First-episode schizophrenia

Early intervention and medication discontinuation in the context of course and treatment

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Background The concept that early intervention with antipsychotic medications improves the long-term course of schizophrenia is discussed.

Method This report reviews the literature concerning early intervention with antipsychotic medications for people with first episodes, and how it affects long-term morbidity. It also studies the effects of discontinuing antipsychotic medications on relapse for people with first episodes.

Results Early intervention with antipsychotic medications appears to decrease the long-term morbidity of schizophrenia.

Conclusions Early intervention with antipsychotic medications should be encouraged for people experiencing their first episode of schizophrenia. This report proposes that studying the various phases of subject response to treatment can be helpful in elucidating when antipsychotic medications should be tapered or withdrawn.

The concept of prevention is not new to psychiatry (Cameron, 1938), and has long been recognised in general medicine. In psychiatry, however, putting prevention into action has proven difficult. One of the many areas in psychiatry where secondary prevention may prove beneficial is in the treatment of first-episode schizophrenia. Here, we examine the evidence that treating individuals with schizophrenia early in the course of their illness decreases their long-term morbidity, and explore what is known about discontinuing antipsychotic medications for people suffering first episodes in relation to preventing relapses. We also introduce the issue of phases and change points in the course of recovery from the first episode of schizophrenia, and explore other factors that may be of value in preventing relapse/recurrence for people with first-episode psychosis.

A REVIEW OF EARLY INTERVENTION STUDIES

There are four lines of evidence indicating that early intervention with antipsychotic medications may decrease the long-term morbidity of schizophrenia. Taken individually, each kind of study has its own interpretative difficulties. Taken as a group, however, the studies appear to indicate that early intervention with antipsychotic medications does decrease the long-term morbidity of schizophrenia.

Epidemiological data

Epidemiological data look for evidence of changing incidence or severity of illness from a historical perspective. While a number of investigators (Eagles & Whalley, 1985; Parker *et al*, 1985; Munk-Jorgensen & Jorgensen, 1986; Joyce, 1987; Munk-Jorgensen, 1987; de Alarcon *et al*, 1990; Der *et al*, 1990; Waddington & Youssef, 1994) have pointed to a substantial body of evidence suggesting that the incidence of schizophrenia has decreased over the past 50 to 60 years, Kendell *et al* (1993), and others (Bamrah *et al*, 1991; Castle *et al*, 1991; Häfner & Gattaz, 1991; Harrison *et al*, 1991), have emphasised the many potential difficulties in making such estimates. Notably, there have been many changes in the way schizophrenia is diagnosed (Hegarty *et al*, 1994).

There appears to be less disagreement about whether or not the severity of schizophrenia has decreased during the past 50 to 60 years (Ey *et al*, 1957; Achté, 1961; Astrup & Noriek, 1966; Hare, 1983), and it is unlikely that changes in severity could be attributed to changes in diagnostic methods. For example, although people with severe nutritional deficiencies and viral encephalitis might at times have been confused with people suffering from schizophrenia, there is no reason to suspect that they would have often confused good clinicians such as Bleuler, Astrup, Ey and Achté. Furthermore, mistaking people with affective disorders for those with schizophrenia, which was common in North America until relatively recently (Gurland *et al*, 1969), would probably have made cases of schizophrenia in the earlier part of the century seem less rather than more severe. Hegarty *et al* (1994), however, point out that there may have been cycles in diagnosis which could account for some of these differences. Eugen Bleuler attributed the decrease in the 1930s and early 1940s of what was called catastrophic schizophrenia (schizophrenia with sudden onset and severe deterioration) to improved psychosocial care (Bleuler, 1978). The decrease in severity could also be attributed to the introduction of convulsive therapies in the early 1940s. In fact, one well-controlled study carried out in the late 1950s and early 1960s (May *et al*, 1976*b*) demonstrated that electroconvulsive therapy does decrease the long-term morbidity of first-episode schizophrenia. The results of a meta-analysis carried out by Hegarty *et al* (1994) also supports the conclusion that the introduction of convulsive therapies, and then antipsychotic medications, improved the course of schizophrenia, although that study did not focus on individuals experiencing first episodes.

