Medication Noncompliance in Schizophrenia: Codification and Update

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Risk of relapse and recidivism makes the failure to take antipsychotic medication as prescribed a significant issue in forensic psychiatry. This question may arise in such contexts as the setting of bail, plea bargaining, the insanity defense, and sentencing. We have reviewed the literature on medication noncompliance in schizophrenia and present here the results, organized by topics relevant for the work of forensic mental health experts.

Reported rates of noncompliance vary widely, reflecting major differences in the populations studied and the methods used as well as the complexities involved in defining noncompliant behavior. A noncompliance rate of 50 percent has been attributed globally to chronic patients, both medical and psychiatric.

The tendency of significant factors to interact precludes a simple typology of noncompliance. However, environmental security and supportiveness correlate positively with adherence; whereas anxiety, paranoia, grandiosity, depression, and side effects correlate negatively.

Clinicians' assessments of whether medication is being taken have proven to be unreliable. Although monitoring by chemical measurement, particularly a radioreceptor assay for urine samples, can be useful, depot injection ensures that prescribed medication is being taken. Less invasive means of promoting compliance are described; psychodynamic and ethical issues to be considered in the monitoring and promotion of compliance over extended time periods are presented.

We also probe the link between medication noncompliance and behavioral relapse. The time between default and relapse is most often measured in weeks. Whether due to medication withdrawal or not, the relapse pattern of each individual tends to repeat, allowing its recognition before recidivism occurs. Restarting medication at this stage, especially with a dosage increase, is usually effective.

In sum, the forensic mental health expert can now readily use a large and diverse literature to assist with a variety of significant issues.

Medication noncompliance, a focus of forensic evaluations, is also the subject of a rapidly growing medical literature.[1-3] It first emerged in the psychiatric literature as an aspect of drug effectiveness research. Currently, this subject commands considerable attention[4] in relation to deinstitutionalization. It is also a focal point in the growing concern for patients' rights[5] and informed consent,[6] and is a relevant topic in general discus-

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sions of society's attitude toward the mentally ill.[7]

The forensic psychiatrist's opinion on the issue of medication noncompliance, followed by risk of relapse into a psychotic state with attendant potential for recidivism, is useful at several stages of the judicial process. Before trial, these risks may be deliberated in order to set bail. In jurisdictions requiring treatment in the least restrictive setting, this issue strongly influences the disposition of a person found not competent to stand trial. Its relevance continues in similar fashion as the judicial process moves forward to plea bargaining, requests for accelerated rehabilitation, and other pretrial motions. During trial, notably in insanity defense cases, the relationship between the defendant's past compliance or default regarding medication and his mental state may be in dispute.[7] After trial, the sentencing proceedings may call for an expert opinion on the offender's prospective medication compliance. Examples include motions for parole, for sentence modification, and for the release of insanity acquittees. In addition, movements for insanity defense reform point to an increasing postverdict role for expert opinion on medication compliance. The same is true of more general reform proposals, including those for alternatives to incarceration.

In these situations, the mental health expert becomes involved in questions concerning the "curability" of mentally ill individuals, the role of medication in their treatment, and the extent of their ongoing need for medication. When such a need is established, the debate centers on the likelihood of compliance with prescribed medication versus the risk that an individual will discontinue medication and then experience relapse. Our purpose is to comprehensively organize and update this material for the use of the expert faced with the question of whether an accused individual is likely to comply with prescribed antipsychotic medication and maintain a state of remission. Focusing on schizophrenia, the predominant diagnosis[8] in these situations, we explore the nature and extent of compliance and its relationship to relapse. We describe risk factors for noncompliance and evaluate current means for preventing, detecting, and dealing with it.

