence of significant psychotic symptomatology. In short, would early intervention abort or merely ameliorate an impending psychotic episode? In spite of existing clinical experience,
the relative efficacy and the generalizability of such an approach to medication are yet to be established. Toward this end, we are studying a heterogeneous group of schizophrenic patients in which an intermittent drug strategy, termed the "targeted" medication approach, is compared with continuous drug use. This article will describe the clinical care strategies we use in our targeted medication approach, and report preliminary research data supporting its feasibility.

**Description of Program**

Patients attending the Walnut Street Clinic of the Maryland Psychiatric Research Center are referred to this research setting if they have a diagnosis of schizophrenia and a preliminary willingness to participate in a comparison of intermittent medication with continuous medication in a randomized trial. In addition to a clinical judgment that the patient has schizophrenia and that treatment with antipsychotic drugs is appropriate, Research Diagnostic Criteria (Spitzer, Endicott, and Robins 1978) for schizophrenia, or schizoaffective, mainly schizophrenic, illness are met by all study subjects. Patients are recruited in most instances at the time of discharge from inpatient psychiatric units, the majority of which are in the public sector. Chronic and subchronic conditions in the poor- to mid-prognostic range predominate.

Upon referral and admission to the research clinic, all patients enter a 4- to 8-week stabilization and evaluation period. In almost all cases, patients are receiving significant doses of neuroleptic drugs upon entering the clinic, and medication is continued at a level judged optimal to induce a stable state with minimal symptoms. The initial stabilization and evaluation phase has proved an important aspect of the research because in these times of brief hospitalizations most patients enter aftercare treatment in only partial remission. This period also serves to establish a relationship and treatment alliance with the patients and their families (about half of our patients live with spouse or relatives) through weekly visits with a clinician/evaluator. Also, during this time a detailed clinical history is obtained from the patient and relatives. Signs and symptoms characteristic of the prodromal phase preceding past psychotic episodes are emphasized.

All patients next enter a drug-free period during which they are closely monitored. In most cases medication is discontinued abruptly. Although probably not the optimal strategy for drug discontinuation, it is helpful in performing one of the primary tasks of this phase, i.e., the recognition of overt tardive dyskinesias (Carpenter 1978). The drug-free period also provides an opportunity to form baseline impressions of patients' clinical condition off medication. During this period patients are seen weekly, with more frequent consultations with patient and family as needed to assure prompt recognition of any clinical deterioration. If significant clinical worsening is noted, medication is promptly reinstituted; if not, patients continue drug free for 4 weeks. In patients requiring medication before completion of the prescribed drug-free period, medication is continued until restabilization of the patient's condition, drugs are continued for a period not exceeding 4 weeks, at which time the patient returns to the drug-free condition. The same effort to detect signs of early decompensation is made with patients in the continuous medication assignment. When signs of decompensation are detected, the dose of medication is immediately raised to therapeutic levels appropriate for treating a psychotic episode. Upon restabilization of the patient's condition, medication is reduced to a maintenance level.

We believe an integrated, multimodality therapeutic approach is optimal when treating patients with psychotic illness. Polemics among mental health professionals, and the fact that clinicians have often focused on their favorite treatment approach while ignoring others, have impeded meaningful integration. Even today, when most workers accept a role for pharmacotherapy and for some form of psychosocial treatment, clinical approaches may be multimodal without integration. The physician medicates, the case manager oversees living requirements, the social worker deals with relatives, etc. Each therapeutic intervention takes place in relative isolation. The integration
of these seemingly disparate elements of clinical care is crucial to an approach which relies on early recognition of symptom change and rapid change in treatment approach. Hence, the pharmacotherapeutic treatment described above is integrated with a psychosocial treatment program. The core therapeutic experience for all patients in this aspect of the program is an ongoing individual relationship with a therapist/case manager. This clinician typically has professional training at the master's level in social work or psychology. The psychiatrist (usually an advanced resident on research elective) is readily available to the therapist/case manager for brief consultation or rapid intervention. Also, by attending weekly clinic meetings, all clinically involved staff members maintain an ongoing dialogue concerning patients and integration of various treatments. Finally, the psychiatrists interview their patients initially and maintain personal familiarity with their patients by brief, occasional meetings. While not very time consuming, the meetings enable the person making critical drug decisions to have a personal grasp of the patient, as well as to be informed by other members of the team. For the patient, the regular meetings avoid the sense of dealing with a stranger at crucial points in the course of treatment. The case manager/therapist plans weekly meetings with each patient and has four primary functions with respect to therapist/patient interaction.

