Full Disclosure: Toward a Participatory and Risk-Limiting Approach to Neuroleptic Drugs

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Following the many clinical studies of neuroleptic treatment and the resulting practice guidelines and algorithms that have been established by various psychiatric associations, there seems to be little room for considering other treatment concepts that may be at variance with these guidelines: the earlier and the more sustainedly that neuroleptics are taken, the better-this is currently the widely accepted basic principle. If this were indeed correct, service users would have only negligible input into their treatment with neuroleptics. For therapists, there would be little more to do than to inform patients fully about these medications and their untoward effects. The elbow room could be substantially increased if clinical experiences and scientific results that are frequently ignored were to be considered. Such information will be presented in this article, with the aim of enhancing the agency and creativity of users and mental health professionals and of advocating for patient-centered and context-oriented advances in psychiatry. Critical assessments of neuroleptic treatment will be followed by a presentation of the therapeutic potential of complex psychosocial interventions, which enable the avoidance of neuroleptic medications in 40%-70% of instances; and finally, the principles of an approach that we would call participatory neuroleptic treatment will be outlined.

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ost drug studies within the heterogeneous pool of "schizophrenia" studies (e.g., Cullberg, 2003) do not further differentiate the variety of disturbances, elements of the familial context, doctor-patient relations, personality styles, individual experiences with medications. and subjective models of illness, even though these have a demonstrable impact on the effectiveness of pharmacological interventions. Therefore, generalizable recommendations based on these studies remain highly problematic and limited.

Most drug studies permit only limited conclusions due to the fact that the control groups generally consist of patients on placebo who are not receiving any type of intensive

psychosocial treatment once their medications have been discontinued. Even under such placebo conditions there are still considerable rates of "spontaneous remissions," which are rarely mentioned (e.g., Beasley et al., 1996). Ultimately, only studies with at least one comparison group that receives a complex and competently executed psychosocial intervention can offer useful information.

The selected outcome criteria in most studies (e.g., maximal remission of symptoms) frequently do not correspond with individual needs and experiences and the goals of individual patients. Whenever these seem at odds with each other, study results cannot provide exclusive guidance for the treating professional. Furthermore, important elements that have considerable bearing on outcome are often not incorporated in the study design, such as the extent of comorbidity, particularly the consumption of other noxious psychotropic substances (i.e., illegal drugs).

Worldwide there is a serious lack of studies about services and implementation strategies, as well as networks of clinicians and researchers whose funding is independent of the pharmaceutical industry and who are therefore free of market-driven conflicts.

Results of Prospective Outcome Studies

"The long-term outcome of schizophrenia has not changed significantly, in spite of the demonstrated effectiveness of antipsychotic medications in the treatment of acute psychoses as well as in the prevention of relapse" (Carpenter, 1997). Hegarty, Baldessarini, Tohen, Waternaux, and Oepen (1994) actually noted a worsening of outcomes in his meta-analysis of studies between the years 1984 and 1994.

The cause of these commonly seen deteriorations over long periods of time is still unknown. It has not been demonstrated that the deteriorations can be attributed to biological factors, such as the much discussed neurotoxicity of acute psychoses (Wyatt, 1997). These poor outcomes may therefore also be the results of current treatment practices, such as the long-term maintenance on neuroleptics and/or the consequences of inadequate psychosocial treatment. Given that the long-term risks and benefits of neuroleptics have not been fully understood (Bockoven & Solomon, 1975; Wyatt, 1991), it is only sensible to make thorough use of all potentially helpful psychosocial interventions.

At least 20% of all individuals first diagnosed with "schizophrenia" never experience a relapse in their lifetime.

A total of 20%–30% of individuals diagnosed with "schizophrenia" should largely be considered nonresponders to neuroleptics (Conley & Buchanan, 1997; Kane, 1999). For example, when they are treated with Clozaril, these nonresponders experience no more than a temporary and partial reduction of primarily positive symptoms, along with considerable side effects (Schäfer, Lambert, & Naber, 2004). A total of 5%–10% of all patients experience absolutely no improvement of symptomatology from any type of neuroleptic treatment (Pantelis & Lambert, 2003).

Approximately 40% of patients diagnosed with "schizophrenia" decompensate in spite of taking the prescribed medication within one year after hospital discharge (Hogarty & Ulrich, 1998).

Approximately 20% of individuals with schizophrenia experience a relapse within one year in spite of taking long-acting depot medications (Kane et al., 2002).

Course and outcome can be significantly improved with integrated psychosocial interventions, especially those including family approaches (Hogarty & Ulrich, 1998).

ADHERENCE RESEARCH

Under routine treatment conditions, more than 50% of service users either cease taking their medications altogether, or take them at variance with their doctors' orders (Fenton, Blyler, & Heinessen, 1997). A similarly high nonadherence rate can be found among patients taking medicine for physical illnesses.

In contrast to the initial high expectations and assertions, even the atypical neuroleptics have not changed this picture. Here too—according to a randomized comparison of typical and atypical neuroleptics prescribed for 1493 patients over 18 months (Lieberman et al., 2005b)—about the same number of patients discontinue treatment prematurely when they are taking atypical neuroleptics versus the traditional drug perphenazine (Stelazine). With an overall discontinuation rate of 75%, certain atypicals are faring even worse than perphenazine. Only olanzapine has relatively better results, with a 64% discontinuation rate within 18 months. However, its common side effects of weight gain and other metabolic changes correspond to a potentially higher mortality (see below).

Dosing Strategies

The atypicals have initially favored lower-dose regimens, although there had already been a trend toward lower dosages of first-generation antipsychotics (FGAs) during the 1980s, at least in the United States. By 2002–2003 this trend had started to reverse, with dosages of 40 mg olanzapine per day becoming much more common. Presumably, the improved tolerability of the newer drugs is mostly related to their relatively lower dosing. This fact is generally being obscured, as they are traditionally being compared in industry-sponsored trials to more than double the equivalent dosages of haloperidol (2 mg risperidone = 10 mg olanzapine = 2.5 mg haloperidol). In 94% of the comparison studies in the United States, the haloperidol doses were above the upper border of the official recommended doses (Hugenholtz et al., 2006). We can assume that 4 + / 2 mg of haloperidol equivalents is the generally required average dosage in acute treatment situations (McEvoy, Hogarty, & Steingard, 1991). However, individual dosages can vary by a factor of 30. In first-break episodes, the average minimally effective dosage of 2 mg is even lower, less than half of the above-mentioned average required for acute situations in general.

Studies using PET only scans have shown that a receptor blockade of 50%–60% is sufficient to achieve an antipsychotic effect. Kapur, Zipursky, Jones, Remington, and Houle (2000) studied individuals diagnosed with schizophrenia during their first episode and found that clinical improvement occurs at 65% of D2-receptor blockade in the striatum; a 75% blockade results in hyperprolactinemia generally accompanied by sexual dysfunction; and 78% corresponds with extrapyramidal side effects.

These findings support a cautious attitude among service users toward neuroleptic medication, and justify a low-dose approach with slow and limited upward titration, without the ability of predicting which dosage will be appropriate for each individual. On the other hand, in consideration of these findings, the age-old and still widespread practice of rapid upward titration to high dosages must in hindsight be viewed as malpractice. At the same time, this very practice has been sold to users as the "state of the art" without having methodologically sound studies to back it up. This is a rather astonishing deficiency, one that may actually result in legal challenges by ex-users.

Addressing Toxicity

Negative Neuronal Effects of Neuroleptics. Recent PET only studies have shown that subjects diagnosed with schizophrenia have a normal number of D2 receptors (e.g., Farde et al., 1990; Laakso et al., 2000; Nordstrom, Farde, Eriksson, & Halldin, 1995; Martinot et al., 1990). A temporary increase of dopamine production has been demonstrated only during acute psychotic episodes (Abi-Dargham et al., 1999, 2000; Breier et al., 1997; Laruelle, Abi-Dargham, Gill, Kegeles, & Innis, 1999). Positive psychotic symptoms can also develop in relation to non-dopaminergic mechanisms (Laruelle, 2000). This may also explain why more than 25% of acutely psychotic patients are showing a resistance to neuroleptics that block D2 receptors.

Nevertheless, all patients with psychotic symptoms are being treated with dopamine antagonists (neuroleptics), mostly in dosages that block more than 65% of the receptors, and also after symptom remission, which leads to the establishment or the aggravation of so-called negative symptoms and neuropsychological deficits (Breggin, 1990, 1996). This neuroleptic-induced attenuation of the dopaminergic system, which regulates attention, initiation, motivation, affect, and the assignment of importance to incoming stimuli, is not being studied systematically and is consistently being obscured by the questionable suggestion of illness-related processes. Service users and their families are quite familiar with these effects, often erroneously attributing them to the "illness" rather than to its "treatment."

When dopamine receptors are blocked by neuroleptics, compensatory regulatory mechanisms are soon called upon, which promote the development of new receptors and collateral nerve endings (up-regulation) (Abi-Dargham et al., 1999, 2000; Baldessarini & Tarsy, 1980). This leads to an overall increase in dopaminergic activity and a concomitant reappearance of symptoms and exacerbations ("supersensitivity psychosis," "tardive psychosis") (Chouinard & Jones, 1980). In clinical practice this is reflected in the current increase in polypharmacy, combining several atypical neuroleptics and typical ones, and in the difficulties experienced by patients who attempt to discontinue neuroleptics after long use. There appears to be proof of a partial tolerance that develops in conjunction with taking a neuroleptic. Therefore, we should assume that the high incidence of relapse following premature or prescribed discontinuation is significantly related to the neuroleptics themselves. This is why drug studies with patients in a so-called placebo group, who are rapidly withdrawn from neuroleptics, erroneously demonstrate a higher rate of relapses (Ross & Read, 2004).