Definition and Extent of Noncompliance

Blackwell[9] has pointed out that noncompliance includes a wide spectrum of patient behavior: "failure to enter a treatment program, premature termination of therapy, and incomplete implementation of instructions, including prescriptions." Since Haynes *et al.*[1] have explored that point in detail, the focus of this review is noncompliance with prescribed antipsychotic medications, including both complete failure to begin or continue taking them as prescribed and partial failures considered to be serious enough to be clinically significant.[10] Stimson[11] and Conrad[12] have aptly commented on the rather myopic orientation of the bulk of past research in this area. In Stimson's words,[11] "Studies of patients' 'compliance' with doc-

tors' instructions have generally used an ideal image of the patient as a passive, obedient and unquestioning recipient of medical instructions. . . . The blame for 'default' is seen as lying with the patient." Still more aptly for the present discussion, he went on to liken the situation to research in criminology: "This image of the delinquent and of the patient has led to a research approach that precludes investigation of the broader social setting in which delinquency or default takes place, or of the meaning attached to the behavior by the delinquent or patient."

Our review of the literature on the extent of noncompliance among schizophrenic outpatients on oral neuroleptics generated a series of 21 reports. The median default rate reported was 41 percent, with a range falling between 10 and 76 percent. As indicated above, the term default as used here includes any significant deviation from the prescribed medication. This incorporates the spectrum from not taking any medication to missing several doses.

Table 1 summarizes this group of studies[13-33] in order of increasing default rate. Illustrative highlights include the report of Parkes *et al.*[22] that, of 68 male patients discharged from the hospital with medication, 40 percent had stopped taking medication within two months of discharge. As ascertained from careful questioning of patients and relatives, 53 of 120 drug courses prescribed during a one-year period were probably not taken as intended. Of these, 22 percent were terminated prematurely, often when the patient returned to work or exhausted the given supply of medication. Twenty percent of prescribed drug courses were terminated by the patient within one month of discharge; eight percent were not taken at all. These findings agree with the report of Hogarty and Goldberg[19] that one-half of their patients who relapsed within two months after discharge from the hospital were not taking medication. Of 124 schizophrenics seen during a one-year outpatient study in Edinburgh, 24 percent stopped taking neuroleptics for at least four weeks and 7 percent took no medication at all.[26] In a survey by Serban and Thomas[33] of 516 chronic schizophrenic outpatients, 42 percent reported no use of prescribed medication between their hospitalizations. In fact, 19 percent of chronic patients and 21 percent of acute patients indicated no intention of taking medication.

In a study of two different populations of chronic schizophrenic patients, Herz and Melville[18] reported that 50 percent of one group and 26 percent of the other stated that they were taking medication as prescribed. Approximately 24 percent of the first group and 33 percent of the second group claimed that no medication had been prescribed for them. Interestingly, when relapse did occur, only 2 percent attributed it to stopping or incorrectly using their medication and less than 4 percent of all patients and family members stated that the patient took more medication when symptoms became serious.

Assessment of patient default rates is more complex with regard to antipsychotic medication given in the form of

Table 1
Results Reported from Investigations of Compliance with Oral Medications among Schizophrenic Outpatients

Reference	% Default Rate (N)	Subjects	Observation Period	Method of Detection
Quitkin *et al.*[13]	10 (3/30)	Stable outpatients	1 year	Clinic nurse's report
Carman *et al.*[14]	12 (5/40)	Patients stabilized on low potency medications	6 months	Serum and urine assays
Raskin[15]	21 (37/179)	Patients at 22 VA clinics	8 weeks	Interview of patient and therapist
Leff and Wing[16]	21 (24/116)	Patients leaving hospitals	6–12 weeks	Interview of patient, riboflavin marker
McClellan and Cowan[17]	24 (69/286)	Patients at a VA clinic	Single point	Urine assay
Herz and Melville[18]	26 (26/99)	Stable outpatients	Single point	Interview of patient and relatives
Hogarty *et al.*[19]	29 (120/412)	Patients at three clinics	Up to 1 year after discharge	Interview of patient and others
Willcox *et al.*[20]	31 (8/26)	Maudsley Hospital clinic patients	Single point	Urine assay
Irwin *et al.*[21]	35 (14/40)	Walter Reed clinic patients	Single point	Urine assay
Parkes *et al.*[22]	40 (27/68)	Discharged patients in London	2 months	Interview of patient and relatives
Crawford and Forrest[23]	40 (6/15)	Reliable outpatients	40 weeks	Staff reports
Herz and Melville[18]	41 (19/46)	Recently hospitalized patients	Time of current relapse	Interview of patient
Rajotte and Denber[24]	44 (7/16)	Relapsing female outpatients	2 years	Interview of patient
Van Putten[25]	46 (39/85)	VA teaching service patients	Single point	Interview of patient
Renton *et al.*[26]	46 (57/124)	Royal Edinburgh Hospital releases	1 year	Interview of patient and others
Falloon *et al.*[27]	50 (22/44)	Patients leaving hospital	Up to 1 year	Pill counts, riboflavin marker, interview
Michaux[28]	52 (74/142)	VA clinic patients	Single point	Interview of patient
Pollack[29]	58 (183/316)	State hospital releases	6 months to 1 year	Interview of patient

