during the first 6 weeks of treatment. Clinical Global Impression (CGI) scores were used to evaluate the therapeutic efficacy of clozapine. Side effects were assessed by using the Columbia University Rating Scale (4) for parkinsonian symptoms and the Hillside Akathisia Scale (5) and the UKU Side Effect Rating Scale (6) for general side effects. The occurrence of side effects was analyzed by following operationalized criteria that are defined by cutoff points on each of the rating scales. Along with weekly WBC counts we determined clozapine plasma levels. Response to treatment was defined as an improvement in the patient's CGI score of two or more points. Side effects were assessed in all patients who received at least one dose of clozapine. Patients were entered into the efficacy analysis if they completed at least two ratings (i.e., 1 week of treatment).

Survival analysis, Cox proportional hazard regression analysis, and a Wilcoxon matched-pairs test that used a last-observation-carried-forward approach were used for statistical analysis.

The 52 patients (73.1% [N=38] of whom were men) had a mean age of 29.0 years (SD=9.4) and a mean duration of illness of 41.6 months (SD=52.2). There was a significant decrease in CGI scores from baseline (mean score=5.4, SD=1.0) to week 2 (mean=4.7, SD=1.2) ($z=-3.9$, $p=0.0001$, Wilcoxon matched-pairs signed rank test) that continued at week 6 (mean score=4.1, SD=1.4) ($z=-4.9$, $p<0.0001$, Wilcoxon matched-pairs signed rank test). This improvement was accomplished by using a mean clozapine dose of 225.1 mg/day (SD=117.1). Mean plasma levels were 132.2 ng/liter (SD=83.6). With a two-point or greater improvement in CGI score as the response criterion, 63.5% (N=33) of the patients responded during the first 6 weeks of treatment.

The most endorsed side effects were sedation and hypersalivation. A Cox regression analysis that used the response criterion as the dependent variable showed no significant influence of the covariates mean dose, plasma level, age, duration of illness, side effects, or comedication.

Our results suggest that lower doses of clozapine, as used in many European countries, can be as effective as the higher doses that are generally employed in the United States. With the exception of seizures and confusion, which are generally reported more often in the U.S. studies than in European trials, the frequency of side effects appears comparable across studies (3). Studies that use positron emission tomography, which has shown that D_2-receptor occupancy really does not increase beyond doses of 300–400 mg/day and that 90% of the $5\text{-}HT_2$ receptors are already occupied at a dose of 200 mg/day (Farde, personal communication, 1994), also do not support the use of higher doses. We conclude that controlled dose-finding studies are badly needed to resolve the problems of dose-response correlations in the treatment with clozapine.

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Inclusion of Psychological Torture in PTSD Criterion A

TO THE EDITOR: Criterion A for the diagnosis of posttraumatic stress disorder (PTSD) defines the nature of an event that can be regarded as traumatic and that may lead to the symptoms listed under criteria B, C, and D. The DSM-IV definition of a traumatic event differs from the old definition in DSM-III-R, which stated that the event must be "outside the range of usual human experience and . . . would be markedly distressing to almost anyone." In DSM-IV this fairly broad definition has been restricted to "events that involved actual or threatened death or serious injury, or a threat to the physical integrity of self or others" (criterion A1). Additionally, "the person's response [must have] involved intense fear, helplessness, or horror" (criterion A2). We are concerned that the DSM-IV definition does not include those forms of psychological torture in which the physical integrity of a person is not threatened.

In the German Democratic Republic (East Germany), political prisoners were regularly exposed without warning to the following extreme stressors: frequent, repressive, and long interrogations; isolation and no contact with other people apart from the prison service and the interrogators; systematic sleep deprivation with the lights being switched on and the person being called every 10 minutes; degrading treatment and discrimination; and complete uncertainty regarding their own and other family members' future. Prisoners clearly felt helpless and often experienced intense fear in the face of harassment that was arbitrary and unpredictable (which fulfills criterion A2). Although physical attacks did sometimes occur, between 1970 and 1989 most political prisoners were not beaten or physically injured (and thus would not meet criterion A1). The techniques employed caused psychological suffering and were inflicted with the express purpose of coercing the victims to cooperate with their interrogators and to give as much information as possible. These techniques may thus be regarded as a psychological form of torture according to the United Nations (1). Case reports and an empirical study (2) show that some subjects who were victims of the aforementioned coercive treatment during their political imprisonment in East Germany now suffer from enduring mental sequelae, the symptoms of which would qualify for the diagnosis of PTSD—regardless of whether DSM-III-R, DSM-IV, or ICD-10 criteria are applied.

