Letters to the Editor

Carnitine for Valproic Acid-Induced Hyperammonemia

TO THE EDITOR: Valproic acid, a mainstay in the treatment of acute mania and a prophylaxis for bipolar disorder (1), is usually well tolerated. Nonetheless, some patients report lethargy, cognitive slowing, or a general sensation of malaise. When a patient develops such symptoms while taking valproic acid, the manufacturer suggests closer monitoring of liver function test results. When a patient has suspected or apparent liver dysfunction, the manufacturer recommends that clinicians discontinue treatment until the clinical situation is clarified.

In addition to liver function test results, serum levels of ammonia should be monitored. Chronic treatment with valproic acid can lead to elevated serum ammonia levels because of valproic acid's reversible toxic effects on the liver and kidneys (2). Hyperammonemia may not produce symptoms and can occur regardless of whether liver function test results are elevated or not (1996 *Physician's Desk Reference*, pp. 414–416). When symptoms are present, however, treatment with carnitine can be beneficial (2). Carnitine, an important nutrient found in meat and dairy products, is a cofactor necessary for the oxidative metabolism of long-chain fatty acids. It is also necessary for the metabolism of valproic acid. Moreover, carnitine stores can be depleted by long-term treatment with valproic acid (2). I present here the cases of two patients who were taking valproic acid and for whom treatment with carnitine relieved lethargy and cognitive slowing and decreased serum ammonia levels.

Ms. A was a 24-year-old woman with an axis II diagnosis of borderline personality disorder. She had been admitted to an inpatient unit for treatment of major depression, atypical subtype, after she had threatened to commit suicide. She was a strict vegetarian who did not consume any milk, milk products, or red meat. Until her hospitalization, she had been treated as an outpatient with an oral regimen of sertraline, 150 mg/day. After a 2-week washout, she was started on a regimen of tranylcypromine. Over a period of 2 weeks her daily dose was raised to 40 mg/day. Other medications included in her regimen were oral doses of liothyronine, 50 μg/day; thioridazine, 10 mg t.i.d.; and clonazepam, 0.5 mg t.i.d. After 50 days in the hospital, she began an oral regimen of valproic acid, 250 mg b.i.d., in an attempt to reduce her impulsivity. Three days later, the dose was increased to 250 mg t.i.d. and was further increased to 500 mg b.i.d. after 5 days. On her 60th day in the hospital, Ms. A complained of fatigue, lethargy, and persistent nausea; her daily dose of valproic acid was suspended. The serum level of ammonia was 101.5 μmol/liter (normal level=11–35). Her valproic acid dose was adjusted to 250 mg in the morning and 500 mg in the evening. Despite the adjustment, her lethargy persisted. Results of liver function tests were normal, and her serum level measurements were 89.9 μmol/liter of valproic acid and 51 μmol/liter of ammonia. Carnitine treatment was initiated at 1 g b.i.d., and her lethargy disappeared after 10 days. The serum level of ammonia had decreased to 28 μmol/liter.

Ms. B was a 38-year-old woman with a diagnosis of bipolar I disorder that had begun at age 16 and for the past 2 years had shown evidence of rapid cycling. Because of cholelithiasis, she had adopted a mostly vegetarian regimen that included dairy products every day and occasional consumption of red meat and poultry. Her episodes of rapid cycling were controlled with the following regimen: venlafaxine, 300 mg/day; L-thyroxine, 0.15 mg/day; lithium, 900 mg/day; and valproic acid, 1000 mg/day. Within 6 months on this medication regimen, she reported increasingly frequent periods of cognitive slowing and lethargy that hindered her work performance. Her serum ammonia level was 101 μmol/liter, her valproic acid level was 73 μmol/liter, and her liver function test results were normal. She was started on a regimen of carnitine, 1 g b.i.d. The frequency of the lethargic episodes diminished after 2 weeks. Her serum level of ammonia had decreased to 22 μmol/liter.

The hyperammonemia thought to be responsible for the clinical symptoms of cognitive slowing and malaise appears to arise from the inhibitory action of valproic acid on the enzyme carbamyl phosphate synthetase, which is the first enzyme involved in the urea cycle. Inhibition of this enzyme prevents the incorporation of ammonia into urea (3). Valproic acid also causes an elevation in renal vein serum ammonia (3). Thus, hyperammonemia results from greater renal production of ammonia along with reduced hepatic production of urea. Carnitine's restoration of serum levels of ammonia to normal is accomplished most likely by removing valproic acid's inhibition on carbamyl phosphate synthetase and urea synthesis.

As stated earlier, long-term treatment with valproic acid can lead to carnitine deficiency (4). Individuals most at risk for this complication are children less than 2 years old (whose ability to synthesize carnitine is limited), those with inborn errors of metabolism, and those with a restricted dietary intake of carnitine (2). Like the first patient, those who receive valproic acid while following a strict vegetarian diet could harbor a heightened risk of carnitine deficiency, which could lead to elevated serum levels of ammonia.