Table 1 (continued)

Reference	% Default Rate (N)	Subjects	Observation Period	Method of Detection
Mason *et al.*[30]	62 (30/48)	Patients entering hospital	Single point	Urine assay
Reilly *et al.*[31]	64 (39/61)	VA hospital readmissions	Single point	Interview of patient
Carman *et al.*[14]	65 (52/80)	Patients stabilized on high potency medications	6 months	Serum and urine assays
Wolff and Colacino[32]	73 (79/108)	State hospital releases	6 months	Interview of patient
Serban and Thomas[33]	76 (449/591)	Bellevue Hospital admissions	Single point	Interview of patient and others

Table 2
Results Reported from Investigations of Compliance with Depot Medications among Schizophrenic Outpatients

Reference	% Default Rate (N)	Subjects	Observation Period	Method of Detection
Crawford and Forrest[23]	14 (2/14)	Reliable outpatients	40 weeks	Staff reports
Johnson and Freeman[40]	16 (30/182)	Recently discharged patients	1–33 months (mean = 13.5)	Staff reports
	26 (37/142)	Clinic patients	1–31 months (mean = 11)	
Carney and Sheffield[41]	43 (52/122)	Chronic outpatients	1–84 months (mean = 41)	Clinician and patient reports
	24 (23/97)		3–71 months (mean = 33)	
	23 (46/199)		1–42 months (mean = 21)	
Quitkin *et al.*[13]	27 (8/30)	Chronic outpatients	1 year	Clinic nurse reports
Falloon *et al.*[27]	36 (16/44)	Patients leaving hospital	1 year	Interview of patient

long-acting depot injections. One report[34] mentions patients not completing the study, but does not describe a defaulting group. Several others[35–39] mention dropouts without enough description of them to evaluate whether they in fact defaulted. In contrast, the authors of five reports[13,23,27,40,41] do recognize and measure the extent of outpatient noncompliance with depot neuroleptics. Their work is summarized in Table 2. Carney and Sheffield[41] reported that of 122 patients treated with injections of fluphenazine enanthate, 97 with

fluphenazine decanoate, and 199 with fluphenthixol decanoate and followed for mean periods of 41, 33, and 21 months, respectively; 43, 24, and 23 percent, respectively, failed to continue their medication. In another report on injectables,[27] 16, or 36 percent, of 44 patients missed at least one injection during a one-year period despite home visits by a community nurse.