Mirror-image studies

Mirror-image studies compare the outcomes of similar subject populations from the pre-antipsychotic and antipsychotic

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eras. Of nine such studies (Wyatt, 1991, 1995*a*), all but two indicate an improvement in the long-term course of schizophrenia after the introduction of antipsychotic medications. One study by Astrup & Noreik (1966) found that people with first-episode psychosis admitted to Oslo's Gaustad Hospital were more likely to deteriorate if they were admitted in the pre-antipsychotic era (1938–1950) than if they were admitted between 1951 and 1957 and given antipsychotic medications.

A major obstacle to accepting these studies as valid is that subject matching was likely to have been inexact, and, even when only a few years separated the two subject groups, other variables in addition to the use of antipsychotic medications during the first hospital admission may have influenced the individuals' outcomes. During the mid-1950s, for example, when antipsychotic medications were introduced, there was also a recognition that the large, impersonal, psychiatric hospitals of the period had to be improved; steps were already underway to make the conditions for patients more habitable by the time antipsychotic medications became available (Isaac & Armat, 1990).

Delayed intervention studies

Delayed intervention studies compare the outcome of people with schizophrenia who were treated in the early phases of their illness with those for whom treatment was delayed. Eight fairly well-controlled studies of this nature have now been identified (Astrup *et al*, 1962; Astrup & Noriek, 1966; Wyatt, 1991; McEvoy *et al*, 1991; Loebel *et al*, 1992; Szymanski *et al*, 1995; Waddington *et al*, 1995), and all but one of these indicate that delayed intervention leads to poorer long-term outcome. A similar conclusion has been drawn from a number of less well-controlled studies (Angrist & Schulz, 1990; Wyatt, 1995*a*).

Caution is necessary in interpreting these studies, because individuals who get treatment early in their illness may have a different form of schizophrenia than those for whom treatment is delayed. There are numerous studies demonstrating that people with an acute onset have a better prognosis than people whose onset is more gradual (Stephens, 1970) and, because of the florid nature of acute symptoms, it is likely that those with an acute onset would get treated more quickly than those people whose onset is gradual. A study by Loebel *et al* (1992) attempted to control for the type of onset, gradual *v.* sudden, and found that people who had been ill longer, as measured by either the time elapsed between their first prodromal or first psychotic symptoms and their first treatment, had a worse outcome. The time elapsed between the onset of prodromal and the onset of psychotic symptoms was not related to outcome. Other prospective studies are now needed to confirm these findings.

Contemporaneous control studies

These studies compare people who received treatment with antipsychotic medications to people who received a non-somatic treatment. While these studies should provide the most information about the role of early intervention on the long-term morbidity of schizophrenia, they are associated with their own set of confounding issues. Most of these studies were organised because the investigators felt that their version of psychosocial treatment had an advantage over antipsychotic medications. Often, considerable attention was paid to people receiving the psychosocial treatment, while individuals receiving antipsychotic medication were given 'usual care', which could often be wholly inadequate. Follow-up treatment, for example, was usually not equivalent for the two groups. There was much greater continuity of care, and perhaps caring, given to those people assigned to the psychosocial treatment groups. Individuals treated with antipsychotic medications were often discharged sooner and to a less adequate treatment facility than those who received the psychosocial treatment. It is also possible that some of the psychosocial treatments themselves might have produced benefits similar to those of antipsychotic medications. From the point of view of the question addressed here, however, the most important and rigorous study was carried out by May and colleagues (1976*a*,*b*; 1981). They found that antipsychotic medications given to people with first-episode schizophrenia improved the long-term outcome of such people when compared with those people initially treated by *milieu* – or psychotherapy alone.

THE COURSE OF FIRST-EPISODE SCHIZOPHRENIA

This section, which emphasises the period of post-florid psychosis, introduces the issue of phases and change points in the course of schizophrenia, and discusses how these concepts might be useful in the timing of medication discontinuation for individuals with first-episode psychosis. Precise definitions of phases and their change points in the course of schizophrenia are not available (Brown *et al*, 1972; Falloon, 1984; Lukoff *et al*, 1986); nevertheless, an attempt has been made to define change points for the course of major depressive disorders during pharmacological treatment (Frank *et al*, 1991). These concepts are useful in beginning to outline several theoretical phases, the corresponding change points, and their conceptual bases in the course of schizophrenia. People experiencing first-episodes who recover or go into remission pass through roughly seven phases illustrated in Fig. 1: non-psychotic decompensation (also known as the prodrome), psychotic decompensation, florid, resolving, transition, remission and recovery. Of these, it is the final four which are central to the issue of timing medication discontinuation. However, the first three may foreshadow the severity of the course