Hence, in patients treated with valproic acid, lethargy, cognitive slowing, and general malaise may represent the emergence of symptomatic hyperammonemia rather than imminent hepatic failure. Treatment with carnitine can alleviate these symptoms with practically no side effects. This approach may allow these patients to continue receiving valproic acid, a medication for which there are currently few substitutes.

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Koro and Homicidal Behavior

TO THE EDITOR: Koro is a disorder that is characterized by complaints of genital retraction with concomitant anxiety and fear of death. Koro initially was described as a culture-bound syndrome that occurred in the Far East (1). Subsequent research has suggested the prevalence of koro-like symptoms in Western populations (2–4). Self-injurious and assaultive behavior have been observed in psychotic patients with koro (3). We report a case of koro that was related to homicidal behavior in an American man with schizophrenia.

Mr. A, a black, 25-year-old American man, was admitted to a forensic hospital after murdering a stranger and being found not guilty by reason of insanity. At the time of admission, he presented with symptoms that were consistent with his 6-year diagnosis of chronic paranoid schizophrenia: paranoid ideation, ideas of reference, visual hallucinations, and auditory hallucinations that commanded that he kill himself or someone else. He had had these symptoms in the past but had not engaged in violent behavior. He noted a new complaint: "My penis draws up in me at times . . . into my stomach . . . there's only skin left." He expressed the delusion that if he did not obey the voices to kill he would be punished by having his penis permanently retract, which would cause his death. He described the murder as self-defense, stating, "It was him or me . . . I didn't want to die."

At the time of his offense, Mr. A was on an oral regimen of trifluoperazine, 2 mg q.i.d.; perphenazine, 4 mg b.i.d.; and amitriptyline, 25 mg b.i.d. He had never travelled abroad, had no legal problems, and had no history of assaultiveness, familial mental illness, or substance abuse. His clinicians felt that he was medication compliant. They noted that he had been curious about his sexual functioning (e.g., asking how erections "work") for about 6 months before the murder but had not expressed fears of penile retraction.

Mr. A eventually improved on a regimen of fluphenazine decanoate, 87.5 mg every 2 weeks, and was able to be transferred to a state hospital. At the time of transfer, he had no fears of penile retraction but did remain preoccupied with questions about dating and sexual function. He would not discuss his past koro-like delusion and denied any past or present difficulties with sexual performance.

This case describes a patient who had engaged in homicidal behavior and had reported a koro-like delusion in the context of an acute schizophrenic episode. The patient had shown increasing preoccupation with sexual function before developing koro-like symptoms. This case underscores the serious nature of koro in psychotic patients and suggests a potential link between anxiety about sexual function and the development of a koro-like delusion.

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Clomiphene-Induced Psychosis

TO THE EDITOR: Clomiphene citrate induces ovulation and improves the quality of semen. The psychiatric side effects of clomiphene (greater nervous tension, restlessness, insomnia, depression, and mood swings) are few and limited. Clomiphene-induced psychosis has been reported only rarely in women (1). We present two cases of this condition; one is the first report of clomiphene-induced psychosis in a man.

Ms. A, a 27-year-old woman with no previous psychiatric history, had been taking clomiphene at a dose of 175 mg/day for 3 weeks. Ten days before admission, she had become frightened, anxious, irritable, and hypervigilant; she also complained of insomnia. Two days before admission, she had become restless and had developed delusions of reference and persecution. On admission, clomiphene treatment was stopped. She began a regimen of haloperidol, 15 mg/day, that was discontinued after 2 weeks because of severe akathisia and parkinsonism. After six ECT sessions she improved sufficiently to be discharged and subsequently returned to her premorbid level of functioning.

Mr. B, a 25-year-old-man with no history of psychiatric illness, had been taking clomiphene for 2 weeks at a dose of 50 mg/day to treat infertility. He was hospitalized because he was in an acute psychotic state that was characterized by irritability, suspiciousness, labile affect, delusions of reference, persecution, and megalomania with auditory hallucinations. Clomiphene treatment was stopped, and he was prescribed a regimen of haloperidol, 10 mg/day. His psychotic features slowly receded over a 2-month period. In the 6-month follow-up period during which he was treated with a maintenance regimen of neuroleptic medication, there was no recurrence of his psychotic symptoms.

Both cases of clomiphene-induced psychosis were first episodes that were temporally related to the administration of clomiphene and did not rapidly resolve after its discontinuation. No organic or toxic symptoms were observed. The mechanism of the clomiphene effect in these cases is unclear. There have been suggestions that estrogens participate in the modulation of limbic areas and act on catecholaminergic target cells in the hypothalamus and maybe in other CNS regions. Therefore, clomiphene might have exerted its effect and resulted in a psychotic state through catecholaminergic or estrogenic activity in the limbic area. Before they were hospitalized, these two patients appeared to have well-balanced personali-

ties, which suggests that the psychotic episodes were an idiosyncratic response to clomiphene.