Neurodegeneration Through Neuroleptics

The use of neuroleptics can lead to the destruction of cells (apoptosis). Depending on the chemical substance, the dosage, and the length of use, haloperidol, perphenazine, and clozapine, for example, induce cell death via the activation of the enzyme Caspase 3, which can also occur with risperidone, albeit at a six times lower rate than with haloperidol (Gil-ad, Shtaif, Shiloh, & Weizman, 2001; Ukai, Ozawa, Tateno, Hashimoto, & Saito, 2004). Transglutaminase in the cerebrospinal fluid, a marker for apoptosis, was found to be similarly elevated with

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typical and atypical neuroleptics, raising the possibility that a degenerative process is being initiated by these drugs. An even stronger influence was found for women, suggesting a "female vulnerability to antipsychotics" (Bonelli et al., 2005), which may account for the higher incidence of neuronal apoptosis and tardive dyskinesia (Yassa, Nastase, Dupont, & Thibeau, 1992) among women. The clinical effects of these insidious atrophies are probably rather diffuse and poorly understood. Many research findings are also intentionally suppressed. Breggin assumed quite early that 10%–40% of all treated patients are affected by this destructive process in one way or another (Breggin, 1990).

Lieberman et al. (2005a) showed in an MRI study that haloperidol causes a reduction of gray matter volume especially in the prefrontal area within 12 weeks, which decreases by 1.7% in one year and by 1.9% in two years. Neurodegeneration related to olanzapine is disavowed in the summary by these authors, but appears to be still at 0.5% after 52 weeks (just like the rate for haloperidol after 3 months) and seems to be more aggravated in the frontal area with 1%, which is 41.8% of the haloperidol of 2.4% in this area. For the haloperidol-treated patients, a correlation between the frontal gray matter reduction and less improvement in neurocognitive functioning is affirmed, but the possible correlation for the olanzapine-treated subsample is not mentioned. Due to the higher discontinuation rate in the olanzapine group, statistical analyses for the later time points could not be conducted. Atrophy of gray matter is especially pronounced during the first 6 months of treatment, but the fact that patients had been treated with neuroleptics for at least 40 days prior to their baseline assessments has to be taken into consideration. The methodological deficiencies of this study make the asserted differences between haloperidol and olanzapine as well as the extent of neurodegeneration uncertain: high rates of exclusion; differential dropout rates; uncertain adherence to medication regimes; unaccounted-for effects of prestudy treatment; longer exposure to neuroleptics prior to the study among the haloperidol group; relatively higher maximal doses of haloperidol (20 mg) than olanzapine; and relatively higher rates of schizophrenia diagnoses as opposed to schizophreniform disorder in the haloperidol group. The negative effect of olanzapine on gray matter volume after one year appears to be similar to the haloperidol effect at 3 months. The assertion of the authors that olanzapine partially counterbalances a neurodegenerative effect of psychosis itself appears to be unsubstantiated, since any new development of pyramidal cells under second-generation antipsychotics (SGAs) has not been demonstrated.

Based on animal research, even the atypicals are suspect of causing substantial neurodegenerative effects. Dorph-Petersen et al. (2005) have shown a global reduction of gray and white matter in Macaque monkeys amounting to 7%–11%, with a preponderance in the frontal and parietal regions, following 17–27 months of neuroleptic administration at plasma levels that are comparable to those for patients diagnosed with schizophrenia and receiving haloperidol or olanzapine. The histological correlate of these findings has not been ascertained, and a direct translation onto patients being treated for psychotic disturbances is of course not feasible. Most likely, such effects among human subjects would be less pronounced and more localized.

Needless to say, a more prolonged exposure to neuroleptics is likely to result in further cumulative effects, possibly at lower levels. How can we assess the long-term effects after 10 or 20 years of exposure? McGlashan (2006) has pointed out in a critical commentary that the long-term (9- and 10-year) outcome data emerging from two well-treated, first-episode samples (Andreasen, Moser, O'Leary, & Ho, 2005; Hoff, DeLisi, & Maurizio, 2005; Milev, Arndt, & Andreasen, 2005) suggest that deterioration in schizophrenia does

not plateau as seen in older, long-term follow-up patient samples where exposure to medication was absent or intermittent (Harding, Brooks, Ashikaga, Strauss, & Breier, 1987a; Harding, Brooks, Ashikaga, Strauss, & Breier, 1987b; McGlashan, 1988; McGlashan & Fenton, 1993). In other words, the cognitive decline proceeds in relation to neuroleptic exposure and not due to illness-related factors. It is still unresolved whether there is a difference in neurotoxicity between first- and second-generation antipsychotics. Studies by Bonelli et al. (2005) and Dorph-Petersen et al. (2005) suggest that the neurotoxic effects are identical and that women are at particularly high risk for them.

Liebermann's study appears to favor SGAs, but has considerable methodological problems. Even if SGAs had a certain advantage in neurotoxicity (Ukai et al., 2004), their greater cardiovascular and metabolic risks in morbidity and mortality would have to be balanced against that.

Methodologically speaking, any neuroimaging studies on the course of "schizophrenia" in which neuroleptic effects are not systematically controlled are unlikely to yield usable results. It is rather surprising how little attention these problems have received to this date, even though they have been basically identified since the middle of the 1990s.

These results also reveal that to this day—contrary to common assertions—no neurobiological model of illness has been formulated that can account for the complexity and contradictory nature of the findings associated with schizophrenia. Therefore, professionals would be well advised to act even more perspicaciously in their clinical practice. A "repression" or "denial" of these uncertainties in clinical situations often leads to intolerable simplifications, which are meant to convey to patients a kind of certainty that simply does not exist.

MORTALITY

Obesity, diabetes, hypertension, and hyperlipidemia are likely side effects of neuroleptics. They lead to cardiovascular morbidity and an increase in mortality for this patient group within a period of 10 or 17 years (Henderson et al., 2005; Joukamaa et al., 2006). With the liberal use of these medications and the potential for serious side effects over the long term, decisions with potentially huge consequences are being made. The limited amount of research in this area gives credence to the impression that this dilemma is hardly being discussed adequately within psychiatry or given its due consideration.

INFLUENCE OF THE PHARMACEUTICAL INDUSTRY

All this illustrates in a rather compelling fashion that clinical psychiatry has been subject to a great many errors till this day, errors that have caused substantial suffering among patients. At the same time it is becoming clear that so-called scientific findings—not least due to one-sided or even frankly manipulative strategies by the pharmaceutical industry cannot be valued as reliable practice guidelines but frequently seem to serve economic interests.

Based on the decades of experience, the demand for psychopharmacological research free of industry meddling is hard to refute. Enmeshments of clinicians, scientists, and the pharmaceutical industry have become increasingly public (Angell, 2005; Mosher,

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Gosden, & Beder, 2004) and are frightening, but remain remarkably effective in spite of all the scandals.

It is quite possible that politicians and the public are not being awakened as a result of individual suffering, but must await more clear-cut economic consequences of bad psychiatric services.

We are still far from achieving a meaningful and critical involvement of users in research and service provision. In our daily clinical practice we can at least try to respond to these information gaps and contradictions by discussing the ambiguous aspects of medications as openly as possible with our patients.

THERAPEUTIC POTENTIAL OF PSYCHOSOCIAL TREATMENTS

Family Interventions

It is proven that relapse rates can be cut in half by adjunctive psychosocial treatments. These interventions are currently not available to a majority of patients (Hogarty & Ulrich, 1998; Naber & Krausz, 2001).

Interventions that aim to enhance communication and problem-solving strategies within families contribute to much higher rates of relapse prevention than medication alone (Hahlweg, 1995). Amelioration of the intrafamilial climate, interactions, problem-solving capacities, and increased contact with the identified patient have always been the primary aims of these interventions.

Leff, Kuipers, Berkowitz, Eberlein-Vries, and Sturgeon (1982) and Leff, Kuipers, Berkowitz, and Sturgeon (1985) used relatives-groups without the participation of the patients for families with "high expressed emotion." After two years, the relapse rate was 33%, compared to 75% in the control group. If the family climate was effectively improved and the duration of general contact between patient and family lessened, there were no relapses. When patients are included, the acceptance of the intervention increases, and the dropout rate is significantly lowered. Hogarty et al. (1991) also achieved a zero relapse rate within two years, if the family climate had improved due to ongoing family-oriented interventions.

Longer term benefit occurs only in conjunction with longer term family support. Six family sessions during the early phase of a psychotic condition (Goldstein, Rodnick, Evans, May, & Steinberg, 1978) are quite effective at first, and help to curtail neuroleptic use, but 3 years later no further effects can be demonstrated.

Falloon et al. (1985) used structured, informative, and training-oriented sessions in the family home with a frequency decreasing from once a week to once a month. Relapse rates after two years were 17%, compared to 83% among subjects receiving only individual treatment, obviously a great advantage for the family approach. No studies have been extended beyond this time period; therefore it remains unclear whether psychotic relapses can be entirely averted or whether they are merely postponed for a period of several years. Tarrier, Lowson, and Barrowclough (1991) showed that family-oriented interventions can save up to 27% of treatment costs.

In spite of the fact that these results have been widely known for over 10 years, familyoriented interventions are now offered even less frequently than before in the treatment of individuals with psychosis. This is being justified with the untenable hypothesis that the new atypical neuroleptics can address the root causes of "schizophrenia-as-brain-disease" and therefore obviate the need for all forms of psychosocial intervention, aside from merely informative psychoeducation. After more than 10 years of atypicals combined with psychoeducation we now have long-term outcome studies (e.g., Lieberman et al., 2005b) showing that this is not the case. Neither will it occur with neuroleptics of the third and fourth generation. The scientific attempt to reduce "schizophrenia" to a pure brain disease (for example, on the home page of the National Institute of Mental Health [www.nimh.nih.gov]: "Schizophrenia is a chronic, severe and disabling brain disorder that affects about 1% of people all over the world") is tied to a propaganda campaign to deny any partially etiological effects of the familial milieu in the development, course, and outcome of psychoses.

This position is controverted by the longitudinal results of Tienari's sophisticated adoption studies (Tienari, 1991; Tienari et al., 2004; Tienari, Wynne, & Läksy, 2003) about the interactions between genes and the environment. Mental disorders diagnosed in adoptive children at adult age clearly correlated with disordered family environments. Schizophrenia and schizophrenia spectrum disorders were more common among the adoptive children in the genetically high-risk group (i.e., those with a schizophrenic biological mother), but occurred only when the atmosphere of the environment in which the child was growing up was dysfunctional. An adoptive family environment classified as healthy, on the other hand, protected even high-risk adoptive children against severe psychiatric morbidity.

Based on factor analysis, the most significant risk factors identified in the family environments in this study were divided into three groups: (1) critical/conflictual families characterized by intensive emotional outbursts, parental conflicts, and lack of mutual empathy; (2) emotionally constricted families; and (3) chaotic families with boundary problems (Tienari et al., 2004).