Although in the literature the term "psychological torture" is not employed according to any clear definition, we suggest that any diagnostic criterion that characterizes the traumatic

stressors leading to PTSD should be expressed in such a way that psychological forms of torture are included.

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On the Words "Mental Illness"

TO THE EDITOR: As a practicing psychiatrist, I have benefited greatly from the inspiring advances in neuroscience and psychopharmacology, as have my patients. I share an office with a rheumatologist and dermatologist. The great majority of my patients act no differently and are no more obviously "mentally ill" than the rheumatology or dermatology patients. However, I must advise my patients who are being treated for mood or anxiety disorders that they would be ill-advised to talk frankly about their illness to anybody but the most trusted family members or friends, since disclosing such information may be injurious to their reputations or careers. In addition, every time a bill is submitted to an insurance company, there is the possibility that my patients and their families may be unable to obtain necessary insurance coverage (life, disability, or health) in the future. Indeed, if a patient is well-to-do, I may advise him or her not to file for insurance to avoid these possible consequences. My patients' office visits and prescriptions for psychotropic medications are reimbursed at 50% of the cost; the patients of the rheumatologist and dermatologist, in contrast, are reimbursed at 80%. When physicians of other specialties refer patients to me, these patients often tell me that they were told by the referring physician that there was nothing "organically" wrong, hence the referral to me. My patients clearly are viewed as "second class" by both insurance companies and our medical colleagues.

One of the most helpful things I do for my patients is to explain that diseases of the brain are just as organic as—and no more "mental" than—diseases of other body organs. I clearly state they are *not* "mentally" ill and are no different than the patients of the rheumatologist or dermatologist. I have found that this educational effort raises my patients' self-esteem and enables them to feel less stigmatized. I explain, however, that although they are not "mentally" ill, they must be discreet, since the insurance companies and many physicians will think of them as "mentally" ill.

I would implore the American Psychiatric Association (APA) to do a risk-benefit analysis regarding the continued use of the words "mental illness" by the APA, its organs, and its members. Is it not clear now that our patients are harmed by having this label attached to them? Doesn't this label create a continued rationale for society, legislators, insurance companies, and other physicians to split our patients off from the mainstream of medicine and into second-class status? Is it not time for APA to take the lead in educating society, legislatures, insurance companies, and general medicine practitioners that the diseases we diagnose and treat are just as physical as, just as deserving of first-class status as, and no more mental than diseases of other body organs?

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Schizophrenia: A 100-Year Retrospective

TO THE EDITOR: James D. Hegarty, M.D., M.P.H., et al. (1) concluded that between 1895 and 1985 the proportion of schizophrenic patients who were considered improved at the end of follow-up periods grew from 27.6% to 48.5%. However, this figure diminished to only 36.4% after 1986, a level statistically indistinguishable from that found in the first half of the century. We believe that the authors overlooked an important phenomenon that may cast light upon this unexpected finding.

We have found four post-mortem studies—with a total of more than 800 schizophrenic inpatients who died between 1954 and 1988—in which a remarkably high prevalence of Alzheimer's disease pathology was found. The percentages of schizophrenia with comorbid Alzheimer's disease in these four studies were 41% (2), 28% (3), 30% (4), and 74% (5), which yields an unweighted mean Alzheimer's disease comorbidity rate of 43% among elderly schizophrenic patients. This prevalence is many times that reported in age-matched general populations. The frequent comorbidity of Alzheimer's disease was masked clinically by the primary diagnosis of schizophrenia. The schizophrenic subjects generally received neuroleptics over prolonged periods.

We suggest that the decline in favorable outcome for schizophrenic subjects since 1986 may reflect a high prevalence of Alzheimer's disease in the schizophrenic population. It is even possible that this regrettable diminution of improvement is iatrogenic.

We suggest that the frequent comorbidity of Alzheimer's disease might be prevented, or its progression in the early to intermediate stages inhibited, by treatment with nonsteroidal anti-inflammatory drugs, which penetrate the blood-brain barrier. In a clinical trial of indomethacin, Rogers et al. (6) found that the progression of Alzheimer's disease was arrested. A co-twin study by Breitner et al. (7) indicated that in addition to nonsteroidal anti-inflammatory drugs, ACTH or steroids might be effective in preventing or delaying the onset of dementia. However, steroids are notorious for causing major adverse side effects, especially in the elderly (8). They do not appear appropriate, therefore, for the purpose discussed herein. It will be important to conduct ante-mortem surveys of elderly schizophrenic subjects to determine if symptoms of Alzheimer's disease can be reliably detected, as well as post-mortem studies to determine the degree, if any, to which neuroleptic treatment contributed to Alzheimer's disease-type pathology. The arresting or slowing of the Alzheimer's disease process might produce an improved long-term outcome for patients with schizophrenia.

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