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Risperidone Treatment of Methamphetamine Psychosis

TO THE EDITOR: Risperidone effectively treats the positive and negative symptoms of schizophrenia (1) and is of benefit to those schizophrenic patients who have not responded to other neuroleptic medications. Recent studies have demonstrated the usefulness of risperidone in the treatment of other disorders, including Tourette's syndrome (2), pervasive developmental disorder (3), and bipolar disorder (4). We describe here a case in which risperidone was used to treat psychosis in a methamphetamine-dependent patient.

Mr. A, a 45-year-old married Caucasian man, had become dependent on methamphetamine 12 years earlier and had increased his use during the past 5 years. There had been no psychiatric symptoms until 4 months before admission, when he reported the onset of hallucinations. Two weeks later he experienced telepathic communications with God and his deceased father. He saw devils entering the bodies of acquaintances and also saw half-man and half-dog creatures. In response to accusatory and command auditory hallucinations, he drove his truck through freshly poured concrete. He reached a truck stop and started wandering and spitting on people. He was hospitalized for 3 days. He discontinued using methamphetamine and smoking cigarettes, since he believed that this was God's will.

Four weeks later, Mr. A presented for outpatient addiction treatment. His mood was neutral, and he displayed constricted affect. His thoughts showed disorganization and blocking. He described telepathic capabilities and persistent auditory hallucinations. He complained of insomnia, impulsivity, and paranoia. Results of a mental and physical examination revealed depression, disorganized thinking, avoidance, and alienation but no clinically significant organic dysfunction.

Mr. A consented to a trial of risperidone, 1 mg b.i.d. Within 3 days he noted reduced hallucinations, delusions, and paranoia. After 1 week mood, affect, organization of thought, delusional beliefs, memory, attention, insight, and judgment improved. After the dose was increased to 1.5 mg b.i.d., the auditory hallucinations and delusions ceased. Two weeks into treatment he stopped taking risperidone, and his auditory hallucinations recurred. He also resumed smoking and craved methamphetamine. Upon resumption of risperidone treatment 1 week later, his hallucinations and craving for methamphetamine promptly ceased. Insomnia, impulsivity, and anhedonia also improved.

To our knowledge, this is the first report of treatment of methamphetamine-associated psychosis with risperidone. In addition to symptomatic improvement, use of risperidone was associated with reduced craving. Despite obvious limitations of this nonblind single patient case report, the findings suggest the value of further investigation, particularly in view of increases in methamphetamine use and complications since 1991 (5).

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Metronidazole-Induced Psychotic Disorder

TO THE EDITOR: Metronidazole, a 5-nitroimidazole, forms a cornerstone of antibiotic therapy regimens, particularly for the treatment of peptic ulcer disease because of its eradication of *Helicobacter pylori* infection (1). Although metronidazole is well tolerated in general, there are some known neuropsychiatric side effects (e.g., encephalopathy, cerebellar dysfunction, and seizures) as well as other side effects such as vertigo, impaired sleep, dizziness, and states of confusion, excitation, and depression (2). We report here the case of a metronidazole-induced psychotic disorder.

Ms. A, a 26-year-old woman with no family or personal history of psychiatric illness, was admitted for treatment of acute psychosis. The onset of psychotic symptoms took place at the end of a 5-day regimen of intravenous metronidazole (1 g/day) for treatment of adnexitis. The clinical picture was dominated by thought blocking with delusions of persecution and an intense experience of depersonalization, derealization, and thought insertion. Ms. A complained of impaired short-term memory and of a comprehension deficit. Her affect was timid and irritable, with increasing psychomotor agitation, but there was no evidence of autoaggressive behavior or suicidal potential. No impairment of consciousness that would be indicative of acute delirium was found. Results of thorough physical and laboratory examinations, including an EEG recording, revealed no pathological findings. She was given a diagnosis of metronidazole-induced psychotic disorder with delusions.

Ms. A recovered completely from the psychotic symptoms after a 14-day, neuroleptic-anxiolytic therapy combination of haloperidol, 10 mg/day, and lorazepam, up to 6 mg/day. After an 8-month follow-up period, the symptoms remained in full remission.

To our knowledge, this is the first report of a metronidazole-induced psychotic disorder. The inconspicuous premor-

bid personality, the immediate onset of the disorder in close temporal vicinity with metronidazole treatment, and the rapid, full, and stable recovery after 2 weeks of neuroleptic treatment strongly underline the assumed capacity of metronidazole to induce psychosis.

Although it is a well-established fact that metronidazole can pass the blood-brain barrier, little is known about its central mode of action. Preliminary findings suggest both direct, i.e., toxic (2), and indirect CNS effects. A highly speculative but innovative perspective was provided by the recent findings of Yurdaydin et al. (3), who focused on the "gut-brain axis." They demonstrated in rats that metronidazole treatment is associated with the growth of a resistant strain of the gut bacterium *Acinetobacter iwoffii*, which produces an inactive benzodiazepine receptor ligand precursor. Consecutively, an active ligand might be synthesized from this precursor in the brain and hence influence central transmission of γ-aminobutyric acid (GABA). Given that GABA transmission is impaired in schizophrenia (4), we suggest that such a metronidazole-mediated effect through antagonism or inverse agonism at the benzodiazepine receptor site might have contributed to this short-term psychotic state.