In the attempt to absolve families from feelings of guilt—thereby confusing guilt, causation, and tragic concatenation—the baby has been thrown out with the bathwater, and every potentially problematic aspect of familial interaction, including physical and sexual abuse, has been abrogated, with the primary aim of facilitating family involvement in the marketing of neuroleptic drugs. It is not too difficult for families to understand the differences between actual responsibility, that is, intrafamily abuse prior to the onset of psychosis, guilt feelings, and tragic intergenerational concatenation. Simply ignoring these factors would be a rather ineffective therapeutic strategy (Aderhold & Gottwalz, 2004).

Individual Psychotherapy

The effectiveness of individual psychotherapy has been judged to be dependent on the caliber and experience of the therapists within the context of a short-term use of neuroleptics, that is, less than 14 days (Karon & VandenBos, 1981). Under such conditions (Group A), intermediate and long-term treatment effects (up to 20 months) were found to be considerably better than for the groups with less experienced therapists and continuous neuroleptic treatment (Group B) or standard treatment with medication only (Group C).

The frequently quoted study by May et al. (1981), in which "pharmacotherapy alone" showed the best results, has considerable methodological problems and should not convince anyone. Therapists were inexperienced and to some extent unmotivated or

skeptical; subjects received an average of 46 sessions, but only as long as they were in the hospital—psychotherapy ended on the day of discharge. This study is being cited to this day demagogically as evidence against individual psychotherapy.

Scandinavian experience has shown that individual psychotherapy with relatively autonomous patients can be very helpful in conjunction with or following family-oriented treatment. However, unlike family and network approaches, individual therapy should not be considered as an essential component of the optimal psychosocial treatment package for every individual suffering from psychosis. (See below in the section on complex treatment systems.)

Following a first episode of so-called "schizophrenia," the current consensus guidelines recommend a routine attempt to discontinue neuroleptics after two years. This recommendation accepts an 80% risk of relapse. A staggering 80% of patients will fail in such a withdrawal attempt without concomitant family and/or individual therapy and gradual dose-reduction strategies; this becomes a self-fulfilling prophecy that in turn is used to justify open-ended neuroleptic maintenance.

ORIENTATION TOWARD SUBJECTIVE PERSPECTIVES

Subjective models of illness espoused by service users are rarely considered in the therapeutic context. They are often viewed as delusional or as an expression of a purported lack of insight. Psychoeducational approaches might cause a moderate reduction of relapse but are only marginally relevant to subjective systems of meaning and their relationship to participation in treatment (Pekkala & Merinder, 2002). After a 6-month follow-up, service users and family members have long returned to their original explanations or to other beliefs that deviate from professional opinion (Cozolino, Goldstein, Nuechterlein, West, & Snyder, 1988; McGill, McGill, Falloon, Boyd, & Wood-Siverio, 1983). Only a collaborative review and a "translation" into relational language or metaphor would be sensible and therapeutically useful (Aderhold & Gottwalz, 2004). However, such procedures are not part of traditional psychiatric practice. On the contrary, the conclusion that insight is lacking leads to the elimination of the patient from the therapeutic discourse.

Individual attitudes toward medications are all too frequently not taken into consideration in treatment planning. Whenever it seems predictable that a patient will discontinue his medication in an outpatient setting, all efforts should be made to support this "experiment" by bringing every appropriate psychosocial intervention to bear in the individual and social systems context.

COMPLEX SYSTEMS OF TREATMENT

Aside from individual approaches, the specific situational context of the treatment setting and the treatment philosophy have a fundamental bearing on variations in prescribing practices. The Soteria concept is one important example of such an approach (Ciompi, 1982; Mosher & Bola, 1991; Mosher & Burti, 1992).

The Soteria Approach—Milieu Therapy During Acute Psychotic Episodes

Outcome studies of the Soteria projects in California have shown (Bola & Mosher, 2003; Mosher & Menn, 1978) that neuroleptic and psychosocial treatments are not simply additive but at times also complementary to each other. A series of other, even older studies showed that 30% - 40% of first-episode patients with acute psychoses can be treated without neuroleptics, if they are engaged in an adequate treatment environment, such as a specific milieu (Soteria), within the family, or an inpatient setting, as long as sufficient qualified staff members are available (Alanen et al., 1990; Carpenter, McGlashan, & Strauss, 1977; Ciompi et al., 1993; Falloon, 1992; Goldstein, 1970; Marder, van Kammen, Docherty, Rayner, & Bunney, 1979; Rappaport, Hopkins, Hall, Bellaza, & Silverman, 1978; Silverman, 1975/76). Beyond this, the meta-analyses conducted by Bola (2006) revealed that a 6-week delay of selective neuroleptic treatment showed a small statistically nonsignificant long-term advantage in comparison to the control groups, even without additional active psychosocial treatments. Intermittent and time-limited administration of benzodiazepines (mostly lorazepam) was permitted during the first weeks of treatment. Altogether, to this day there are only six randomized clinical studies that address this question. There is certainly a scientific basis for allowing a window of several weeks for the identification of those individuals who could be treated without neuroleptics (de Haan, Linszen, Lenior, de Win, & Gorsira, 2003). This meta-analysis also casts a critical light on the unproven assumption that the immediate administration of neuroleptics at onset of treatment might have a positive impact on long-term outcomes.

PREDICTORS OF DRUG-FREE RESPONSE EXTRACTED FROM VARIOUS STUDIES

Three clinical criteria emerged from Bola and Mosher's meta-analysis (2002) as predictors of positive Soteria-treatment outcomes without neuroleptics (with a predictive power of 75%):

- higher level of social competence prior to onset of illness (Goldstein Scale)
- relatively older age at onset of illness
- · fewer core symptoms (positive symptoms, catatonia, disturbance of affect, speech/thought, behavior)

The first criterion was confirmed in most other studies that addressed this question in traditional clinical settings. The second criterion appeared rarely, and the third one not at all. Acute onset, another frequently replicated positive predictor, was definitely not confirmed in the Soteria study, which found high rates of effectiveness among patients diagnosed with schizophrenia who had a gradual onset (42% treated without neuroleptics). It is important to mention in this context that the Finnish acute psychosis integrated treatment (API) study of minimal neuroleptic use failed to demonstrate that a duration of untreated psychosis of more than 6 months correlates with a negative outcome of medication-free treatment (Bola et al., 2006; Lehtinen, Aaltonen, Koffert, Rakkolainen, & Syvalahti, 2000).

We cannot be certain of the variables that characterize the subgroup of medication-free responders. However, differentiated clinical studies (see Bola, 2006) and clinical observations lead us to give credence to the following attributes common in this group:

- older age at manifestation of psychosis
- onset of psychosis within the past 6 months
- sudden and acute onset
- fewer psychotic symptoms
- disordered speech
- · short duration of earlier psychotic episodes, including those treated with neuroleptics
- shorter hospital stays
- notable trigger factors or life events
- · a psychotic state with confusion
- a preoccupation with death during psychotic experiences
- concomitant affective symptoms
- adequate psychosocial functioning prior to onset of disturbance
- sexual relations until shortly before onset of psychosis
- absence of schizoid personality traits
- · depressive disorders in the family
- absence of parental mental health treatment

These are not definitive prognostic criteria, but rather individual variables that can inform treatment decisions in individual situations. Sudden onset, a clear-cut triggering situation, and a decent premorbid psychosocial level of functioning are probably the most important predictive factors (Bola & Mosher, 2002).

If a treatment environment is available in which these prognostic criteria can be taken into consideration by offering a trial period of several weeks without neuroleptics, a variety of treatment choices and experiences become apparent to service users, and the range of medication options within a cooperative patient-therapist relationship becomes considerably broader.

No long-term damaging effects (so-called neurotoxicity) caused by the experience of acute psychosis without neuroleptic medication over 4–6 weeks have been demonstrated, even if such arguments are persistently made (Bola, 2006). All Soteria studies show at least equal (Ciompi et al., 1993) or better (Bola & Mosher, 2003) treatment results without medication, compared with the immediate use of neuroleptics in the control group. It is not appropriate to evaluate such medication-free strategies given the proper indication (see above) and a calming treatment setting based on longitudinal studies of individuals who have experienced acute psychoses without medication over many months or even years (duration of untreated psychosis; DUP). Moreover, lowering the treatment threshold for a subset of users in the Soteria group who may be averse to neuroleptic treatment means that effective intervention can begin much earlier than under conditions of obligatory neuroleptic administration.

The majority of the remaining 60%–70% of users can be treated with low dosages in a supportive and low-stimulus therapeutic environment. Neuroleptic dosages vary widely among individual patients, and the lowest effective dose can be determined only if a therapeutic milieu is available where subtle dosing strategies can be employed. If this succeeds, the average dose for acute treatment can be brought down to 1.5–2 mg haloperidol equivalents (Alanen et al., 1990; McGorry, Edwards, Mihalopoulos, Harrigan, & Jackson,

1996; Oosthuizen, Emsley, Turner, & Keyter, 2004). Especially for users experiencing a first psychotic episode, such low dosages can be seen as an indicator for the quality of the available psychosocial services. Furthermore, such low dosages have a decisive influence on the incidence of side effects and secondary cognitive deficits.

THE NEEDS-ADAPTED TREATMENT MODEL

Beginning with Yrjö Alanen in Turku, Finland, the past two decades have seen the development of a treatment model within Scandinavia that is firmly oriented toward the potential and the needs of service users and their families. This model has been described in greater detail elsewhere (Aderhold, Alanen, Hess, & Hohn, 2003; Alanen, 1997). A rapid response to psychotic crises within the home environment of the patients, a therapeutic engagement with their social network from the beginning by a specialized team that remains involved over the long term, and the availability of ongoing individual psychotherapy (in 40%–50% of cases) have shown impressive results.

Contacts with the family and with members of the social network take place only with the consent of the client; in those areas of Finland where the research took place, this consented family contact has been the case in a substantial percentage of contacts (67%–95%).