Drug default among schizophrenics is not necessarily higher than among medical patients in general. Integrating a wide range of studies on patient behavior, Zisook and Gammon[42] state that rates of noncompliance fall between 16 and 75 percent of patients, depending on the therapeutic situation. For outpatients in general, a compliance failure rate of 50 percent is the minimum figure in one-third of quoted estimates.[43] A medication compliance rate of 50 percent applies to chronic patients in general, based on reports selected for their soundness.[44]

Factors Associated with Noncompliance

Investigators have associated numerous factors with noncompliance in psychiatric patients. These include form of medication, type of medication, extent of supervision, side effects, type of illness, duration of illness, complexity of prescribed drug regimen, sex, age, socioeconomic status, and the attitudes of both patient and physician. Among recent researchers, consensus is limited on the significance of each factor. Blackwell[9] summarizes this situation with his concept of a complex interaction involving "the patient, the illness, the physician, the treatment setting, and the medication itself." Stuart[3] agrees, to the point of developing a "natural history" of patients' decision making. On a similar tack, Porter[45] concludes his study of drug defaulting across diverse patient groups by stating: "It must be emphasized that it has not proved possible to identify an uncooperative type. Every patient is a potential defaulter. Compliance can never be assumed."

Nonetheless, the expert preparing to testify or advise regarding prospective medication compliance should be conversant with a few reasonably well-established and often mentioned correlations. Specific social factors do have a bearing on prospects for compliance. Several groups of investigators have verified the helpful effects of a supportive[46] family in contrast to a hostile[26,43] one. Brown *et al.*[47] and Vaughn and Leff[48] have refined this work using an index of expressed emotion. This is a measure of hostility and emotional overinvolvement based on critical comments about the patient by close relatives at the time of first presentation. Their studies in England, which have been replicated in the United States,[49,50] demonstrate that such behavior of family members carries over to the home situation during ongoing treatment, a point supported in a careful two-year study by Hogarty *et al.*[51] Social isolation,[52] living alone,[30,53] and poor housing[54] increase the risk of noncompliance. The presence of a spouse,[48] friends who take a responsible role,[22,33] and gainful employment[55] all make compliance more likely.

Certain clinical factors have a straightforward bearing on compliance. Denial makes it less likely, while insight favors it.[56-58] The more acute and less severe the patient's course, the better for compliance.[26] Although most symptoms evaluated for their possible relationship to compliance failure have been found not to correlate with it, there are four exceptions. These are anxiety,[57] paranoia,[26,59] grandiosity,[48,57] and depression.[41,60] Each of these can significantly contribute to medication noncompliance followed by relapse.

Of 12 outpatient studies reporting on the possible association between side effects and noncompliance, 1[20] reports no association and 11[18,22,25-28,31,41,45,53,56] report a positive association. Early studies, such as those by Parkes *et al.*[22] and Reilly *et al.*[31] demonstrated that a significant number of patients who terminated drug therapy did so because of side effects, 13 and 25 percent, respectively. More recently, Seltzer *et al.*[53] reported that experiencing frightening side effects was the most commonly cited variable associated with noncompliance ($p < .05$). Falloon *et al.*[27] demonstrated that patients' ratings of their discomfort caused by side effects showed a significant possible association with irregular tablet taking. Eight of 11 patients with a history of irregular drug taking reported high levels of discomfort while on the drug, whereas only 4 of 13 patients who took medication as prescribed reported high levels of discomfort ($p < .05$). This discomfort seemed to occur primarily within the first month of drug therapy. In a study of patients receiving depot injections, Carney and Sheffield[41] reported that, of patients who failed to continue their medications, 28 percent (34 of 121) did so because of extrapyramidal effects. Fifty-two percent of patients receiving fluphenazine decanoate who discontinued their injections cited extrapyramidal side effects as a reason and 38 percent of patients receiving fluphenazine enanthate who discontinued injections cited extrapyramidal effects.

Van Putten[25] reported akathisia, an intense subjective feeling of restlessness, as being notably associated with reluctance to take medication. Kalinowsky[61] has quoted his patients as stating that this side effect can be "more difficult to endure than any of the symptoms for which they had been originally treated." The problem has been described as easily treated, often overlooked, and sometimes mistaken for exacerbation of psychiatric illness. There is some suspicion that akathisia may be especially prominent among patients receiving injections of fluphenazine decanoate.[27,61,62]

Later studies by Van Putten *et al.*[63,64] identified an association between initial dysphoric response and eventual drug refusal. Among newly admitted schizophrenic inpatients, an initial dysphoric response to a test dose of thiothixene was shown to be a powerful predictor of both immediate and eventual drug refusal. These dysphoric responders experienced significantly more extrapyramidal symptoms, notably akathisia, during the 24 hours following the test dose. However, a failure to confirm these results elsewhere[65] has brought them into question.