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Augmentation of Clozapine Therapy With Ondansetron

TO THE EDITOR: Ondansetron is a novel serotonin (5-HT) antagonist, currently approved in the United States for treatment of the nausea and vomiting associated with chemotherapy, radiotherapy, and surgery. It is a selective antagonist of the 5-HT_3 receptor. Ondansetron has shown a possible antipsychotic effect in patients with schizophrenia (1) and in Parkinson's disease patients with dopaminergic medication-induced psychosis (2). We report a case of apparent ondansetron augmentation of clozapine therapy in a patient with chronic schizophrenia.

Mr. A was a black, 31-year-old forensic inpatient. He had been continuously symptomatic since admission in spite of treatment with typical antipsychotic medications (in chlorpromazine equivalents that ranged from 1000 to 4000 mg/day) and risperidone (6 mg/day). Mr. A had received up to 900 mg/day of clozapine continuously for over 3 years. On this clozapine regimen, he was no longer violent but still displayed formal thought disorder with delusions and hallucinations. One month after Mr. A was diagnosed with Hodgkin's lymphoma, treatment started with biweekly administrations of adriamycin, bleomycine, vinblastine, and doxorubicin. Treatment with clozapine, 750 mg/day, was continued throughout chemotherapy, since substantial violent behavior would reemerge upon discontinuation. Mr. A was given ondansetron, 32 mg i.v., before chemotherapy for treatment of nausea and vomiting. For the 72 hours after each chemotherapy administration, Mr. A was given ondansetron, 8 mg p.o., every 8 hours. In addition to clozapine, his regularly scheduled medications included divalproex (for clozapine augmentation), vitamin E (for tardive dyskinesia), insulin and glyburide (for treatment of diabetes), lisinopril (for hypertension), ferrous sulfate (for treatment of anemia), and cisipride (to control gastroesophageal reflux).

While receiving ondansetron, Mr. A appeared to become less delusional, and he reported a decrease in hallucinations. Approximately 2 weeks after ondansetron treatment was discontinued (upon cessation of his chemotherapy), Mr. A's psychotic symptoms returned to their prior level. His score on the Brief Psychiatric Rating Scale (BPRS) was 62. Because of the possible benefit seen with ondansetron treatment, we decided to reintroduce the medication and monitor it through biweekly administration of the BPRS. An oral regimen of ondansetron, 4 mg b.i.d., was initiated. Mild improvement was noticed after 72 hours. Marked improvement was seen within 2 weeks and was still evident after 10 weeks (the average BPRS score was 36, and the BPRS score after 10 weeks was 26). Results from the Abnormal Involuntary Movement Scale administered 2 weeks after initiation of ondansetron revealed no change. No parkinsonian movements were noted according to the Simpson-Angus scale.

Since clozapine blood levels were not obtained, a pharmacokinetic cause for improvement cannot be ruled out. However, clozapine is a substrate of the cytochrome (CYP) enzyme systems CYP 1A2 and CYP 3A34; ondansetron is not a known inhibitor of these systems, nor has it been reported to interact with any other medication.

This report suggests that ondansetron may be effective in augmenting the clinical effects of clozapine. Further research, including controlled clinical trials, is indicated to further determine the effectiveness of the drug.

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Lamotrigine Treatment of Rapid Cycling Bipolar Disorder

TO THE EDITOR: Joseph R. Calabrese, M.D., and colleagues (1) presented a report of a patient with refractory rapid cycling bipolar disorder who responded to lamotrigine monotherapy. We have administered lamotrigine treatment to seven patients with rapid cycling bipolar disorder. The rapid cycling episodes of six of these patients were newly

diagnosed. These six had a mean age of 30.83 years (SD= 15.52), and the mean age at onset of illness was 20.83 years (SD=8.08). The mean number of affective episodes during the previous 12 months was 9 (SD=3, range=6–14). These six patients began a regimen of lamotrigine monotherapy, 25 mg b.i.d. The dose was increased to 50 mg b.i.d. at the beginning of the second week, and the patients remained on this dose for 3 weeks. The dose was further increased to 75 mg b.i.d. if there was no response. Of the six patients, four responded to lamotrigine treatment. One became euthymic by the end of the second week, the other three by the end of the third week. All four have remained in remission. The two who did not respond continued to have depressive or mixed episodes. None of the six developed a rash.