In the course of a 2-year comparative outcome study (Lehtinen et al., 2000), three Scandinavian regions attempted to decrease the use of neuroleptics for first-episode patients as much as possible (69% were diagnosed with schizophrenia or schizophreniform psychoses). During the first 3 weeks of acute treatment, neuroleptics were completely avoided if at all possible (instead, whenever necessary, benzodiazepines were used); if a clear improvement was notable after three weeks, the use of neuroleptics was further postponed. This procedure resulted in the fact that as an average for all three regions, 40% of the service users never used neuroleptics at all. Retrospectively, the medicated patients did not differ significantly from those who avoided neuroleptics with respect to their premorbid adjustment, occupational functioning, number of psychotic symptoms, duration of untreated psychosis, and diagnoses. However, the treatment results for the patients in the experimental group who received neuroleptics were significantly worse. In comparison to the control group, in which subjects received neuroleptics in 94% of instances with otherwise identical treatment according to the needs-adapted approach, the entire experimental sample showed significantly shorter hospitalizations (p = .011) and higher psychosocial functioning (GAF score > 7; p = .019), with a trend toward lower residual psychotic symptoms during the final study year (41% v. 58%; p = .088). The duration of untreated psychosis (DUP) had no influence on treatment outcomes.

Due to the fact that the experimental group received not only fewer neuroleptic dosages but also a larger number of family sessions (67 v. 38), these results cannot be attributed exclusively to factors relating to medication. The Tornio region of Western Lapland has made it a special priority to avoid neuroleptics whenever possible, and compared the outcomes from two different treatment periods when different variations of systemic approaches were being followed. For our purposes, I want to focus on the specific impact of these systemic interventions on neuroleptic usage.

Currently available results (Seikkula, Aaltonen, Alakare, & Haarakangas, 2006) from the 5-year outcomes of the second treatment cohort (recruited between 1994 and 1997) show that only 29% of the 51 first-episode patients were ever treated with neuroleptics, 26% at the onset and 17% continuously over 5 years. Their diagnoses were schizophreniform psychosis (26%); schizophrenia (38%); acute psychotic reaction (15%); and psychosis not otherwise specified (NOS) (21%). A total of 17% of subjects relapsed during the first 2 years, and an additional 19% in years 3 through 5, an exceptionally low rate, especially considering the infrequent use of medication. The total number of family/network meetings during the 5 years was 36 (first cohort) and 29 (second cohort), a realistic number, even though in some cases daily meetings were taking place during the initial treatment phase. After 5 years, 82% of the study participants showed no residual psychotic symptoms, and 86% were engaged in work or study. The dropout rate of 6% (3 out of 51) was extremely low, reflecting a high rate of acceptance of this treatment model.

These results confirm that even with a nonresidential model based on systemic crisis intervention and long-term family therapy, medications can be entirely avoided in 40%–70% of all cases. Whenever a treatment succeeds without medication and with strong family support—which seems to be essential—relapse rates are kept at a minimum and psychosocial functioning is enhanced.

PARTICIPATORY MEDICATION STRATEGIES

Preconditions

Having emphasized the importance of these rarely available therapeutic environments, it is still possible to implement a more participatory approach to psychopharmacological treatment within current everyday clinical practice. Flexibility is of course more limited. But these limitations should be explained to patients even in acute situations. Here are some basic principles of such an approach.

The path out of psychosis should not be a path into an affective void. This calls for a careful dosing strategy in order to avoid drug-induced repression of psychotic affects. Even within psychotic states, affects remain essential for the formation of structure. Therefore, neuroleptics should always be given in a manner that makes affects more tolerable, thereby promoting less delusional thinking, rather than completely extinguishing them, which might lead to postpsychotic depression or a "deficit syndrome."

A lively, supportive, and empathic relationship is essential to promote the sensitive process of "symptom remission." In conjunction, these approaches are likely to prevent affective disintegration due to a shared understanding and a working through of these affects. The greater the personal fit between patient and therapist (Alanen et al., 1990), the better the chance for success in this joint undertaking. Achieving such an optimal fit is probably more important in working with people who experience psychoses than the use of particular treatment methods. While the therapeutic fit is frequently discussed in relation to long-term treatment, its importance in acute interventions is rarely considered, presumably due to the urgency of need. However, when we take into account the long-term consequences and the extent of chronification, a paradigm shift might be indicated. This therapeutic element, that is, the therapeutic fit in acute situations, will be addressed again when we consider the work of specialized teams for psychoses.

Treatment systems that make only limited use of psychosocial elements apply a great deal of pressure on service providers to begin medicating patients rapidly, and thereby contribute to higher initial dosages. Whenever it is possible to develop a holding relationship in a safe therapeutic context, the question of medication can be approached in a more relaxed manner, almost assuming a wait-and-see attitude. For this, it is of great importance to create an atmosphere of hope and the positive expectation that it is possible to overcome psychosis without medication.

Besides developing a trusting relationship, service users can find out whether they can overcome their symptomatology on their own, or whether they will need to resort to neuroleptics after all, with the goal of containing symptoms or eliminating them entirely. In Western Lapland, if the treatment team feels it is advisable to initiate medication treatment, this is discussed in three therapy sessions, which include the family and other significant persons, before a joint decision is made.

Patients experiencing paranoia are often able to identify their own target symptoms, if they can arrive at a precise formulation of their subjective difficulties. Such self-defined target symptoms can provide the patient with a justification for neuroleptic use, and enable him to experience their effectiveness in a subjectively measurable and controllable manner.

In order to promote an appropriate internal position vis-à-vis their treatment, patients with acute psychoses should be viewed as fundamentally capable of making responsible decisions. According to this principle, there will be only rare situations when a patient is no longer capable of making such decisions. Most of the time, he or she will resort to a relationship that is perceived as therapeutic, and will respond with particular trust to the respect he or she is being afforded.

Beyond this, an initial medication-free period in the treatment of psychosis can facilitate a partial return to a greater amount of shared reality and thereby promote a selfdetermined decision for or against medication. The capacity for insight can be assumed even under the conditions of a coerced treatment inpatient service. Following American and German court decisions that patients preserve the right to refuse medications even under legal commitment orders, unless a pronounced deficit in judgment capacity can be proven, the catastrophe that many professionals had predicted did not occur. Instead, professionals were widely induced to cajole and to negotiate, resulting in a learning process on both sides (Warner, 1994).

When a person experiencing acute psychosis receives support in determining his/her own position vis-à-vis neuroleptics, we should always remind ourselves that the taking of medications for psychological problems is not an obvious intervention. In cases of somatic disorders, medication is discontinued by patients at an even higher rate than for psychiatric problems (Ley, 1989). Patients coming from families that are particularly antagonistic toward pharmacotherapy may actually feel that medications are contraindicated or forbidden. In a study of 100 mental health professionals, 30% rejected the use of neuroleptics for themselves, should they ever become psychotic (Amering et al., 1999).

Out of necessity, patients are generally pursuing a path of rapprochement. If professionals respond with too much pressure, overshooting their goal, this can drive the patient toward rejection of treatment. Most users are quite capable of noticing when they are being hoodwinked in order to get them to take medication at the earliest opportunity, or whether they are benefiting from a broad therapeutic approach that might ultimately lead to the realization that medication cannot be avoided. Whenever a patient perceives that a provider is interested in him or her as a person (Nelson, Gold, Hutchinson & Benezra, 1975), the willingness to accept medication is significantly increased. If he or

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she determines that the medication is necessary, fewer side effects will be reported, and the initial dysphoric response will not occur; this also increases the chance of resuming the medication at a later time in a rational manner (van Putten, 1974; van Putten, May, Marder, & Wittmann, 1981).

Ideally we should ask ourselves, as service providers, which treatment situation we would wish for our best friend under optimal conditions, so that we can relate better to the frustrations and reluctance of our patients, and work continually on improving our therapeutic offerings.

In the United States, psychiatrists are obliged by state regulations to inform all patients in the public mental health system about the risks, side effects, and benefits of any medication ("informed consent"), regardless of their level of competency.

It is unethical to lead patients into believing that neuroleptic drugs can have a causally healing effect on psychotic disturbances. Neuroleptic medication remains nothing but symptomatic treatment. With few exceptions, service users will reward honest information with greater confidence. The same goes for the legal obligation to share information about any side effects that may occur, unless a patient can obviously not absorb the information or is in a dangerously aggressive state.

PARTICIPATORY MEDICATION PRACTICE IN ACUTE INTERVENTIONS

It is easier for patients to assess the risks and benefits of a certain medication if they can sense a positive effect. This is why an attempt should always be made to jointly determine the target symptoms, which can then be used to evaluate the effectiveness of a medication. Ideally, a neuroleptic trial should be defined precisely as that—a trial effort that allows the user to determine quite accurately, through self-observation, whether a drug is helpful or not. For this purpose, ideas, emotions, bodily experiences, energy levels, and a basic sense of self are key observational dimensions (Mosher & Burti, 1992). Patients should be encouraged to document their experiences in writing prior to the onset of treatment; this can also be done in a collaborative fashion, in order to have a baseline parameter available for subsequent comparison (Mosher & Burti, 1992). Such written protocols can be continued throughout the treatment period, whenever this seems to facilitate self-observation. For the most part, patients develop a positive attitude toward medication if they have experienced positive effects and greater well-being with a certain drug (Marder et al., 1983; Razali & Yahya, 1995). Service users who are given an unfamiliar drug in an outpatient setting should be informed in detail what they might do in case of unexpected side effects. Quickly getting in touch with the service provider would provide the best reassurance. In this fashion, medication becomes part of the therapeutic dialogue.

A service provider should never approach a patient with the expectation that he or she will be kept on medication for as long as possible, even against all manner of inner opposition. Many studies have demonstrated the value of a positive therapeutic relationship in connection with the amenability to take medication (Frank & Gunderson, 1990; Marder et al., 1983; Nelson et al., 1975). Therefore, therapists should make themselves available to service users as advisors and supporters along the difficult path through the complexity and the contradictory information and emotions: the fear of doing the wrong thing, the

fear of being transformed by introducing a foreign substance into one's body, and the fear of becoming dependent on this substance. It would be unreasonable to expect anything from patients going down this road other than the fact that they will frequently question the need for medication and attempt to wean themselves off it early on.

Whenever discontinuation occurs in an atmosphere of mutual trust and is being supported safely, the cooperation of patients increases, which in return fosters greater trust, subjective satisfaction, self-worth, and self-confidence. A relapse that can be understood is less damaging, and some patients can learn only by going through several such crises.