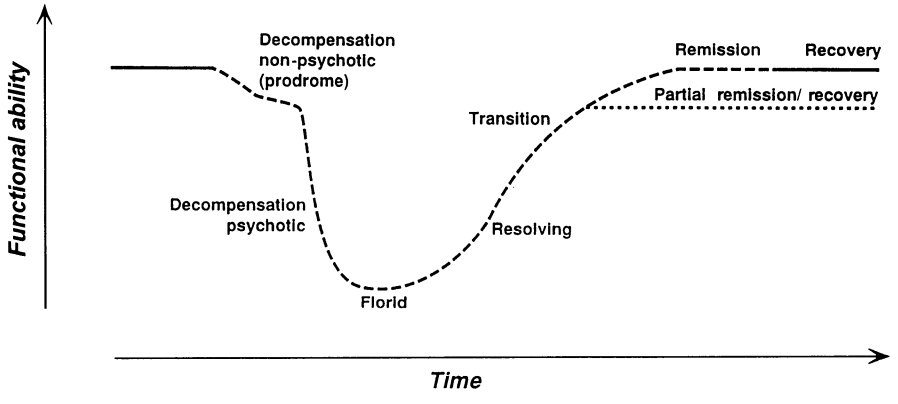


Fig. 1 Functional changes in people with first-episode schizophrenia over time.

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of the illness (Wyatt, 1991, 1995*a*,*b*). While the relationship between the resolving to recovery phases and outcome are discussed in some detail below, non-psychotic decompensation, psychotic decompensation, and florid phases are discussed only in passing.

Resolving phase

Clinical observations suggest that the process of going from a florid psychosis into complete or partial remission is one of resolving both positive and negative symptoms, as well as going through a transition phase in which non-psychotic symptoms such as depression, anxiety, social sensitivity, obsessive thoughts and ideas of self-reference are decreased.

The resolving phase begins when psychotic symptoms start to decrease (see Fig. 1); it continues until both positive and negative symptoms are either no longer present, have stabilised into a partial remission (defined below), or indicate that a chronic form of schizophrenia is present (not shown). In people with first-episode schizophrenia, it is our clinical impression that the length of the resolving phase is proportional to the length of time a person is psychotic or has prodromal symptoms. That is, the longer a person is ill before treatment, the longer the resolving phase will take after treatment is begun. Empirical evidence comes from a study of people with first-episode schizophrenia at Hillside Hospital (Loebel *et al*, 1992). That study found a direct correlation between the length of time until people treated with medications had no psychotic or negative symptoms and the duration of both prodromal (r=0.43, P=0.0001) and psychotic symptoms (r=0.30, P=0.001).

The actual length of the resolving phase has been examined in relatively few studies of people suffering first episodes. Another report from Hillside Hospital on the same group of people with schizophrenia, using a standardised treatment protocol, found that the median time to the disappearance of both positive and negative symptoms was 11 weeks, with a mean of almost 36 weeks; 26% of the people did not achieve full remission (Lieberman *et al*, 1993). If these people are typical, the duration of the resolving phase is extremely variable. In clinical situations and research studies where medications are discontinued in individuals who have not passed through the resolving phase, abrupt relapses might be expected. The results of such studies would look very different than the results of studies in which all the people had passed through the resolving phase before antipsychotic medications were discontinued.

Transition phase

During the transition phase (see Fig. 1), which can be quite lengthy, the person's 'buffering systems' are presumably still equilibrating. When people in this fragile state return to their previous environment – their families, school, or work – psychotic symptoms often re-emerge. The transition phase ends when transient events can no longer cause people to easily decompensate (Docherty *et al*, 1978), and when the non-psychotic symptoms described earlier are no longer present. Since a relapse might be expected to occur in a fairly short period of time, it might be best to wait until the transition phase is over before discontinuing antipsychotic medications.