The seventh patient was an elderly woman with an 8-year history of rapid cycling bipolar disorder. Her 4–6-week depression cycles alternated with euthymia or hypomania. She previously had been treated with lithium, carbamazepine, divalproex sodium alone or in combination, and various antidepressant medications. She had been taking divalproex for 2 years; it had been effective in controlling the hypomanic, but not the depressive, episodes. Addition of bupropion was not successful in preventing depressive relapses. Lamotrigine was added to divalproex therapy during a depressive episode. Depressive symptoms remitted within a week of the lamotrigine addition. However, she developed a rash 4 weeks later, and lamotrigine treatment was discontinued. She recommenced lamotrigine therapy 4 days later and has remained well.

Our experience with lamotrigine suggests that it is very effective in treating patients with rapid cycling bipolar disorder. Rashes, unfortunately, are a common side effect of this medication, and the occurrence of rashes is more likely when lamotrigine is given in combination with divalproex (2). A slow escalation of the lamotrigine dose has been suggested as a method to reduce the occurrence of rash (2). Our experience adds to that of Calabrese et al. (1) and suggests that lamotrigine may prove to be a potentially useful agent for treatment of patients with rapid cycling bipolar disorder.

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Light Visor Maintenance of Light Box Response

TO THE EDITOR: While the efficacy of conventional light therapy for treating seasonal affective disorder has been established (1, 2), the efficacy of the portable head-mounted light visor has been more controversial (3–5). Patients with seasonal affective disorder who are treated with the light box often ask if they may temporarily switch to the visor during times when use of the light box would be impractical. To address this question, we compared the two modalities to determine how well the visor maintained the established antidepressant effect of the light box.

Seven patients who met the Rosenthal-National Institute of Mental Health criteria (1) for seasonal affective disorder and had responded to treatment with the light box entered our study and provided written informed consent after explanation of potential risks and benefits. The institutional review board approved the protocol. All patients were given standard light therapy (twice daily 45-minute sessions in front of an angled light box that emitted 10,000 lux) for 1 week to establish a baseline. The patients then were randomly allocated to receive treatment with either the 2,500-lux visor or the 10,000-lux light box for 1 week; the following week, the patients were treated with the alternate device. Raters who were blind to treatment condition used the 29-item Structured Interview Guide for the Hamilton Depression Rating Scale—Seasonal Affective Disorders Version (6) to evaluate the patients' mood for a 3-day period at the end of the baseline period and each treatment week. Interrater reliability was 0.98.

The mean scale scores for patients at baseline and after treatment with the light box and the light visor were 11.3, 10.7, and 10.4, respectively. A repeated measures analysis of variance revealed no significant difference between treatment conditions and baseline. The data suggest that patients who are being treated with the light box can switch to the visor for a week without losing antidepressant response. This is useful information for patients who travel or temporarily need to switch to the visor for convenience.

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Ritual Handwashing

TO THE EDITOR: Among the many common behavioral disorders in the human population that are characterized by persistent and unreasonable anxiety is obsessive-compulsive disorder. As defined in DSM-IV, individuals with obsessive-compulsive disorder have perseverant or recurrent thoughts or impulses that become inappropriate and time-consuming.

To neutralize these intrusive and ego-dystonic obsessions, the affected individual attempts to neutralize the associated emotional stress with another, usually physical, action, termed a compulsion. These compulsions are performed in a rigid, repetitive, and stereotypic fashion according to personally elaborated rules. Arguably the most common compulsive physical behavior is ritual handwashing, which is associated with obsessive concerns about contamination after touching objects, other people, or even handshaking. Stereotypic handwashing has been recognized for centuries and has been known casually as the "Lady Macbeth syndrome" to acknowledge one of the better recognized historical descriptions.

In view of its substantial prevalence in comparison to other ritual or stereotypic behaviors (e.g., kleptomania, dipsomania, trichotillomania, and polyembolokoilamania [1]), it is astonishing that no formal medical term exists for compulsive handwashing. Fortunately, Homeric Greek offers a suitable root, Χερνιπτομαι (cherniptomai), derived from Χειρ (or *cheir*, meaning hand) and νιζω (or *nizo*, meaning to wash, especially the hands and feet), i.e., "to wash one's (own) hands with holy water" in the sense of cleansing, purging, or purifying, especially before a sacrifice. To proffer a medical appellation that is both respectful to those who suffer from this condition and useful to the professionals who endeavor to comprehend and to manage this disorder, I suggest the proper medical neologism for compulsive stereotypic handwashing: "cherniptomania."

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Neuroleptics and Bone Mineral Density

TO THE EDITOR: The association between neuroleptic use and hyperprolactinemia is beyond question. Work has been done that demonstrates the decrease in bone mineral density in medicated psychiatric patients (1). These same patients often smoke, eat poorly, and take little exercise. Hyperprolactinemia itself has been shown to reduce bone density in female patients (2). In the United States, approximately 1.5 million fractures annually are attributable to osteoporosis, which costs the health services between $5 billion and $10 billion a year (3). With an aging population these figures can only increase, which would thereby impose a phenomenal cost to the health services. The newer neuroleptics purportedly have less propensity to cause hyperprolactinemia, which surely provides a further argument for their greater use. In addition, given our increasing awareness of this problem, although it has not yet been formally proven, the risks of future litigation ought to be considered. Forewarned is forearmed.