Increases or reduction in dosages should always be discussed with the patient in detail. These too have a particular dynamic and meaning, which must be understood. And every step must remain under the control of the patient, with the option of reversing it whenever he or she desires.

The lowest dosage that succeeds in controlling symptoms in a satisfactory manner should be considered an adequate maintenance dose (Gilbert, Harris, McAdams, & Jeste, 1995). Neuroleptics can support the restoration of self-control by establishing a distance from overwhelming psychotic experiences, and aids in stabilizing ego-functions. Neuroleptics do not exert a specifically curative effect on psychotic symptoms. Patients who are feeling better can affirm this by the persistence of more or less subtle side effects and secondary disabilities. When a patient experiences a return of mild psychotic symptoms as medication is being reduced, this should not necessarily lead to an increase in dosage. When the content of these experiences is not too burdensome for the patient, these experiences can lead to a better understanding of their meaning. The user has the opportunity of confronting psychotic experiences directly, which in turn promotes greater self-sufficiency over time.

In this approach, the aim of neuroleptics is not necessarily to remove all psychotic symptoms, but rather to offer sufficient protection, which enables a constructive and integrative way of dealing with these phenomena. Some patients are actually helped by the appearance of short, infrequent, and attenuated psychotic symptoms (e.g., hallucinations, or ideas of reference) in dealing with the external and internal dynamics of their disturbance; for instance, these symptoms might help in identifying covert stressors that have great emotional relevance. Or patients can use certain symptoms as a gauge of inner balance, encountering them with effective, albeit small, changes in daily living. Progress in self-differentiation and an increase in autonomy can be noted by a reduction of these relatively mild symptoms. Of course this presupposes the kind of person who wants to become actively involved with his disturbances and is in search of a corresponding lifestyle.

Schooler (1991) was able to show that lower maintenance dosages are equal to standard dosages with respect to relapse prevention, and superior regarding the occurrence of side effects. Low dosages during acute treatment also allow lower prophylactic (i.e., maintenance) dosages. Hogarty reports dosages ranging from 5 to 12.5 mg fluphenazine decanoate intramuscular every other week. In general, a temporary dose increase is mostly adequate when prodromal symptoms of psychotic decompensation are noticed (Marder et al., 1994).

Carpenter, Buchanan, Kirkpatrick, and Breier (1999) have shown that patients diagnosed with schizophrenia or schizoaffective disorder who are—during a period of stability—not maintained on neuroleptics and begin to experience prodromal symptoms can be managed effectively in 50% of cases with 10 mg diazepam daily for some weeks. Fluphenazine (5 mg per day) was equally effective for the control group. An inadequate response to diazepam led to conventional neuroleptic treatment. Another study, by Johnstone, MacMillan, Frith, Benn, and Crow (1990), demonstrated that a cohort of patients with a short duration of illness prior to treatment had better vocational outcomes if they received placebo at the end of the acute treatment. Obviously, this presupposes that patients, therapists, or relatives are capable of recognizing the prodromal symptoms in a timely fashion.

Following long periods on medication, patients have a greater risk of relapse due to upregulation and supersensitivity of receptor sites (Warner, 1994). In other words, the medication itself creates a higher risk of relapse (Chouinard & Jones, 1980; Viguera, Baldessarini, Hegarty, van Kammen, & Tohen 1997). On one hand, this is a significant argument in favor of an initial drug-free treatment trial, given the appropriate indication and therapeutic setting (see above). In addition, the increased receptor activity mandates a gradual reduction of long-term neuroleptics. Patients who discontinue medications abruptly have a 50% greater risk of relapse within the next 6 months than those who go through a very gradual reduction over a period of 6 to 9 months (Viguera et al., 1997). Psychoses occurring under such circumstances should be considered rebound phenomena and are connected with the development of tolerance and dependence (the rebound effect or so-called withdrawal psychoses) (Lehmann, 2002). Accurate information about these problems should be shared with patients to increase the chance of a successful withdrawal.

PARTICIPATORY MEDICATION STRATEGIES DURING ONGOING TREATMENT

Following the completion of acute treatment, the user is faced with the question of socalled prophylactic or maintenance treatment. In actuality, it would only be sensible to speak about prophylactic medication when such treatment is indeed certain to prevent relapse. Mostly this is not the case, since we are in fact rather dealing with a postponement of relapse (Hogarty & Ulrich, 1977). Recommendations for maintenance treatment are based on a variety of longitudinal studies. It needs to be taken into consideration that these studies involve heterogeneous samples whose members are assumed to have one common disorder. The results of such studies are directly applied to individual patients in treatment settings.

The notion that relapses can be prevented by a suppression of symptoms is controverted by several studies (Gaebel, 1995; Hogarty & Ulrich, 1977). Under optimal treatment conditions, half the patients experience a delay in relapse of over one year, and the other half under one year. Most of the comparison groups used in these studies consist of patients who are switched rather abruptly to placebo following the acute treatment phase, which further increases their relapse risk (Viguera et al., 1997). A proportion of prophylactic effectiveness must therefore be considered as an artifact accounted for by abrupt withdrawal among the control group. A similar phenomenon can be deduced from the Tornio Study (Seikkula et al., 2006) due to their low 5-year relapse rate of patients treated without neuroleptics. Approximately 20% of all patients do not suffer a relapse over a period of 7 years, and remain stable even on placebo (Hogarty, Goldberg, Schooler, & Ulrich, 1974). This confirms the result of the longitudinal studies (e.g., Bleuler, 1978; Ciompi & Müller, 1976). For 50% of patients, using medication as the only relapse-prevention strategy does not eliminate the possibility of relapse within 2 years. This means that 70% of all patients do not need prophylactic medication unless they want to postpone their relapses by no more than several months. Conversely, only 30% of patients experience clear-cut relapse prevention from neuroleptics. Intensive psychosocial treatments, such as family interventions, social skills training, and individual psychotherapy have additional relapse-preventing effects, but generally only during their period of application. They do not seem to have significant enduring or "learned" effects; patients and their families continue to rely on the auxiliary self of the therapist for solving problems, at least through the long period of greatest relapse risk (Harding et al., 1987; Hogarty et al., 1991).

These results show that prophylactic treatment is not necessary at all for 20% of the patients, while the risk of relapse remains quite low for an additional 15%. At the lower end of the spectrum, relapse will occur in spite of neuroleptics for 30% of patients within one year. Therefore, only about 35% of patients will benefit from relapse prevention for a period of over one year. As a general rule, neuroleptics should therefore presumably be considered only as "relapse-postponing" (Hogarty & Ulrich, 1977), while it remains unclear to what extent the long-term prognosis can indeed be improved with the perpetual use of neuroleptics (Bockoven & Solomon, 1975; Wyatt, 1991). Furthermore, there is the additional problem of barely being able to predict who might benefit from a prophylactic effect and who might not.

Consequently, neuroleptics remain a limited instrument to suppress, control, contain, and delay acute symptoms, and the experimental approach of many users toward these drugs should generally not be viewed as reflecting limited insight but rather as a trialand-error method in the face of an uncertain outcome. Even atypical neuroleptics result in subjectively and objectively intolerable side effects for 40% of the mostly young individuals who are suffering from psychosis: weight gain, sexual dysfunction, and cognitive deficits occur at an age when brain development has not been completed, and when the formation of social relationships is a biographical necessity and a communal expectation. Simultaneously, the long-term prognosis of psychotic disturbances depends on the ability to form such relationships, which would imply that neuroleptics might actually thwart individual development.

WITHDRAWAL ATTEMPTS

Nearly 75% of individuals diagnosed with "schizophrenia" for the first time attempt to discontinue their neuroleptics during the first 2 years. Service providers should face this fact squarely. They would be well advised to help create protective environments where such withdrawal attempts can be supported, aiming to limit any undesired consequences. Whenever necessary, a precise agreement concerning the withdrawal should be negotiated, and the patient should be informed about the necessity of a very gradual reduction in dosage to prevent the sudden occurrence of withdrawal psychoses, which might be mistaken for a "true" relapse (Viguera et al., 1997). It is very useful to begin early on with advice and negotiation around medication issues in a collaborative fashion, in order to reduce the intrapsychic pressure toward noncompliance. Such collaboration creates "contingent experiences" (Lempa, 1995), which means that the patient can remain influential and effective independently of the other person. In this manner, negotiation related to medication becomes a therapeutic element in itself.

Participatory Approach to Neuroleptic

Patients who are taking medication are given relatively little attention, affection, and engagement in our current service environment. There are many users who discontinue their medications precisely because of these deficiencies, possibly to elicit greater care, concern, and attention from the therapist. Even a rehospitalization due to an exacerbation of psychosis can sometimes have the function of obtaining more intensive care and attention.

It would be preferable for a patient to attempt a withdrawal while he or she is still in a protective setting, like a residence or an inpatient unit, rather than once he or she is left entirely to his or her own devices. Obviously, ever shorter inpatient stays nearly eliminate the possibility of medication reduction in hospital settings.

Patients often experience medications as a symbol of an illness-related identity that permeates every dimension of their self-concept. Little remains, other than being "schizophrenic." Following a psychotic episode and the attendant collapse of patients' habitual identity, nothing remains as it was.

Only with these considerations can we begin to understand some of the loaded dynamics of medication use. A therapeutic dialogue that goes along with the important search for identity and a return to a normalizing social context (ideally through work) is essential if we want to avert the socio-toxic effects of medications and limit chronification and unsupported attempts to reject a negative illness-identity by discontinuing the medication.

Obviously, patients also stop their medications due to the immediate experience of side effects. To experience oneself free of medication and to pursue the desire of finding out who is actually buried "down there" are deeply understandable yearnings that can never be compensated for by information about relapse rates and purported insight into the illness. Only fear can be stronger than those yearnings. The best therapeutic response in such instances would be to empathize with these conflicts and provide a safety net for attempts to withdraw medications, with the aim of finding a credible and autonomous resolution of this dilemma.

THE REJECTION OF NEUROLEPTIC DRUGS

Certain patients will undoubtedly retain a fundamentally negative attitude toward neuroleptics; a proportion, however, that is no greater than in somatic medicine. Fenton and colleagues distinguish between rejection due to the condition itself and rejection due to other causes (Fenton et al., 1997). Rejecting medications does not necessarily reflect a denial of illness but could be a consequence of negative experiences with earlier medications. It could also be based on a fundamental mistrust of the treating physician, when facing the dilemma of expecting to become dependent, while refusing to relinquish complete control over one's body and mind.