1. Beginning early in the treatment experience the case manager/therapist explicitly discusses with the patient the nature of his or her illness, with special emphasis on characteristic signs, symptoms, course, and rationale for treatment. The value of early detection of psychotic episodes is stressed whether the patient is receiving continuous or targeted medication. The therapist helps the patient develop a "checklist" of prodromal symptoms noted to have preceded his past psychotic episodes. The therapist then works together with the patient to maintain continued vigilance for the appearance of these symptoms or other suggestions of early relapse. Should such symptoms emerge, the therapist discusses their possible significance with the patient and addresses any tendencies toward resistance and denial that may be present on the patient's part. The therapist then assists the patient in clearly communicating the symptoms and context of their appearance to the psychiatrist, who makes a decision as to the appropriate pharmacologic intervention.

2. In addition to a direct role in implementing optimal pharmacotherapy, the therapist uses his ongoing relationship with the patient to help the latter recognize the important role of environmental stress in inducing symptomatic exacerbation. Relevant stressors are identified and discussed. The therapist helps the patient improve coping strategies and employs environmental manipulations to minimize such stress. At times the active involvement of the therapist in the patient's environment is required to reduce interpersonal, financial, and other stress in the tradition of social casework.

3. When obvious sources of stress in the patient's life are relatively stabilized, attention is paid to helping the patient gradually improve his or her level of functioning in interpersonal and instrumental spheres. This attempt entails systematic attention to the deficit syndrome, which is accompanied by appropriate cautions against moving too quickly and careful attention to the possible emergence of psychotic symptomatology as increased demands for performance are made.

4. Finally, the therapist serves to coordinate the patient's participation in therapeutic and research procedures. The therapist is responsible for knowing the full range and level of the patient's participation in the program, considering the possible positive and negative interactions of various portions of the program, and monitoring the patient's overall reactions to the clinical and research experience. This function also provides continuity over time for informing and enhancing the consent process for research and treatment procedures.

A second critical component of the psychosocial treatment program is an effort to involve, educate, and assist the family in coping with schizophrenic illness in one of its members. At the beginning of the treatment experience, families are invited to a series of six weekly sessions with the therapist. Instead of being presented as family therapy, these sessions are explicitly presented as an opportunity for family members to learn more about the illness and to have questions and concerns answered. The sessions begin with the therapist asking the patient and family to describe the patient's illness from their respective viewpoints. These exchanges frequently lead to an increased capacity for mutual empathy. Also, many questions are generated by both patient and family about the emergence, nature, prognosis, and treatment of the illness. All questions are answered in a matter-of-fact style, drawing on the existing literature, yet an attempt is made to relate this general information to the patient's specific case. Overly abstract or theoretical explanations are eschewed, and the lack of
specific knowledge on many important facets of schizophrenia is explained. As in individual patient contacts, special attention is paid to describing prodromal symptoms and the importance of early detection and treatment of relapse. In the course of this experience the therapist frequently becomes aware of major emotional concerns among family members, e.g., fear, guilt, shame, disappointment, and hopelessness, that must be empathically acknowledged and addressed. Although the degree of sophistication with which the material is discussed varies with the desires and abilities of the family, the notion of schizophrenia presented always includes the idea that although much is unknown about its underlying etiology, it is a stress-responsive illness. The family sessions consequently involve an attempt to articulate the major sources of stress in the patient's and family's life followed by practical suggestions for reducing them. Additional contact with families beyond the routinely prescribed sessions is individualized at the discretion of the therapist. In all cases, however, continued effort is made to encourage the family to contact the therapist at times of crisis, on encountering difficulty in managing or coping with the illness in the home, or when early decompensation is suspected. Therapists also maintain close contact with the family for periodic followup.

As an additional component of the psychosocial program, all patients are encouraged to participate in a "social club" in which patients, under supervision of a social worker, organize and carry out a range of group activities and projects of general interest. The purpose of this setting is to give patients an opportunity to form social relationships with one another. It also seems to enhance patients' emotional ties to the clinic.