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Physician-Assisted Suicide and Abortion

TO THE EDITOR: Although there are important differences between physician-assisted suicide and abortion, there are profound similarities in the way that the public and clinicians think about and react to the two issues. An application of our perspective on abortion politics and practices to issues that surround physician-assisted suicide may be useful.

Similarities between these two controversial issues can be divided into four general categories. 1) *Individual rights.* Opponents of legal abortion and physician-assisted suicide argue that societal needs or moral standards outweigh the right of individuals to make decisions to end life or pregnancy. Proponents of both procedures argue for the right of individuals to make decisions, often in consultation with physicians, regarding their own bodies and futures.

2) *Consent and competence.* Opponents of both procedures are concerned about individual competency and the process of informed consent. For a time, psychiatrists and "abortion committees" in many states evaluated patients' abilities to make informed decisions regarding abortions. Similarly, there is much talk now of psychiatric evaluation and "safeguard" procedures before physician-assisted suicide.

3) *The role of clinicians.* In abortion and physician-assisted suicide, clinicians perform the procedures, obtain informed consent, and support the patient (and sometimes family) with their decisions. Participation in abortion procedures has become largely voluntary for most clinicians, and there is much current discussion about which clinicians will choose to participate in the physician-assisted suicide process.

4) *Potential for abuse.* The Ninth Circuit Court had feared that *Roe v. Wade* would lead to the coercion of poor and uneducated women to have more abortions (1). Abortion opponents also fear that persons will take advantage of the procedure to avoid taking responsibility for sexual activity, birth control, or for raising children. Likewise, physician-assisted suicide opponents argue that persons who contemplate the procedure may become victims of a family or society hoping to minimize financial or emotional burdens.

How can our perspective on abortion inform our decisions about physician-assisted suicide? Most would agree that greater emphasis on prevention of unwanted pregnancies is desirable to reduce the number of abortions. Similarly, a greater emphasis could be placed on hospice care and improving symptom control and support services for the terminally ill. Over time there has been significant change in the processes necessary to obtain abortions in this country. We might expect to see similar types of change, as well as associated social and political unrest, in physician-assisted suicide processes. As we have seen involvement of psychiatrists and abortion committees decline, we might expect to see less involvement of parties other than patient and primary clinician should physician-assisted suicide become commonplace. The history of abortion in this country suggests that most physicians will not be involved in physician-assisted suicide. While this may appeal to individual clinicians, there is a danger that the procedure will be

left to specialists who are strong proponents of the procedure but who do not necessarily know the patients well. We need to think very carefully how much we want, or do not want, physician-assisted suicide to resemble current abortion practices.

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Antidepressants and Breast-Feeding

TO THE EDITOR: The issues addressed by Katherine L. Wisner, M.D., M.S., and colleagues (1) are of importance to us, particularly with regard to fluoxetine.

In our study (2), 10 women were receiving fluoxetine (mean dose=0.39 mg/kg/day, range=0.17–0.85). The mean fluoxetine concentrations in breast milk ranged from 23.1 ng/ml to 189.1 ng/ml; concentrations of norfluoxetine, an active metabolite of fluoxetine, ranged from 31.0 ng/ml to 169.4 ng/ml. Although not explicitly shown in our article, there was a close correlation between the maternal fluoxetine dose by weight (mg/kg/day) and the mean concentrations of fluoxetine and norfluoxetine in breast milk (ng/ml): fluoxetine concentration=249×(maternal dose by weight) +17; r^2=0.86; norfluoxetine concentration=174×(maternal dose by weight)+17; r^2=0.65.

Thus, when a 60-kg woman is taking 40 mg/day of fluoxetine (about 0.7 mg/kg/day), the estimated steady-state drug concentrations in milk for fluoxetine and norfluoxetine would be 191 ng/ml and 139 ng/ml, respectively. When the milk intake is 150 ml/kg/day, the infant's dose will be about 0.03 mg/kg/day for fluoxetine and 0.02 mg/kg/day of norfluoxetine. Because the infant's serum concentrations are related proportionally to the dose in milk, and inversely to the infant's clearance, these low-level exposures (less than 10% of the weight-adjusted dose of the mother) are unlikely to cause therapeutic serum levels unless the mother's dose is very high or the infant's drug metabolizing capacity (clearance) is substantially low. If the infant's clearance value is half of the mature level, the infant's serum concentrations of fluoxetine may reach 10% of the therapeutic level. Whether the 10% level of exposure is clinically meaningful or not awaits further study, as Wisner et al. suggested.

In this regard, recent findings of uncompromised neurodevelopment of children who are exposed to fluoxetine in utero (3) are important. The information is in favor of breast-feeding, because breast-feeding during maternal fluoxetine therapy results in less exposure than that occurring during pregnancy, and breast-feeding itself has many beneficial effects.