A few studies have reported on the sexual side effects of these drugs and their relationship to compliance. Falloon *et al.*[27] reported that 80 percent of patients taking fluphenazine experienced difficulty in their sexual relationships at a one-year assessment. Carney and Sheffield[41] reported that one patient refused fluphenazine decanoate injection because of loss of sexual powers.

Detecting Default

If default occurs, how easily and reliably can it be discovered? The literature repeatedly points out that it is underreported because of the difficulties in detecting the noncomplying patient. It is worth noting that physicians generally may not be reliable predictors of compliance. Of 27 medical residents who attempted to assess their patients' compliance with an antacid treatment program, 22 were found to overestimate their patients' degree of adherence with an average error of 32 percent.[66] In a study by McClellan and Cowan[17] where therapists were asked to predict their patients' compliance with medication, 20 percent erred in their predictions. The direction of their errors is significant for the forensic expert: in contrast to their nonpsychiatric colleagues, 71 percent of the erring therapists underestimated their patients' compliance. Reports from patients themselves on the amount of drugs taken are notoriously unreliable, as are more objective means of assessment such as pill counts,[4,28] Such outcomes certainly support the suggestion made by Porter[45] that there is no straightforward noncompliant profile; further research on clinicians' efforts to estimate compliance is warranted.

Direct plasma level measurement of antipsychotic medications dates back to the late 1960s. Although this technology has not yet reached the degree of clinical applicability already associated with some antidepressant levels,[67] it does offer the forensic psychiatric witness a powerful tool. Much of the growing literature on the clinical aspects of this topic, including details beyond the scope of this review, has been recently summarized.[67] From the forensic point of view, the major current application of plasma level measurement at present would be the use of random checks to ascertain whether an individual has been recently taking medication.*

However, progress in this area is, for forensic experts, well worth watching as it emerges from its prolonged infancy in the research laboratory to practical application in psychiatric practice.[68] Already speculations about a therapeutic window for antipsychotic drug levels are available[69–72] to guide the expert preparing to testify or advise. Despite fluctuations observed from day to day for some individuals,[73–75] in the future it may prove possible to establish a therapeutic level clinically in order to follow a particular patient over time. In addition, the use of serum prolactin levels has been proposed as a simple means of detecting noncompliance; but problems

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with this approach have also been raised regarding natural variations in prolactin levels over time, differences among the various medications, and changes that might arise over the course of long-term medication use.[75-79]

Fluids more easily obtained than blood offer some obvious practical advantages, and results obtained from them may be quite sufficient for forensic needs. Urine tests date back to the early years of antipsychotic medication[17,20,21,30,80,81] and remain in use.[14,53] Measurement of neuroleptic drug levels in saliva[82,83] has proven to be both reliable and readily accepted by patients.

The addition of various chemical markers to medication for later detection in the urine enjoyed popularity in the early 1960s. Riboflavin has been used with success at doses of 6 mg[45] and 2 mg,[16,27] but did not prove useful at a dose of 0.5 mg.[84] Phenol red, or phenolsulfonphthalein, has proven effective for monitoring compliance in both psychiatric[85] and general[86] work.

As of this writing, the optimal choice among chemical tests available for monitoring compliance appears to be the urine radioreceptor assay.[14] It offers an ideal combination of sensitivity, specificity, range of application, and ease of use.

Of course, the administration of depot injections incorporates the direct monitoring of medication compliance. Contemplating this approach raises an ethical issue: one must weigh the invasiveness of depot injections against the alternatives faced by the patient. Another ethical consideration is that the use of saliva or urine rather than blood for frequent random assays is simpler and less intrusive. In addition, there are potential dangers in long-term exposure to markers added to medication in order to monitor compliance.