Herz *et al* (1977) followed a group of people primarily with schizophrenia (chronicity was not stated), and found that after an average of six months, most patients had returned to a stable state (Herz *et al*, 1977). A few other studies have examined the length of time an individual needs to be in the transition phase before discontinuation of antipsychotic medications is attempted. The one relevant study of people with first-episode schizophrenia found that those people whose transition phase (or combined resolving, transition and perhaps remission phases) began at least one year prior to discontinuation of antipsychotic medications appeared to have a reduced risk of relapse compared with people who had shorter transition phases before antipsychotic medications were discontinued (Johnson, 1979). For people with chronic schizophrenia, who were probably in partial remission, it appears to make little difference when antipsychotic medications are discontinued; relapse rates for this population remain extraordinarily high (Johnson *et al*, 1983; Hegarty *et al*, 1994).

The resolving and transition phases have together been termed the 'improving' phase; however, improving has also been used to describe people with chronic schizophrenia who, after years of illness, experience a very gradual decrease in their symptoms (Breier *et al*, 1991). 'Stabilising' is another term which has been used to describe the combined resolving and transition phases, but this term has also been used to indicate a relatively stable nadir of symptoms, rather than a period of improvement (Breier *et al*, 1991).

Remission and recovery phases

For schizophrenia, we propose that recovery and remission be defined as bounded by several points of change, which in turn require further operational definitions.

In the literature, the terms recovery and remission are often used interchangeably (Frank *et al*, 1991). However, we define remission as a state in which the person has been asymptomatic for at least a certain number of days (t_{rm} days) and continued treatment is required for the person to remain asymptomatic. Recovery is defined as a state in which the person has been asymptomatic for at least a certain number of days (t_{rc} days) without the use of prosthetics such as antipsychotic medications. Partial remission is a state in which the person still has symptoms; though these have been stable for a given number of days (t_{prm} days), they would worsen if treatment were discontinued. Partial recovery is a state in which the person has had residual symptoms for a given number of days (t_{prc} days) and where symptoms remain stable in the absence of continued treatment. Any significant return of, or increase in, symptoms, either of a psychotic or non-psychotic nature, while a person is in remission is defined as a relapse; in contrast, any significant return of, or increase in, symptoms which occur when an individual has recovered is considered a recurrence.

Ideally, before the individual's antipsychotic medications are discontinued, that person should have reached the recovery or partial recovery phase. Since it is not now possible to know in advance if antipsychotic medications taken by people who are asymptomatic are suppressing symptoms, keeping the person stable, or have become unnecessary, in practice, individuals suffering from first episodes should be in remission, or at least partial remission, prior to discontinuation of antipsychotic medications.

DISCONTINUATION OF ANTIPSYCHOTIC MEDICATIONS

Evidence from early intervention studies and the concept of phases in the course of illness, both described above, could have a significant impact on the way researchers

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and clinicians use medication in the treatment of people with first-episode psychosis. If early intervention does decrease long-term morbidity, it might be that subsequent recurrences and relapses might also alter the long-term outcome, by working through the same mechanism that increases long-term morbidity for people untreated early in the course of their illness. Szymanski *et al* (1995) published preliminary results of an important prospective study of people with first-episode schizophrenia. With each relapse following medication discontinuation, individuals took longer to respond when antipsychotic medications were restarted. The observations of Szymanski *et al* are perhaps similar to the step-like changes found following each relapse which have been described in a number of longitudinal studies (Kraepelin, 1913; Snezhnevsky, 1966; Bleuler, 1978; Ciompi, 1980; Watt *et al*, 1983). Although it must be tested scientifically, it seems reasonable to assume that the increased length of time to treatment response which accompanies each relapse might eventually progress to non-responsiveness and intractability.

It is important to know at what point after a person has been treated for the first episode of schizophrenia to consider discontinuation of antipsychotic medications. Although there are no experimentally derived data suggesting how long to maintain first-episode people on antipsychotic medications, there are numerous reasons why a person should not remain on them longer than necessary. Discontinuation studies have not generally examined the effects of discontinuing antipsychotic medications on the long-term morbidity of schizophrenia, or generally dealt with people suffering first episode; instead, they have been more likely to include those who have relapsed at least once. The phases in the courses of illness described above may account for some of the variance following the discontinuation of antipsychotic medications in the few controlled studies of people with first-episode schizophrenia.