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TO THE EDITOR: The recent literature review by Dr. Wisner and colleagues on antidepressant use during breast-feeding was a timely one. Regarding the available data on infant plasma tricyclic antidepressant levels in breast-fed infants, the authors noted: "healthy full-term infants over 10 weeks of age have a low risk of negative effects secondary to maternal tricyclic treatment, since neither parent compounds nor metabolites have been detected, and no reports of adverse effects have been published." We report here data on two healthy older breast-fed infants in whom we detected an active hydroxymetabolite of nortriptyline.

The patients gave written informed consent for treatment and venipunctures to assess simultaneous mother and baby plasma drug concentrations. Samples were drawn at least 3 weeks after the mothers were on a stable dose of medication, 12–15 hours after the last medication dose, and 2–3 hours after the infants' last breast-feeding. High performance liquid chromatography was used to identify and measure nortriptyline and hydroxynortriptyline. Sensitivity of the assay was 4 ng/ml for reproducible quantitation and 2 ng/ml for limit of detectability.

The first baby was 20 weeks old when the mother started nortriptyline treatment. Plasma drug concentrations were examined when the infant was 31 weeks old. Solid foods had been introduced 3 weeks earlier. At the time of venipuncture the baby was breast-fed five times a day and ate solids four times a day. Maternal drug concentrations were as follows: nortriptyline: 66 ng/ml, E-10-hydroxynortriptyline: 162 ng/ml, and Z-10-hydroxynortriptyline: 12 ng/ml. Nortriptyline and Z-10-hydroxynortriptyline were not detected in the infant, but E-10-hydroxynortriptyline was detected at <4 ng/ml.

The second baby was 7.5 weeks old when the mother started nortriptyline treatment. Plasma drug concentrations were examined when the infant was 16 weeks old. Maternal concentrations were as follows: nortriptyline: 95 ng/ml, E-10-hydroxynortriptyline: 302 ng/ml, and Z-10-hydroxynortriptyline: 28 ng/ml. In this exclusively breast-fed infant, nortriptyline and Z-10-hydroxynortriptyline were not detected, but E-10-hydroxynortriptyline was detected at <4 ng/ml.

Potential sources of E-10-hydroxynortriptyline in these infants are maternal hydroxynortriptyline from the breast milk and hydroxynortriptyline produced by nortriptyline metabolism in the infant. We believe this is the first report on detecting and identifying the metabolite of a tricyclic antidepressant in breast-fed infants older than 10 weeks. Consistent with the review of Wisner and colleagues, these babies did not show adverse effects during the period that they were breast-fed. These cases suggest that although hydroxynortriptyline may be found in infants older than 10 weeks, it is not likely to have short-term adverse effects on the infant. Hydroxynortriptyline is an active compound (1), and the long-term safety of low-level infant exposure to antidepressants has not yet been established. As noted by Wisner and colleagues, until data on long-term safety accrue, patients and physicians will need to make individualized decisions as they weigh the risks and benefits of tricyclic use in breast-feeding mothers.

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Dr. Wisner and Colleagues Reply

TO THE EDITOR: We appreciate the comments on our article. We also applaud the publication of additional data on serum levels of nortriptyline and its hydroxymetabolites in breast-feeding mothers and their infants. Dr. Mammen et al. studied two older infants who had no detectable nortriptyline in their sera. However, both infants' sera had detectable amounts of E-10- hydroxynortriptyline at <4 ng/ml. The sensitivity of assay was 4 ng/ml for reproducible quantitation and 2 ng/ml for limit of detectability. Our interpretation is that these two infants had 2–4 ng/ml of E-10-hydroxynortriptyline in their sera. Less than 2 ng/ml would lead to *non*detectability of the drug according to their definition. At 2 to <4 ng/ml, the drug is detectable but not reliably quantifiable.

At the time of publication of our serum level data (1, 2), nortriptyline and hydroxymetabolite levels were reported (by the same laboratory used by Dr. Mammen and colleagues) as quantifiable only at 4 ng/ml (or greater); less than 4 ng/ml was identified as below the level of detectability. Mammen and colleagues have established that in some infants, the nortriptyline E-10-hydroxymetabolite can be detected (but not specifically quantified) at 2–4 ng/ml.

It is likely that as assay techniques in research laboratories continue to improve, smaller amounts of drugs and their metabolites will be detected and eventually quantified in sera. Improved estimates of risk for breast-fed newborns will progress through these technical advances as well as through accumulation of serum level data from greater numbers of cases. With the additional information presented by Dr. Mammen and colleagues, we would update the statement from our review as follows: "healthy full-term infants over 10 weeks of age have a low risk of negative effects secondary to maternal tricyclic treatment, since neither parent compounds nor metabolites have been *quantified within current assay limits*, and no reports of adverse effects have been published." We are pleased to know that the infants studied by Dr. Mammen and colleagues also experienced no adverse effects during breast-feeding.