Promoting Compliance

Although promoting compliance is primarily the treating psychiatrist's concern, a thorough knowledge of this important area enhances the expert witness' effectiveness. This is especially obvious in regard to planning the administration of medication. For example, the use of depot injections combines the monitoring of medication adherence with the ultimate in promoting it.[87] Depot injections usually need be given only every one to three weeks[88] and every eight weeks is sufficient in some cases.[89]

New evidence has appeared favoring reduced doses,[90,91] an issue which remains under investigation.[92] Since their introduction in the mid-1960s, they have been associated with improvement in long-term course, particularly when combined with good supervision.[51,93] Thus, a careful strategy directed toward reducing maintenance neuroleptic dosage, itself a good clinical practice with chronic schizophrenic patients,[94] may increase compliance[95-100] both directly and by reducing side effects. Such observations as these will be useful for the forensic expert.

Other adaptations of dosing strategy are readily available for decreasing the risk of default. Simplifying the regimen is effective, both reducing the frequency

of doses and reducing the number of pills or drugs.[101] Oral antipsychotics, as is well known, usually need to be taken only once each day for maintenance. Continued acceptance of depot antipsychotics may be enhanced by having the injections given at home by a visiting nurse who deliberately adopts an unintrusive style[102] Although the responsibility to apply them to treatment lies elsewhere, knowledge of these details is of obvious value to the expert called to participate in a court's effort to settle on a treatment plan.

There may be a role for pill-dispensing devices in certain situations. Examples include a willing individual who is forgetful due to a personality trait or an organic deficit, or who has difficulty due to anxiety or compulsiveness. Also, a thoughtfully chosen device may prove to be a practical means for engaging the appropriate help of available family members. Several devices have been developed. One is an inexpensive and compact unit[103,104] which records on an hourly basis whether an attached medication bottle has been opened. Its memory has a three-week capacity and can be read using an EKG recorder. More simply, a dispenser[105] with dated medication packets for each day received favorable review from the majority of a small patient sample. Also, a pill bottle cap programmed to signal when a dose is due to be taken has proven effective, although this work was with healthy subjects on frequent doses of a placebo.[106]

Promoting compliance also involves psychologic and psychosocial aspects of treatment planning. Such aspects do not readily lend themselves to concrete debate about an individual's risk for default and relapse. However, they are of crucial importance, especially when looking ahead to the long periods of time[107] that are often at issue in forensic discussions. Furthermore, the reality of interactions,[108] between pharmacologic and psychosocial interventions makes this area one worth the expert consultant's consideration.

In particular, side effects merit special attention. Their emotional significance for the individual patient is an important but neglected area. Sarwer-Foner,[109] in a review of the psychodynamic aspects of neuroleptic therapy, states that "sometimes a patient may react . . . to an unpleasant side effect, with the feeling that therapy is not 'benevolent' but is 'sadistically cruel.'" Paranoid patients may interpret side effects as particularly threatening or invasive. For example, Van Putten[25] began his discussion of akathisia by suggesting that there appears to be "an interaction between extrapyramidal involvement, drug reluctance, and type of schizophrenia in that the hostile paranoid schizophrenics were most intolerant of any extrapyramidal side effects." The majority of the most drug-reluctant patients were "chronic paranoid schizophrenics who interpreted the subtlest extrapyramidal symptoms as further proof that they were being poisoned or controlled by sinister outside forces." It is hardly surprising that direct treatment of compliance-impairing side effects improves compliance.[110]

The influence of the prescribing physician and other caregivers through their

relationships with the patient thus remains a fundamental locus for promoting medication adherence.[111-115] Van Putten *et al.*[64] have also reemphasized the importance of rapport and specified some of its important qualities. Careful instruction is of basic importance[28,42,116,117] and must be sensitive[118] and carefully timed,[119] a goal which calls for the application of basic psychotherapeutic principles.[120-122] There is a particular need for accommodation to family factors[123-125] which inhibit or enhance compliance.