Rejection can also be the manifestation of a family system that is basically hostile toward medicine, or the result of a fatalistic or guilt-compensating subjective theory of illness. What can we offer these individuals? What kind of an attitude or inner position are we, as treaters, developing toward them? Are we punishing them for their critical responses to our offerings with neglect or coercive measures? Or are we trying to understand them, staying "on the case" and struggling together for a resolution that works for them? Countertransferential reactions triggered by these patients often require particular attention in supervision (Fenton et al., 1997). These clients need therapeutic approaches that can provide them with a gradual and continuous engagement over long periods of time.

DEPOT-NEUROLEPTICS

Depot-neuroleptics are generally used when the therapeutic relationship is inadequate, for client- or provider-related reasons, and when there is instead an expectation that the patient and his symptoms need to be controlled. Usually, providers are pointing to certain difficulties and risk behaviors that the patient fails to acknowledge. An advantage of depot-medicine in such situations might be to give the therapist some extra time to jointly develop a durable relationship with the patient. Thus, it might be possible to begin a psychotherapeutic relationship even under the condition of the patient's agreeing to take depot-neuroleptics for a period of time, at which point a more autonomous decision might become feasible.

The disadvantage of depot-neuroleptics is that they seem to replace the necessary relational work at least for some time, substituting control for a supportive relationship. Experience shows that nearly every patient is capable of finding a way, sooner or later, to extricate himself from such a coercive situation, although the risks involved with depot preparations may be more pronounced than with oral drugs, especially concerning loss of autonomy, depression, and suicide potential.

SUMMARY

Fostering empowerment and autonomy by assuring the greatest possible degree of selfdetermination and by showing respect toward the subjectivity of each person are important goals for providers and users of services. All this requires a readiness and dedication, a cooperative or even "co-evolutionary" attitude, and a proactive treatment setting or rather an environment that promotes development and recovery.

Such treatment systems should be flexible, needs-adapted, with a low threshold, largely community-based, and have the capacity to respond early and rapidly, while being context-oriented and minimally stigmatizing.

Ideally, a therapeutic involvement of individuals belonging to the social context of the patient should occur from the beginning, and a continuity of service providers should extend over several years. They should largely be able to replace inpatient treatment with intensive ambulatory or partial hospital services. These kinds of treatment systems are a prerequisite for the possibility of avoiding medication, and for impacting positively on the familial, biographical, and dynamic factors on the road toward psychosis. Within this context, early intervention means early on reaching individuals who are experiencing incipient psychotic symptoms, and better understanding their relevant situational problems. It also means utilizing psychosocial kinds of interventions by working directly and intensively with important members of the individual's support system, before an attempt to treat with neuroleptics is even considered. In this way, early detection offers the chance to reach a patient early enough with a psychotherapeutic method that might permit the circumvention of neuroleptics to the greatest extent. So far, none of the early detection studies have employed a family-oriented therapeutic approach.

The percentage of situations in which neuroleptics can be avoided could serve as a yardstick for the quality of a psychosocial treatment system. The obstacles to such a desirable development are not only the old encrusted structures and internal power dynamics of psychiatry, but also important marketing interests of the pharmaceutical industry. In the past few decades this industry has succeeded in maximally penetrating psychiatry and its associates with its ideology, thereby rendering psychiatric workers largely dependent on the industry's interests. Gradually, however, even some leaders of American psychiatry are showing opposition to these developments, for example, Steven Sharfstein, the chairman of the American Psychiatric Association, who has begun to speak about a misguided development toward a "bio-bio-bio-model" (as opposed to the bio-psycho-social model), about "over-medicalization" and "bribery" by the pharmaceutical industry, and about the necessity of reforming the fragmented American health system from the bottom up (Sharfstein, 2005).

Finally, we should be developing a truly independent research program, free of meddling by industry, that can help achieve a true integration of biological psychiatry, social psychiatry, and psychotherapy toward a subjectively oriented human science.

REFERENCES

- Abi-Dargham, A., Kegeles, I., Zea-Ponece, Y., et al. (1999). Removal of endogeneous dopamine reveals elevation of D2 receptors in schizophrenia. *Journal of Nuclear Medicine*, 40(Suppl.), 30.
- Abi-Dargham, A., Rodenhiser, J., Printz, D., Zea-Ponce, Y., Gil, R., Kegeles, L. S., et al. (2000). Increased baseline occupancy of D2 receptors by dopamine in schizophrenia. Proceedings of the National Academy of Sciences USA, 97, 8104–8109.
- Aderhold, V., Alanen, Y. O., Hess, G., & Hohn, P. (Eds.). (2003). Psychotherapie der Psychosen— Integrative Behandlungsansätze aus Skandinavien. Germany: Psychosozial Verlag.
- Aderhold, V., & Gottwalz, E. (2004). Family therapy and schizophrenia: Replacing ideology with openness. In J. Read, L. R. Mosher, & R. P. Bentall, *Models of madness* (pp. 335–348). Hove, UK: Brunner-Routledge.
- Alanen, Y. O. (1997). Schizophrenia. Its origins and need-adapted treatment. London: Karnac.
- Alanen, Y. O., Anttinen, E. E., Kokkola, A., Lehtinen, K., Ojanen, M., Pylkkänen, K, et al. (1990). Treatment and rehabilitation of schizophrenic psychoses. The Finnish treatment model. Nordisk Psykiatrisk Tidsskrift (Suppl. 22), 1–65.
- Amering, M., Denk, E., Griengl, H., Sibitz, I., & Stasny, P. (1999). Psychiatric wills of mental health professionals: A survey of opinions regarding advance directives in psychiatry. Social Psychiatry and Psychiatric Epidemiology, 34, 30–34.
- Andreasen, N. C., Moser, D. J., O'Leary, H. S., & Ho, B. C. (2005). Longitudinal changes in neurocognition during the first decade of schizophrenia illness. Schizophrenia Bulletin, 31, 348.
- Angell, M. (2005). The truth about the drug companies: How they deceive us and what to do about it. London: Random House.
- Baldessarini, R. J., & Tarsy, D. (1980). Dopamine and the pathophysiology of dyskinesia induced by antipsychotic drugs. Annual Review of Neuroscience, 3, 23–41.
- Beasley, C. M., Jr., Sanger, T., Satterlee, W., Tollefson, G., Tran, P., & Hamilton, S. (1996). Olanzapine versus placebo: Results of a double-blind, fixed-dose olanzapine trial. *Psychopharmacology*, 124, 159–167.

- Bleuler, M. E. (1978). The long-term course of schizophrenic psychosis. In L. C. Wynne, L. R. Cromwell, & S. Matthysse (Eds.), The nature of schizophrenia: New approaches to research and treatment (pp. 631–636). New York: Wiley.
- Bockoven, J. S., & Solomon, H. C. (1975). Comparison of two five-year follow-up studies: 1947 to 1952 and 1967 to 1972. American Journal of Psychiatry, 132, 796–801.
- Bola, J. R. (2006). Medication-free research in early episode schizophrenia: Evidence of long-term harm? Schizophrenia Bulletin, 32, 288–296.
- Bola, J. R., Lehtinen, K., Aaltonen, J., Räkköläinen, V., Syvälahti, E., & Lehtinen, V. (2006). Predicting medication-free treatment response in acute psychosis: Cross-validation from the Finnish needadapted project. Manuscript submitted for publication.
- Bola, J. R., & Mosher, L. R. (2002). At issue: Predicting drug-free treatment response in acute psychosis from the Soteria project. Schizophrenia Bulletin, 28, 559–575.
- Bola, J. R., & Mosher, L. R. (2003). Treatment of acute psychosis without neuroleptics: Two-year outcomes from the Soteria project. *Journal of Nervous and Mental Disease*, 191, 219–229.
- Bonelli, R. M., Hofmann, P., Aschoff, A., Niederwieser, G., Heuberger, C., Jirikowski, G., et al. (2005). The influence of psychotropic drugs on cerebral cell death: Female neurovulnerability to antipsychotics. *International Clinical Psychopharmacology*, 20, 145–149.
- Breggin, P. R. (1990). Brain damage, dementia and persistent cognitive dysfunction associated with neuroleptic drugs: Evidence, etiology and implications. *Journal of Mind and Behavior*, 11(3, 4), 425–464.
- Breggin, P. R. (1996). Toxic psychiatry, New York: St. Martin's Press.
- Breier, A., Su, T. P., Saunders, R., Carson, R. E., Kolachana, B. S., de Bartolomeis, A., et al. (1997). Schizophrenia is associated with elevated amphetamine-induced synaptic dopamine concentrations: Evidence from a novel positron emission tomography method. *Proceedings of the National Academy of Sciences USA*, 94, 2569–2574.
- Carpenter, W. T. (1997). The risk of medication-free research. Schizophrenia Bulletin, 23, 11-18.
- Carpenter, W. T., Jr., Buchanan, R. W., Kirkpatrick, B., & Breier, A. F. (1999). Diazepam treatment of early signs of exacerbation in schizophrenia. *American Journal of Psychiatry*, 156, 299–303.
- Carpenter, W. T., McGlashan, T. H., & Strauss, J. S. (1977). The treatment of acute schizophrenia without drugs: An investigation of some current assumptions. *American Journal of Psychiatry*, 134, 14–20.
- Chouinard, G., & Jones, B. D. (1980). Neuroleptic-induced supersensitivity psychosis: Clinical and pharmacologic characteristics. *American Journal of Psychiatry*, 137, 16–22.
- Ciompi, L. (1982). Affektlogik. Stuttgart, Germany: Klett-Cotta.
- Ciompi, L., Kupper, Z., Aebi, E., Dauwalder, H. P., Hubschmid, T., Trütsch, K., et al. (1993). Das Pilotprojekt "Soteria Bern" zur Behandlung akuter Schizophrener. Ergebnisse einer vergleichenden prospektiven Verlaufsstudie über 2 Jahre. Nervenarzt, 64, 440–450.
- Ciompi, L., &. Müller, C. (1976). Lebenslauf und Alter der Schizophrenen. Eine katamnestische Langzeitstudie bis ins Senium. Berlin: Springer.
- Conley, R. R., & Buchanan, R. W. (1997). Evaluation of treatment-resistant schizophrenia. Schizophrenia Bulletin, 23, 663–674.
- Cozolino, L., Goldstein, M. J., Nuechterlein, K. H., West, K. L., & Snyder, K. S. (1988). The impact of education about schizophrenia on relatives varying in expressed emotion. *Schizophrenia Bulletin*, 14, 675–687.
- Cullberg, J. (2003). Das dreidimensionale Entstehungsmodell der psychotischen Vulnerabiliät— Konsequenzen für die Behandlung. In V. Aderhold, Y. O. Alanen, G. Hess, & P. Hohn (Eds.), Psychotherapie der Psychosen—Integrative Behandlungsansätze aus Skandinavien. Gießen: Psychosozial Verlag.
- de Haan, L., Linszen, D. H., Lenior, M. E., de Win, E. D., & Gorsira, R. (2003). Duration of untreated psychosis and outcome of schizophrenia: Delay in intensive psychosocial treatment versus delay in treatment with antipsychotic medication. *Schizophrenia Bulletin*, 29, 341–348.