**Preliminary Findings**

Experience thus far with this experimental approach supports the feasibility of an early intervention, targeted pharmacotherapeutic approach. We earlier cited favorable experience in the European long-term reports and in the open study by Herz, Szymanski, and Simon (1982). We have now discontinued antipsychotic drugs in over 100 patients. About two-thirds go 4 weeks without requiring the reinstatement of medication. About one-third show at least prodromal symptoms, but these patients are successfully treated on an outpatient basis, with restabilization occurring within a month in most instances. Eight of the first 102 patients placed on the drug-free regimen were rehospitalized. On this basis, we assume that the base rate for rehospitalization during a 28-day drug-free period is probably no greater than 8 percent, provided that patients are carefully monitored. Details of the drug discontinuation experience will be reported separately. In accordance with expectations, the period also proved useful for detecting covert tardive dyskinesia (Carpenter, Rey, and Stephens 1982).

We have now followed over 40 patients for 24 months in the treatment study and results are in keeping with preliminary data reported elsewhere (Carpenter et al. 1982) and reproduced in table 1. These data reveal that outcomes, as measured by positive symptoms, social and work performance, and negative symptom course, are essentially similar in continuous and intermittent drug treatment. Minor, nonsignificant differences show the expected mild shifts toward more symptomatology in the targeted group counterbalanced by slight

Table 1. Outcome variables at 6 months in two drug treatment conditions

<table>
<thead>
<tr>
<th>Outcome variables</th>
<th>Targeted drug (n = 14)</th>
<th>Continuous drug (n = 27)</th>
<th>p values^2</th>
</tr>
</thead>
<tbody>
<tr>
<td>Strauss-Carpenter outcome score</td>
<td>21.5</td>
<td>22.9</td>
<td>NS</td>
</tr>
<tr>
<td>Global assessment score</td>
<td>52.0</td>
<td>54.8</td>
<td>NS</td>
</tr>
<tr>
<td>BPRS total score</td>
<td>1.93</td>
<td>1.75</td>
<td>NS</td>
</tr>
<tr>
<td>Number of hospitalizations</td>
<td>4</td>
<td>2</td>
<td>NS</td>
</tr>
<tr>
<td>Days in hospital</td>
<td>35</td>
<td>32</td>
<td>NS</td>
</tr>
<tr>
<td>Numbers of weeks on drugs</td>
<td>8.8</td>
<td>25.2</td>
<td>.001</td>
</tr>
<tr>
<td>Total drug dose per patient in CPZ</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>equivalents over 6 months</td>
<td>28,095</td>
<td>69,210</td>
<td>.001</td>
</tr>
</tbody>
</table>

^1 Cohort size is different since two of each three patients were randomized to the continuous drug group at the beginning of this project.

^2 Based on nonpaired t tests.
Scores above are means except for number of hospitalizations.
advantages in interpersonal and intrapsychic functioning. In any case, global outcome and clinical measures reveal no difference between treatment groups. As for the need for hospitalization, the targeted drug patients appear to require more frequent hospital admissions, but hospital stay is appreciably shorter, resulting in similar overall hospital utilization in the two groups. The hypothesized extensive reduction in use of antipsychotic drugs was achieved in the targeted drug group, as measured both by weeks on medication (one-third of the time) and total dose.

Discussion

It appears feasible to apply the targeted approach to a broad range of schizophrenic patients without incurring the dire consequences often presupposed, such as extending hospitalization, disruption of living and work arrangements, harm to self and others, and progressive deterioration. It also appears that many schizophrenic patients can be managed with targeted interventions, with an outcome, as measured by symptomatology and days of hospitalization, that is comparable to that achieved with the traditional maintenance therapy. Furthermore, it is evident that the targeted medication strategy yields a significant reduction in exposure to neuroleptic drugs for schizophrenic patients and thereby presumably reduces the risks inherent in such exposure.