Studies examining relapse rates during the first year after discontinuation of antipsychotic medications in people experiencing first episodes have produced strikingly different results. For example, Johnson (1979), Kane *et al* (1982) and Crow *et al* (1986) found one-year relapse rates of 29%, 41% and 56% respectively; the subjects in the study of Crow *et al* (1986) had been further subdivided into two groups: those who had less than one year between onset of illness and treatment, and those who had more than one year between onset of illness and treatment. This contrasts with findings for people maintained on medication. Although only four people were maintained on antipsychotic medications in the study of Johnson (1979), Kane *et al* (1982) found relapse rates of 0% for the people in their sample, and Crow *et al* (1986) found relapse rates of 20% for those people who had been ill less than one year before treatment, and 67% for those people who had been ill more than one year before treatment. As Fig. 2 illustrates, the disparate relapse rates may be due to a number of factors, including medication administration, the use of psychosocial interventions, and length of illness prior to the first admission. Although results from these studies are widely varied, the conclusion which can be drawn is clear – maintenance treatment with antipsychotic medications is integral to prevention relapse in people with first-episode schizophrenia.

Another explanation for the disparate findings from the above studies may be the various lengths of time people spent in the resolving, transition and remission phases before antipsychotic medications were discontinued. For example, in the study conducted by Crow *et al* (1986), individuals were randomly assigned to one of two treatment groups if they had not relapsed within 30 days of their discharge from a treatment facility; the short period between discharge and further treatment assignment suggests that a number of people may still have been in the resolving phase. Johnson (1979) gave individuals depot medications for a minimum of three months prior to medication discontinuation, while the sample in the study by Kane *et al* (1982) included people treated with depot medications for 1–12 months following their first hospital admission. In

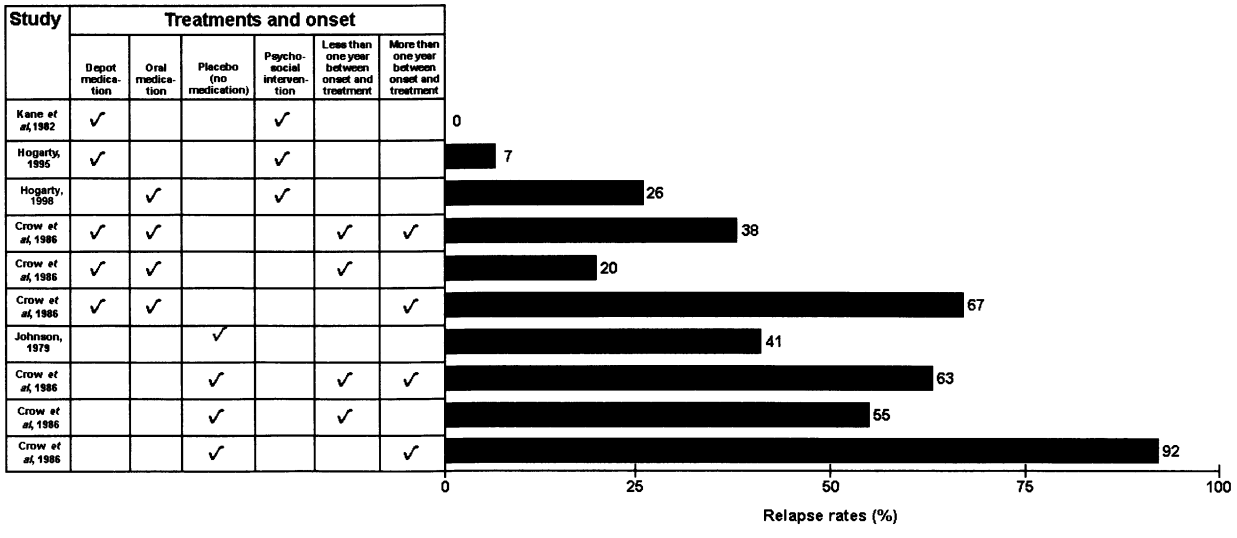


Fig. 2 Relapse rates for people with first-episode schizophrenia. Horizontal bars represent the results of several studies showing the percentage of people with first-episode schizophrenia who relapsed during one year. Treatments during the one year are noted by the checked columns. When the authors noted the length of illness prior to treatment, is also indicated.

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addition to the likelihood that people in these studies were in different phases of their illnesses when medication was discontinued, the differences in availability of psychosocial therapy may also have contributed to the different relapse rates; Kane *et al* (1982) offered many types of psychological and social interventions to their subjects, including mandatory standardised psychotherapy.

OTHER RELAPSE-RELATED VARIABLES

Regardless of the phase of an individual's illness and the timing of medication discontinuation, other factors, described below, appear to be important in both predicting and preventing relapse in people with first-episode schizophrenia. It is important to note that, with the exception of the study by Crow *et al* (1986), the people described were maintained on antipsychotic medications; it is unclear how the results might differ if antipsychotic medications had been discontinued.