For some individuals, specific forms of treatment interventions are useful to promote adherence. These include group therapy[126] and focused supervision.[20-22,26,33,51,127] Finally, useful descriptions of the comprehensive approach required to promote compliance and discourage relapse are available.[43,128-131]

Relapse Containment

Although careful attention to the prediction, monitoring, and encouragement of medication compliance can reduce the incidence of default, it cannot eliminate the problem. Ordinarily, default involves a risk of relapse,[16,132,133] with potential for recidivism. Moreover, just as some schizophrenic patients can do well without medication[16,134-138] others are unfortunately subject to relapse in spite of their medication adherence.[139,140] Evaluation of chronic patients upon relapse has shown that one-third[30] to one-half[19] were taking their medication as prescribed when relapse occurred. Likewise, longitudinal evaluation of chronic patients in remission has demonstrated relapse in spite of compliance with treatment, including drugs.[19,36] The risk of relapse on medication decreases as the patient continues on medication[51,141-143] and varies according to patient selection criteria.[144] Importantly, relapse occurring despite medication compliance tends to be less severe than that following default.[133,145]

Efforts to characterize patients prone to relapse despite medication compliance show general trends rather than a specific pattern. They tend to be more severely ill[146] with longer hospitalizations, stronger medication doses, and greater symptom distress. With very rare exceptions,[147] they do not metabolize their medication any more rapidly than patients with less severe courses,[148] but they do have lower serum levels.[149-151] However, patients in remission on depot fluphenazine decanoate injections also have strikingly low serum levels of the drug.[152]

Especially crucial is the question of whether default can be diagnosed and the resulting relapse contained. There is no substitute here for a good history: interviews and the record can readily establish the first signs of relapse for a particular individual.[18,153] One may also withdraw the patient's antipsychotic medications in the hospital and observe both how much time elapses before relapse occurs and what particular symptom pattern it assumes. For each patient, the time interval between default and relapse is likely to be the same across episodes.[154]

Two literature reviews[88,155] up to 1975

conclude that relapse within a few days of default is rare and that some cases take up to several months. Patients on oral medications in one longitudinal study[16] required at least one week of withdrawal in order to relapse, and most patients withdrawn from depot injections took 12 or more weeks to relapse.[16,37,39,156–159] One early review[134] suggested an upper limit of six months. On the other hand, a recent report[160] has pointed to a small group of patients prone to early relapse, proposing a theoretical explanation which is coherently related to a set of identifying characteristics.

The efficacy of prompt restarting of medication for aborting relapse has become clear.[88,157,161,162] Often a temporary increase in dosage is helpful.[71,93] In fact, intermittent use of medication is sufficient when patients are monitored in weekly groups for early signs of relapse.[163,164] Less frequent monitoring, however, failed to prevent relapse in a small group of patients taking lithium but not taking antipsychotics.[165] These reports and others[128,129] have emphasized the usefulness of engaging appropriate relatives or friends in the early detection of relapse. Since each patient's prodrome, the pattern of symptoms associated with the beginning of a relapse, tends to be predictable from a good history,[18,159] such individuals can be effective at detecting a relapse in time to abort it. On a more general level, the literature[166,167] on stages in the natural history of schizophrenia provides a further basis for optimism about the efficacy of timely intervention.

Conclusion

The forensic expert called upon to address the issue of medication noncompliance will find a varied and challenging literature on the subject. Issues raised include the nature of compliance itself, factors which either promote or discourage it, techniques for detecting noncompliance, means for promoting adherence to prescribed medication, and strategies for the containment of relapse. The value of the expert's contribution lies in applying a literature written from diverse points of view to a variety of court-related situations in keeping with both clinical and legal priorities.

Ethical matters also come up for consideration in the monitoring and promotion of compliance. The expert willing to address issues related to compliance faces a demanding task which requires familiarity with a wide-ranging literature which continues to grow. We expect that this update and codification will be of significant assistance.

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