There are certain requirements of both the patient and the treatment program if the targeted strategy is to work effectively. The patient’s psychosis must have episodic features with a prodromal phase or gradual onset of relapse. Specifically, those patients characterized by continuously severe psychosis which worsens on drug withdrawal are not good candidates for this approach. Typically, these patients show an exacerbation of symptomatology within hours to days of drug discontinuation or reduction. This suggests that the medications are not simply prophylactic but are an active treatment of an ongoing psychotic process. Beyond this, there are a few patients whose psychotic episodes have a sudden catastrophic onset. Included are those who develop full-blown, florid psychosis without prodromal features or a gradual rise in severity. Also included are patients whose earliest signs of relapse are either characterized by destructive or disruptive behavior or such blatant denial of illness as to make them ill-disposed for further treatment. On the other hand, patients who are noncompliant with maintenance drug approaches may be good candidates for targeted drug use. Some patients, who find taking medication every day regardless of how they feel unacceptable, enthusiastically embrace the idea of using medicine only at times of identifiable need. Patients with infrequent episodes in the past may also be good patients for the targeted approach.

In order to develop information on the range of patients for whom the targeted approach is suited, we have chosen to enter a wide range of diagnostically appropriate patients into the study. An alternative and complementary approach is that used by Herz, Szymanski, and Simon (1982) in their ongoing study. While they use essentially the same strategy of targeted intervention, their patients are limited to a group that would be presumptively judged as optimal candidates, namely remitted patients who have been stable as outpatients for at least 6 months and who do not decompensate during drug withdrawal.

Another program requirement in implementing a targeted medication approach is to establish a framework for cooperation with the patient. We use an educational approach to develop a shared view of the illness experience. Patients must accept at some level, however basic or tentative, that they are subject to a disruptive inner process that, when left untreated, leads to undesirable consequences. Instilling this level of awareness is an achievable objective for most patients. For example, patients who do not question the validity of delusional beliefs can frequently understand that the anxiety engendered by these beliefs and the urge to act on them can cause both personal discomfort and difficulty with others. Such a narrow consensus between patient and therapist can be enough to build a needed framework for cooperation. Patients must be as informed as possible about their illness so that they recognize their vulnerability to episodes of psychosis and become intimately familiar with the subjective and behavioral warning signs of impending relapse. Furthermore, they should be aware of the rationale for treatment interventions, including pharmacotherapy, designed to abort these episodes. Again, this is possible with most patients, including some formerly viewed as uncooperative because of resistance to the traditional maintenance medication approach. The latter is not surprising since it is well known that with such chronic illnesses as hypertension and diabetes people are disinclined to take medication daily in the absence of current symptoms. This is especially true when the medications induce negative subjective effects.

In the targeted approach it is
likewise critical to engage the families (or important others) of patients. For the approach to be optimally effective, it is necessary to educate families about the illness, to include them in the process of identifying and articulating prodromal patterns and remaining vigilant with respect to the recurrence of prodromal symptoms. It is also important that they be encouraged to take a role in assuring the initiation of appropriate intervention when relapse threatens. Families are often best at recognizing subtle behavioral changes in the patient that precede psychosis. In the retrospective study by Herz and Melville (1980), over 90 percent of families interviewed could describe prodromal symptoms versus about 70 percent of the patients themselves. Family input is particularly valuable in those cases in which patients experience cognitive impairment or a reduction in communication skills early in the prodromal phase.

Families can play a crucial role in making both patient and therapist aware of these changes and in assuring that treatment recommendations are carried out. This is vital in an illness where apathy and poor insight so often interrupt treatment. In addition to the useful information gained, the inclusion of families in the treatment process has the benefit of helping them feel that they are valued allies in the effort to control the effects of illness. For many families, this is a welcome shift in perspective from what they formerly perceived to be an accusatory and rejecting attitude on the part of mental health professionals.

To work effectively and securely within the above framework, both patients and their household members need to feel that the treatment team is readily available at times of need and that continuity in clinical care is assured. In our system the therapist provides an organizing focus for this continuity for both patient and family. Whenever possible all clinical issues are directed to the therapist. It remains the therapist’s responsibility to bring together those members of the treatment team whose special expertise is required for dealing with a given problem. To ensure immediate availability of staff members, a psychiatrist and a nonphysician mental health professional are on call and available to patients and families 24 hours a day, 7 days a week. We stress the importance of prompt intervention as soon as prodromal experiences are noted, and this degree of availability is necessary for rapid treatment intervention. In the intermittent approach, assurances of availability are also important to reduce the understandable anxiety experienced by many patients and their families about medication discontinuation.