Early assessment/treatment as a predictive variable

In the study by Crow *et al* (1986), people experiencing first episodes for whom more than one year elapsed between onset of schizophrenia and start of treatment tended to have higher relapse rates than those with less than one year between onset and treatment; this was true regardless of whether medications were continued or discontinued (see Fig. 2). When the individuals in that study were followed-up after two years, however, those who had been placed on placebo but who also had been ill for less than one year before treatment was started had higher occupational functioning than similar people who had been maintained on antipsychotic medications for the same length of time (Johnstone *et al*, 1990). It is possible that this somewhat paradoxical finding is associated with the cognitive blunting, as well as other secondary negative symptoms (Carpenter *et al*, 1988), caused by prolonged use of antipsychotic medications. As these findings and the ones described earlier suggest, the need for early assessment, accurate diagnosis and prompt treatment of schizophrenia is important, since timely introduction of therapy may reduce the risk of relapse and decrease the need for long-term use of antipsychotic medications (Wyatt, 1991, 1995*a*; Lieberman *et al*, 1993).

Expressed emotion as a predictive variable

Studies examining the importance of high levels of expressed emotion in family members and significant others of people with first-episode schizophrenia have produced inconsistent results (MacMillan *et al*, 1986; Barrelet *et al*, 1990; Stirling *et al*, 1991; Neuchterlein *et al*, 1992). Furthermore, when expressed emotion has been found to predict relapse, not only is the direction of causality unclear, but there may be intervening factors, such as severity of illness (Neuchterlein *et al*, 1992), that underlie the process of expressed emotion and confound the results. In order to gain knowledge about the role of expressed emotion in influencing relapse, it may be important to isolate the causes of the differential relapse rates found in the published studies of expressed emotion, such as: the culture of the patients studied, definitions of relapse, the aspects of expressed emotion under investigation (critical comments, emotional overinvolvement, hostility), cut-off points for high *v.* low expressed emotion, and definitions of high *v.* low contact with relatives.

Short-acting *v.* long-acting antipsychotic medications

Relapse prevention data from studies comparing short- *v.* long-acting antipsychotic medications are presented in Fig. 2. Hogarty (1998) examined data from an earlier study comparing oral with depot antipsychotic medications in people experiencing first episodes who were also receiving a psychosocial intervention. As Fig. 2 illustrates, people receiving long-acting depot antipsychotic medication had a zero (Kane *et al*, 1982) to seven (Hogarty, 1998) per cent relapse rate, while those receiving short-acting oral medications had a relapse rate of 26% (Hogarty, 1998). The Scottish Schizophrenia Research Group (1988) followed 49 people with first episodes given either a very high daily dose of pimozide once per week (which was thought to provide long-acting protection) or depot flupenthixol injections, and found that the two forms of administration were equally effective. Pimozide, however, appears to have more significant adverse effects than conventional antipsychotic medications (Teuth & Cheong, 1993) and is therefore not usually used in the treatment of schizophrenia. Another study by Kane *et al* (1982) found no significant differences between oral (short-acting) and depot (long-acting) antipsychotic medications in preventing relapse in these people. The studies comparing short- with long-acting antipsychotic medications in people with first-episode schizophrenia are too few and the results too disparate to conclude anything about the relative value of the two forms of medication administration. Nevertheless, since there is evidence that long-acting antipsychotic medications decrease the incidence of relapses in more chronic patients (Davis *et al*, 1993), until further controlled studies with people experiencing first episodes become available, data gathered from more chronic forms of the illness should be used as a guide.

Psychosocial intervention

While there are no studies which directly compare those experiencing first episodes treated with and without psychosocial interventions, at least one study (Goldstein *et al*, 1978) found that, in a group of people suffering from first- and second-episodes, six crisis-oriented family treatment sessions dramatically decreased relapse rate for six months following discharge in people who were treated with antipsychotic medications. Until research is conducted that examines this question directly, it may, again, be necessary to generalise from studies not restricted to people suffering first episodes, and conclude that psychosocial interventions are probably useful when combined with antipsychotic medications.