- Dorph-Petersen, K. A., Pierri, J. N., Perel, J. M., Sun, Z., Sampson, A. R., & Lewis, D. A. (2005). The influence of chronic exposure to antipsychotic medications on brain size before and after tissue fixation: A comparison of haloperidol and olanzapine in macaque monkeys. *Neuropsy*chopharmacology, 30, 1649–1661.
- Falloon, I. R. H. (1992). Early intervention for first episodes of schizophrenia: A preliminary exploration. Psychiatry, 55, 4–15.
- Falloon, I. R. H., Boyd, J. L., McGill, C. W., Williamson, M., Razani, J., Moss, H. B., et al. (1985). Family management in the prevention of morbidity of schizophrenia. Clinical outcome of a two-year longitudinal study. Archives of General Psychiatry, 42, 887–896.
- Farde, L., Wiesel, F. A., Stone-Elander, S., Halldin, C., Nordstrom, A. L., Hall, H., et al. (1990). D2 dopamine receptors in neuroleptic-naive schizophrenic patients. A positron emission tomography study with [11C]raclopride. Archives of General Psychiatry, 47, 213–219.
- Fenton, S. W., Blyler, C. R., & Heinssen, R. K. (1997). Determinants of medication compliance in schizophrenia: Empirical and clinical findings. Schizophrenia Bulletin, 23, 637–651.
- Frank, A. F., & Gunderson, J. G. (1990). The role of the therapeutic alliance in the treatment of schizophrenia: Relationship to course and outcome. Archives of General Psychiatry, 41, 228–236.
- Gil-ad, I., Shtaif, B., Shiloh, R., & Weizman, A. (2001). Evaluation of the neurotoxic activity of typical and atypical neuroleptics: Relevance to iatrogenic extrapyramidal symptoms. *Cellular* and Molecular Neurobiology, 21, 705–716.
- Gilbert, P. L., Harris, M. J., McAdams, L. A., & Jeste, D. V. (1995). Neuroleptic withdrawal in schizophrenic patients. Archives of General Psychiatry, 52, 173–193.
- Goldstein, M. J. (1970). Premorbid adjustment, paranoid status and patterns of response to phenothiazine in acute schizophrenia. *Schizophrenia Bulletin*, 1, 24–27.
- Goldstein, M. J., Rodnick, E. H., Evans, J. R., May, P. R., & Steinberg, M. R. (1978). Drug and family therapy in the aftercare of acute schizophrenics. Archives of General Psychiatry, 35, 1169–1177.
- Hahlweg, K., Dürr, H., & Müller, U. (1995). Familienbetreuung schizophrener Patienten. Weinheim, Germany: Psychologie Verlags Union.
- Harding, C. M., Brooks, G. W., Ashikaga, T., Strauss, J. S., & Breier, A. (1987a). The Vermont longitudinal study of persons with severe mental illness, I: Methodology, study sample, and overall status 32 years later. *American Journal of Psychiatry*, 144, 718–726.
- Harding, C. M., Brooks, G. W., Ashikaga, T., Strauss, J. S., & Breier, A. (1987b). The Vermont longitudinal study of persons with severe mental illness: II. Long-term outcome of subjects who retrospectively met DSM-III criteria for schizophrenia. American Journal of Psychiatry, 144, 727–735.
- Hegarty, J. D., Baldessarini, R. J., Tohen, M., Waternaux, C., & Oepen, G. (1994), One hundred years of schizophrenia: A meta-analysis of the outcome literature. *American Journal of Psychia*try, 151, 1409–1416.
- Henderson, D. C., Nguyen, D. D., Copeland, P. M., Hayden, D. L., Borba, C. P., Louie, P. M., et al. (2005). Clozapine, diabetes mellitus, hyperlipidemia and cardiovascular risks and mortality: Results of a 10-year naturalistic study. *Journal of Clinical Psychiatry*, 66, 1116–1121.
- Hoff, A., DeLisi, L. E., & Maurizio, A. (2005). Longitudinal neuropsychological findings of firstepisode schizophrenia after ten years of illness. *Schizophrenia Bulletin*, *31*, 326.
- Hogarty, G. E., Anderson, C. M., Reiss, D. J., Kornblith, S. J., Greenwald, D. P., Ulrich, R. F., et al. (1991). Family psychoeducation, social skills training, and maintenance chemotherapy in the aftercare treatment of schizophrenia. Archives of General Psychiatry, 48, 340–347.
- Hogarty, G. E., Goldberg, S. C., Schooler, N. R., & Ulrich, R. F. (1974), Drug and sociotherapy in the aftercare of schizophrenic patients: Two year relapse rates. Archives of General Psychiatry, 31, 603–608.
- Hogarty, G. E., Kornblith, S. J., Greenwald, D., DiBarry, A. L., Cooley, S., Flesher, S., et al. (1995). Personal therapy. A disorder-relevant psychotherapy for schizophrenia. Schizophrenia Bulletin, 21, 379–393.

Hogarty, G. E., & Ulrich, R. F. (1977). Temporal effects of drug and placebo in delaying relapse in schizophrenic outpatients. Archives of General Psychiatry, 34, 297–301.

- Hogarty, G. E., & Ulrich, R. F. (1998). The limitations of antipsychotic medication on schizophrenia relapse and adjustment and the contributions of psychosocial treatment. *Journal of Psychiatric Research*, 32, 243–250.
- Hugenholtz, G. W., Heerdink, E. R., Stolker, J. J., Meijer, W. E., Egberts, A. C., & Nolen, W. A. (2006). Haloperidol dose when used as active comparator in randomized controlled trials with atypical antipsychotics in schizophrenia: Comparison with officially recommended doses. *Journal of Clinical Psychiatry*, 67, 897–903.
- Johnstone, E. C., MacMillan, J. F., Frith, C. D., Benn, D. K., & Crow, T. J. (1990). Further investigation of the predictors of outcome following first schizophrenic episodes. *British Journal of Psychiatry*, 15, 182–189.
- Joukamaa, M., Heliovaara, M., Knekt, P., Aromaa, A., Raitasalo, R., & Lehtinen, V. (2006). Schizophrenia, neuroleptic medication and mortality. British Journal of Psychiatry, 188, 122–127.
- Kane, J. M., Davis, J. M., Schooler, N., Marder, S., Casey, D., Brauzer, B., et al. (2002). A multidose study of haloperidol decanoate in the maintenance treatment of schizophrenia. American Journal of Psychiatry, 159, 554–560.
- Kane, J. M. (1996). Factors which can make patients difficult to treat. British Journal of Psychiatry (Suppl. 31), 10–14.
- Kane, J. M. (1999). Management strategies for the treatment of schizophrenia. Journal of Clinical Psychiatry, 60 (Suppl. 12), 13–17.
- Kane, J. M., Davis, J. M., Schooler, N., Marder, S., Casey, D., Brauzer, B., et al. (2002). A multidose study of haloperidol decanoate in the maintenance treatment of schizophrenia. American Journal of Psychiatry, 159, 554–560.
- Kapur, S., Zipursky, R., Jones, C., Remington, G., & Houle, S. (2000). Relationship between dopamine D 2 occupancy, clinical response and side effects: A double-blind PET study of first-episode schizophrenia. American Journal of Psychiatry, 157, 514–520.
- Karon, B. P., & VandenBos, G. R. (1981). Psychotherapy of schizophrenia. The treatment of choice. New York: Aronson.
- Laakso, A., Vilkman, H., Alakare, B., Haaparanta, M., Bergman, J., Solin, O., et al. (2000). Striatal dopamine transporter binding in neuroleptic-naive patients with schizophrenia studied with positron emission tomography. *American Journal of Psychiatry*, 157, 269–271.
- Laruelle, M. (2000). The role of endogenous sensitization in the pathophysiology of schizophrenia: Implications from recent brain imaging studies. Brain Research. Brain Research Reviews, 31, 371–384.
- Laruelle, M., & Abi-Dargham, A. (2000). Dopamine in the history of the schizophrenic brain: Recent contribution of brain-imaging studies. *Dialogues in Clinical Neuroscience*, 2, 359–372.
- Laruelle, M., Abi-Dargham, A., Gil, R., Kegeles, L., & Innis, R. (1999). Increased dopamine transmission in schizophrenia: Relationship to illness phases. *Biological Psychiatry*, 46, 56–72.
- Leff, J., Kuipers, L., Berkowitz, R., Eberlein-Vries, R., & Sturgeon, D. (1982). A controlled trial of social intervention in the families of schizophrenic patients. *British Journal of Psychiatry*, 141, 121–134.
- Leff, J., Kuipers, L., Berkowitz, R., & Sturgeon, D. (1985). A controlled trial of social intervention in the families of schizophrenic patients: A two-year follow-up. British Journal of Psychiatry, 146, 594–600.
- Lehmann, P. (Ed.). (2002). Psychopharmaka absetzen. Erfolgreiches Absetzen von Neuroleptika, Antidepressiva, Lithium, Carbamazepin und Tranquilizern. Berlin: Antipsychiatrieverlag.
- Lehtinen, V., Aaltonen, J., Koffert, T., Rakkolainen V., & Syvalahti, E. (2000). Two-year outcome in first episode psychosis treated according to an integrated model. Is immediate neuroleptisation always needed? *European Psychiatry*, 15, 312–320.
- Lempa, G. (1995). Zur psychoanalytischen Behandlungstechnik bei schizophrenen Psychosen. Forum der Psychoanalyse, 11, 133–149.