The effective implementation of a sophisticated pharmacologic strategy in the context of a broad-based psychosocial treatment program requires that psychiatrists and other mental health workers cooperate closely within an integrated medical model. A shared perspective on treatment goals and rationales for various treatment components requires considerable discussion among members of the treatment team. For example, the psychiatrist is interested not only in therapist reports of the signs and symptoms suggesting relapse, but in discussion with both therapist and patient seeks to obtain a clear understanding of the social and environmental context in which symptoms are occurring. Psychosocial interventions to complement the prescription of medication are also planned and discussed in a three-way exchange among patient, therapist, and psychiatrist. In addition, twice-weekly clinical rounds led by the clinic director and attended by physicians, therapists, and nursing staff help assure that all members of the clinical team are aware of the overall treatment strategy for each patient.

This approach contrasts sharply with more usual settings in which physician and nonphysician clinicians have a clearer division of labor and expertise. It is considered essential that therapists appreciate the basis for pharmacotherapeutic decision-making and that physicians consider treatment needs in the broad context of the psychological and social context of each patient. We have found that this type of approach adds interest and satisfaction to the roles of physician and nonphysician alike without obscuring role definitions. Engel (1977) has explicated the medical model used, and Strauss and Carpenter (1981) have discussed its application to schizophrenia.

Although certainly not limited to targeted drug intervention, we have found that attention to stress management has come to play a central role in the psychotherapeutic work with our patients. Patients need to learn that medication is not the sole or even the most effective technique for dealing with life stressors. The stress-responsive nature of schizophrenic psychosis suggests that effective anticipation of stressful circumstances and the prophylactic management of stressors by personal, interpersonal, and environmental means can significantly reduce psychotic relapses and enhance the efficacy of pharmacotherapy (Goldstein et al. 1978; Leff and Vaughn 1981; Liberman, Marshall, and Burke 1981; Falloon et al. 1982; Leff et al. 1982). The result is often to reduce the need for neuroleptic drugs and increase the feasi-
bility of noncontinuous drug use.

An unanticipated challenge experienced in our work is the need to help patients manage the consequences of the affective brightening, increased energy, and renewed interest in life that frequently accompany drug discontinuation. We find that when drugs are discontinued, about two-thirds of the nondecompensating patients show such a brightening. Despite the positive aspects of this phenomenon, patients often feel more frustrated and discontented with the limited lives they are leading. A frequent response is for patients to develop overly ambitious plans, often with a sense of urgency that seems to derive from a need "to make up for lost time." Unfortunately, the increase in energy and enthusiasm is not usually accompanied by an increase in the social and instrumental skills necessary to fulfill renewed ambitions. As a consequence, unrealistic plans and ambitions often lead to considerable stress as patients attempt to fulfill them. The end result can be demoralization and depression in the face of inevitable failures and/or psychotic relapse in response to the significant increase in stress. In the therapeutic management of these patients, it is important to recognize the emergence of this pattern quickly and to teach patients to modulate the demands they put on themselves and thus reduce the stress to which they are subjected. The importance of making gradual but steady progress in manageable increments is emphasized. At such times, patients often express sadness or shame over their past failure to achieve and the painful awareness that they are so far behind their peers in self-actualization. An empathic acknowledgment of these feelings by therapists is necessarily accompanied by supportive confrontation when patients' plans are unrealistic. They are reminded that each step toward fuller functioning is a time of heightened vulnerability for psychosis. But this vulnerability is more manageable if progress is taken gradually and if patient and therapist remain vigilant for early signs of decompensation and respond promptly with medication and psychosocial support. It is made clear to the patients that emergence of symptoms may require a transient reduction in level of activity but that this is temporary and that as stability is reestablished, progressive steps will again be possible.

Another added therapeutic challenge that has arisen is the need to help patients distinguish between early relapse and the increase in affective response, including dysphorias, that unmedicated patients experience in reaction to the normal vicissitudes of living. This requires mutual phenomenologic exploration of their subjective experience and support of their efforts at adapting to heightened awareness and reactivity. Finally, some patients consider the increased sense of well-being to indicate that they do not need antipsychotic drugs at any future time. Educational efforts which stress the rationale for antipsychotic drug therapy are essential.