CONSIDERATIONS FOR CLINICAL PRACTICE AND RESEARCH

Today, when clinicians delay treating people with first-episode schizophrenia for a few days, it is usually for diagnostic purposes. Longer delays occur when the clinician remains unsure of the diagnosis, and does not want to unduly subject the person to the risks of antipsychotic medications. Although delays in treatment might be of immediate importance (for example, they might increase the risk of violence), there are no data even hinting that such minor delays in instituting treatment can increase long-term morbidity. Unless such

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data become available, it would seem prudent to be more concerned about balancing the person's immediate discomfort and risks against delaying institution of treatment to produce a clinical or research gain.

Studies of people with first-episode schizophrenia indicate that maintaining people on antipsychotic medications prolongs the time until relapse. There is also evidence that early treatment of first-episode patients may decrease the risk of relapse (Crow *et al*, 1986). The decreased relapse rate for people whose treatment begins early, in turn, appears to increase the probability that once antipsychotic medications are discontinued, the individual will be able to function at a higher level (Johnstone *et al*, 1990). Nevertheless, a few people will want to stay on antipsychotic medications indefinitely, and this is what makes the issue of medication discontinuation so crucial. Most people find the side-effects of antipsychotic medications unpleasant. Furthermore, the longer a person remains on these medications the greater the risk of tardive dyskinesia. Even if these considerations were not a factor many studies from other branches of medicine have noted that, once acute symptoms have subsided, individuals begin to forget to take their medications. It follows that people whose cognitive and motivational abilities may be impaired by their illness, such as individuals with schizophrenia, will be less likely than most to continue taking medications unless they are encouraged to do so or unless they perceive a risk in not doing so.

A percentage, perhaps as high as 20–30% of people with first-episode schizophrenia will not require rehospitalisation and perhaps do not require antipsychotic medications after they have recovered from their psychosis (Eaton *et al*, 1992; Ram *et al*, 1992). It is thus incumbent upon the clinician to have a rational approach to offer after a person with first-episode schizophrenia has stabilised at his or her best level of function. There is no experimentally set standard for how long to wait, but there is some consensus that, after a person has been stable for a year or two, there should be a gradual reduction in the dose of antipsychotic medication (Kissling, 1991). The clinician must also learn, from experience, how fast to taper the medication. Our personal experience suggests that the dose needs to be reduced very slowly, perhaps over a period of a year or more. This gives the individual, their family and their clinician time to evaluate possible prodromal symptoms and, if these occur, the dose of antipsychotic medication can be immediately augmented, usually by doubling it.

In contrast, researchers will fairly commonly discontinue antipsychotic medications to answer a number of questions. Justification for this is a controversial topic (Carpenter, 1997; Wyatt, 1997). The evidence that taking people off antipsychotic medications produces benefits is about equal to the evidence suggesting that it may cause long-term harm. Even if this were not the case for the average person, it is important to determine which people will need to continue taking antipsychotic medications. Clinical practice dictates that individuals be given the opportunity to determine whether they will need to continue taking these medications indefinitely. Such determinations might be done in a research setting where control over the person is usually better than in the general clinical setting, and where there is an opportunity to learn (generalise) from the experience. Such control is important because, as medications are withdrawn, predetermined thresholds can be drawn for where 'rescue' medication will be used if it is needed. This issue is particularly crucial for people suffering their first episode. For example, Hogarty (1998) studied the differences between people with first-episode schizophrenia and those who had a greater number of relapses. During the first year after their first episode, people who were maintained on depot medications had a 0–7% rate of relapse. Individuals with more than five prior episodes had a greater than 50% rate of relapse.

Other factors which may decrease the relapse rate of people with first-episode schizophrenia (particularly when combined with maintenance medications) include: the absence of expressed emotion in the family, the use of long-acting antipsychotic medications, early treatment and assessment and the use of psychosocial interventions. Unfortunately, there is no consistent body of literature to support the relevance of any of these factors in preventing relapse in these people. In order to make recommendations regarding the treatment of these people, generalisations from studies of more chronic individuals may have to suffice.

As suggested by the studies reviewed above, discontinuing an individual's medication during different phases of their illness may lead to disparate relapse rates. To help place the existing studies into perspective, but, more importantly to help guide future studies, we have proposed generic definitions of the phases that people with first-episode schizophrenia go through on their way to remission and recovery. In proposing these definitions, we hope to commence a dialogue, which will help provide better operational definitions, and thus create improved treatment strategies.

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