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- Ley, R. (1989). Improving patients' understanding, recall, satisfaction and compliance. In A. K. Broome (Ed.), *Health psychology*. New York: Chapman and Hall.
- Lieberman, J. A., Strup, T. S., McEvoy, J. P., Swartz, M. S., Rosenheck, R. A., Perkins, D. O., et al. (2005b). Effectiveness of antipsychotic drugs in patients with chronic schizophrenia. *New England Journal of Medicine*, 353, 1209–1223.
- Lieberman, J. A., Tollefson, G. D., Charles, C., Zipursky, R., Sharma, T., Kahn, R. S., et al. (2005a). Antipsychotic drug effects on brain morphology in first-episode psychosis. Archives of General Psychiatry, 62(4), 361–370.
- Marder, S. R., Mebane, A., Chien, C.-P., Winslade, W. J., Swann, E., & Van Putten, T. A. (1983). Comparison of patients who refuse and consent to neuroleptic treatment. *American Journal of Psychiatry*, 140, 470–472.
- Marder, S., van Kammen, D. P., Docherty, J. P., Rayner, J., & Bunney, W. E. (1979). Predicting drugfree improvement in schizophrenic psychosis. Archive of General Psychiatry, 36, 1080–1085.
- Marder, S. R., Wirshing, W. C., Van Putten, T., Mintz, J., McKenzie, J., Johnston-Cronk, K., et al. (1994). Fluphenazine vs placebo supplementation for prodromal signs of relapse in schizophrenia. Archives of General Psychiatry, 51, 280–287.
- Martinot, J. L., Peron-Magnan, P., Huret, J. D., Mazoyer, B., Baron, J. C., Boulenger, J. P., et al. (1990). Striatal D2 dopaminergic receptors assessed with positron emission tomography and [76Br]bromospiperone in untreated schizophrenic patients. *American Journal of Psychiatry*, 147, 44–50.
- May, P. R., Tuma, A. H., Dixon, W. J., Yale, C., Thiele, D. A., & Kraude, W. H. (1981). Schizophrenia. A follow-up study of the results of five forms of treatment. Archives of General Psychiatry, 38, 776–784.
- McEvoy, J. P., Hogarty, G. E., & Steingard, S. (1991). Optimal dose of neuroleptic in acute schizophrenia. Archives of General Psychiatry, 48, 739–745.
- McGill, C., McGill, C. W., Falloon, I. R., Boyd, J. L., & Wood-Siverio, C. (1983). Family educational intervention in the treatment of schizophrenia. *Hospital and Community Psychiatry*, 34, 934–938.
- McGlashan, T. H. (1988). A selective review of recent North American long-term followup studies of schizophrenia. *Schizophrenia Bulletin*, 14, 515–542.
- McGlashan, T. H. (2006). Rationale and parameters for medication-free research in psychosis. Schizophrenia Bulletin, 32, 300–302.
- McGlashan, T. H., & Fenton, W. S. (1993). Subtype progression and pathophysiologic deterioration in early schizophrenia. Schizophrenia Bulletin, 19, 71–84.
- McGorry, P. D., Edwards, J., Mihalopoulos, C., Harrigan, S. M., & Jackson, H. J. (1996). EPPIC: An evolving system of early detection and optimal management. *Schizophrenia Bulletin*, 22, 305–326.
- Milev, P., Ho, B. C., Arndt, S., & Andreasen, N. C. (2005). Predictive values of neurocognition and negative symptoms on functional outcome in schizophrenia: A longitudinal first-episode study with 7-year follow-up. American Journal of Psychiatry, 162, 495–506.
- Mosher, L. R., & Bola, J. R. (1999). Das Soteria-Projekt—Einschätzung des Affekts und Interventionsformen. In W. Machleidt, H. Haltenhof, & P. Garlipp (Eds.), Schizophrenie—eine affektive Erkrankung? (pp. 243–256). Stuttgart: Schattauer.

Mosher, L. R., & Burti, L. (1992): Psychiatrie in der Gemeinde. Bonn, Germany: Psychiatrie Verlag.

- Mosher, L. R., Gosden, R., & Beder, S. (2004). Drug companies and schizophrenia. Unbridled capitalism meets madness. In J. Read, L. R. Mosher, & R. P. Bentall, Models of madness (pp. 115–130). Hove, UK: Brunner-Routledge.
- Mosher, L. R., & Menn, A. Z. (1978). Community residential treatment for schizophrenia: Two-year follow-up. Hospital and Community Psychiatry, 29, 715–723.
- Naber, D., & Krausz, M. (2001). Integrative Schizophrenietherapie—Behandlungsphilosophie und Intervention. Basel: Karger.
- Nelson, A. A., Gold, B. H., Hutchinson, R. A., & Benezra, E. (1975). Drug default among schizophrenic patients. American Journal of Hospital Pharmacy, 32, 1237–1242.

- Nordstrom, A. L., Farde, L., Eriksson, L., & Halldin C. (1995). No elevated D2 dopamine receptors in neuroleptic-naive schizophrenic patients revealed by positron emission tomography and [11C]N-methylspiperone. Psychiatry Research, 61, 67–83.
- Oosthuizen, P., Emsley, R., Turner, H. J., & Keyter, N. (2004). A randomized, controlled comparison of the efficacy and tolerability of low and high doses of haloperidol in the treatment of firstepisode psychosis. *International Journal of Neuropsychopharmacology*, 7, 125–131.
- Pantelis, C., & Lambert, T. J. R. (2003). Managing patients with "treatment resistant" schizophrenia. Medical Journal of Australia, 178(Suppl.), 62–66.
- Pekkala, E., & Merinder, L. (2002). Psychoeducation for schizophrenia. Cochrane database of systematic reviews. Retrieved from http://www.cochrane.org/reviews/index.htm
- Pietzcker, A., Gaebel, W., Köpcke, W., Linden, M., Müller, P., Müller-Spahn, F., et al. (1993). Continuous vs intermittent neuroleptic longterm treatment in schizophrenia—Results of a German multicenter study. *Journal of Psychiatric Research*, 27, 321–339.
- Rappaport, M., Hopkins, H. K., Hall, K., Bellaza, T., & Silverman, J. (1978). Are there schizophrenics for whom drugs may be unnecessary or contraindicated? *International Pharmacopsychiatry*, 13, 100–111.
- Razali, M. S., & Yahya, H. (1995). Compliance with treatment in schizophrenia: A drug intervention program in a developing country. Acta Psychiatrica Scandinavica, 91, 331–335.
- Ross, C. A., & Read, J. (2004). Antipsychotic medication: Myths and facts. In J. Read, L. R. Mosher, & R. P. Bentall, Models of madness (pp. 101–113). Hove, UK: Brunner-Routledge.
- Schäfer, I., Lambert, M., & Naber, D. (2004). Atypische Antipsychotika bei therapieresistenter Schizophrenie. Nervenarzt, 75, 79–91.
- Schooler, N. R. (1991). Maintenance medication for schizophrenia: Strategies for dose reduction. Schizophrenia Bulletin, 17, 311–324.
- Seikkula, J., Aaltonen, J., Alakare, B., & Haarakangas, K. (2006). Five-years experiences of firstepisode nonaffective psychosis in open-dialogue approach: Treatment principles, follow-up outcomes, and two case studies. *Psychotherapy and Research*, 16, 214–228.
- Sharfstein, S. S. (2005, August 19). Big pharma and American psychiatry: The good, the bad and the ugly. Psychiatric News, p. 3.
- Silverman, J. (1975/76). Altered states of consciousness: Positive and negative outcomes. Journal of Altered States of Consciousness, 2, 295–317.
- Tarrier, N., Lowson, K., & Barrowclough, C. (1991). Some aspects of family interventions in schizophrenia. II: Financial considerations. British Journal of Psychiatry, 159, 481–484.
- Tienari, P. (1991). Interaction between genetic vulnerability and family environment: The Finnish adoptive family study of schizophrenia. Acta Psychiatrica Scandinavica, 84, 460–465.
- Tienari, P., Wynne, L. C., & Läksy, K. (2003). Genetic boundaries of the schizophrenia spectrum: Evidence of the Finnish adoption study of schizophrenia. American Journal of Psychiatry, 160, 1–8.
- Tienari, P., Wynne, L. C., Sorri, A., Lahti, I., Läksy, K., Moring, J., et al. (2004). Genotype-environment interaction in schizophrenia-spectrum disorder—Long-term follow-up study of Finnish adoptees. British Journal of Psychiatry, 184, 216–222.
- Ukai, W., Ozawa, H., Tateno, M., Hashimoto, E., & Saito, T. (2004). Neurotoxic potential of haloperidol in comparison with risperidone: Implication of akt-mediated signal changes by haloperidol. *Journal of Neural Transmission*, 111, 667–681.
- van Putten, T. (1974). Why do schizophrenic patients refuse to take their drugs? Archives of General Psychiatry, 31, 67–72.
- van Putten, T., May, P. R. A., Marder, S. R., & Wittmann, L. A. (1981). Subjective response to antipsychotic drugs. Archives of General Psychiatry, 38, 187–190.
- Viguera, A. C., Baldessarini, R. J., Hegarty, J. D., van Kammen, D. P., & Tohen, M. (1997). Clinical risk following abrupt and gradual withdrawal of maintenance neuroleptic treatment. Archives of General Psychiatry, 54, 49–55.

Warner, R. (1985). Recovery from schizophrenia. London: Routledge.

Warner, R. (1994). Recovery from schizophrenia (2nd ed.). London: Routledge.

Wyatt, R. J. (1991). Neuroleptics and the natural course of schizophrenia. Schizophrenia Bulletin, 17, 325–351.

- Wyatt, R. J. (1997). Research in schizophrenia and the discontinuation of antipsychotic medications. Schizophrenia Bulletin, 23, 3–9.
- Yassa, R., Nastase, C., Dupont, D., & Thibeau, M. (1992). Tardive dyskinesia in elderly psychiatric patients: A 5-year study. American Journal of Psychiatry, 148, 1206–1211.

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