If the targeted drug strategy is to have wide applicability, it must be shown to be both efficacious and compatible with available clinical resources. We purposely chose to employ a clinical staffing pattern similar to that characterizing many mental health centers. The bulk of direct clinical care is provided by nonphysician clinicians, i.e., master's level psychologists and social workers who serve as case manager-type therapists. In accordance with the protocol, they meet with patients on a weekly basis for 30 to 60 minutes. Physicians see the patients briefly (5 to 10 minutes) once or twice a month and at times of clinical change. As indicated, these contacts were made more effective by the intermediate involvement of the therapist, who is able to present a clear and succinct description of the clinical problem to the physician. The study protocol was designed so that equivalent clinician involvement is provided for patients in both the targeted and continuous medication groups. Although use of placebo for drug discontinuation might have alleviated some of the apprehension associated with patients being off drugs, we did not use this strategy because it is not used in typical clinics.

There are several factors that would reduce the amount of time needed to implement the targeted strategy below that required in this study. Since patients are randomly assigned to the treatment groups, a number of patients are treated with the targeted strategy who ordinarily would not be chosen—for example, patients who are almost continually psychotic or who suffer from frequent, severe relapses. These patients take a disproportionate amount of clinical time and would not be routinely selected for this treatment approach in a purely clinical setting. At the other end of the spectrum, there is a group of patients who master the targeted strategy not only well enough to cooperate fully with the clinician but to recognize early warning signs of relapse on their own and then seek help. Many of these patients internalize the targeted strategy in 3 to 6 months, after which time regular weekly sessions are probably not required to assure that early decompensations are promptly recognized and treated. There remains a large
group of patients in the middle who can effectively use a targeted strategy but who never fully internalize it. These patients are cooperative with treatment but require regular contact with a clinician to help them detect that an early decompensation is occurring. Even here, however, less clinician time than required by our study protocol, provided in the form of either briefer sessions or the use of a group therapy format, may be sufficient.

Finally, we should add a note indicating that problems found in other clinics treating the chronically and severely ill are common in our research clinic. Missed appointments, angry accusations, uncooperative relatives, arrests, sudden loss of place to live or job, paranoid attitude toward clinic, etc., are everyday problems. The clinical approach described is not an answer to the plethora of problems associated with the treatment of schizophrenia, nor have we selected an innately cooperative patient cohort for study.

Conclusion

The experience of many clinicians and the published descriptions by Bleuler (1978) and Herz, Szymanski, and Simon (1982) suggest that an intermittent, targeted drug strategy is feasible for some schizophrenic patients. Our preliminary results support this feasibility. Such an approach can result in an appreciable reduction in the exposure to neuroleptic medication. It is hoped that such a reduction would be paralleled by the lessening of attendant risks such as tardive dyskinesia and, possibly, tardive psychoses and the exacerbation of deficit symptoms. Beyond this, we have noted an important psychological benefit to patients who have learned to use the targeted drug strategy successfully, i.e., an increase in their sense of self-esteem and mastery over the illness.

For many patients the prescription of continuous medication conveys the message that they are perpetually powerless in the face of a terrifying and mysterious condition that can descend upon them without warning and throw their minds and their lives into utter chaos. This feeling is reinforced by the propensity toward passivity that is such an intrinsic part of the schizophrenic experience. With targeted medication, patients develop the sense that exacerbations of the illness can often be predicted early enough to initiate an effective intervention. Patients come to feel that they are active participants in this process in which their contribution to the therapeutic task is valued and appreciated. In many instances the experience of mastery has been found to generalize to other portions of the patient's life, yielding a global increase in self-esteem and sense of competence. The sense of active mastery is easiest for the patient to appreciate in the targeted strategy where drugs are only used in response to identifiable changes in clinical state. However, the same active participation can be achieved with early intervention approaches in the context of continuous maintenance medication. Hence, as a general clinical strategy, the approach described in this article integrates psychosocial techniques to enhance treatment which relies on continuous use of antipsychotic drugs and provides a basis for alternative pharmacotherapeutics.

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