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Borderline Personality and Bipolar Disorder

TO THE EDITOR: In their Clinical Case Conference, Sara Bolton, M.D., and John G. Gunderson, M.D., appear to argue persuasively for reformulating a diagnosis of bipolar disorder into borderline personality disorder (1). However, in so doing they are fostering an unnecessary split between biologic and dynamic treatment modalities.

Their rather harsh critique of the biologic/pharmacologic approach in the case emphasized that this method encouraged dependency. The patient was viewed making "defensive use of the diagnosis [of bipolar disorder]" and seeking hospitalization "to evade responsibility." This may have been the case, but perhaps she was fighting to survive. Functional improvement and assumption of control are goals that can be sought from either theoretical treatment framework, and iatrogenic disempowerment can pose a danger within both.

The authors deemed the search for a pharmacologic cure "unrealistic" and not worth pursuing further, since their patient's pathology was "embedded in personality." But their case against the bipolar disorder diagnosis would be diminished had she recovered with pharmacotherapy. Hence, their diagnosis of borderline personality disorder depends largely on their observation that the patient was largely unresponsive to numerous trials of medication.

But has the pharmacotherapeutic arsenal for this patient, who clearly has experienced bipolar mood states, been exhausted? I think not. State-of-the-art technology for "treatment-resistant" mood disorders (2) leaves, I believe, many stones unturned. For example, almost completely unexplored is the use of antiepileptic drugs for treatment-refractory depression.

Over the past 7 years, I have noted that patients with recalcitrant depressions have responded considerably when antiepileptic drugs were combined with antidepressants, especially in patients with subtle signs that were consistent with an underlying "subclinical epilepsy." In the case that Bolton and Gunderson described, there were several such clues, including the auditory, olfactory, and visual hallucinations; affective lability and impulsivity; history of "migraine stomach," migraine headache, dysmenorrhea, mild head trauma, and bruxism; clinical destabilization with proconvulsants; and family history of antiepileptic drugs and alcohol responsiveness. The single negative EEG reading does not gainsay this evidence. Therefore, it is notable that in spite of this patient's multiple careful medication trials, which sequentially included two antiepileptic drugs, five antidepressants, two antipsychotics, lithium, and ECT, the combination of an antiepileptic drug with an antidepressant was apparently not attempted.

I agree with the authors' implication that treatment response must be taken into account in diagnostic formulation. However, chronic mood disorders, which can result in the formation and continuation of wide-ranging maladaptive and self-destructive behaviors that are possibly independent of past or present psychosocial environment, theoretically can respond to pharmacological intervention in a time interval that is relatively shorter than that of dynamic intervention. This suggests that personality disorders remain the diagnoses of exclusion. Although dynamic intervention should concurrently take place, patients so viewed need to be simultaneously evaluated over time by detailed and exhaustive pharmacotherapeutic trials.

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N. FRANK FEINER, PH.D., M.D.
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TO THE EDITOR: Drs. Bolton and Gunderson's article is a milestone. Such a communication was overdue, and Dr. Gunderson's authoritative comments are enlightening. We are also impressed that the *Journal* saw merit in the case report and published it in a time and age when data-based research papers preferentially find space. As care providers in an acute adult inpatient service of a university-based hospital, we have seen numerous patients similar to Dr. A. We should like to share the following comments.

A cardinal point that Dr. Gunderson made is the necessary search for both axis I and axis II disorders. Inadequate training in the area of personality disorders also accounts for underidentification of pervasive and malignant psychopathologies. In this context, we all must remember that, as Yorke put it, "The psychiatrist who works with adults needs to be able to look back to the child behind the grown-up" (1). Without careful collection of developmental and other social-historical data, a patient would be denied psychosocial therapies that form the mainstay of treatment in severe personality disorders and that could be complementary to biological therapeutic approaches.

Dr. Gunderson emphasized the value of identifying personality factors in the case of treatment-resistant bipolar disorder. We, however, like to identify these factors early on in the treatment. Why wait for treatment resistance to appear? Early identification of the problem is always better; we can empower the patients by helping them assume responsibility for their actions before maladaptive patterns of behavior are entrenched. A rediagnosis almost invariably triggers an initial split in the patient with borderline personality disorder. In our clinical experience, the misdiagnosed patients are very possessive of the diagnostic label of bipolar disorder and the medications that they might have been taking.

We also find the term "treatment resistant" rather misleading. The prefix "treatment" is much more than pharmacotherapy. Generally, the term assumes that pharmacotherapies as well as nonbiological interventions have been tried. Are the latter as standardized as the former? In order words, if a patient were to receive psychotherapy from two sources, would this patient receive the same product, in the same sense, as would a patient getting a prescription for valproic acid filled at two different sources? Further, in psychotherapy more than pharmacotherapy, a patient's participation is very important for the treatment to be effective. Besides, there are major definitional issues with the concept of treatment resistant.

Multiaxial classification and the required consideration of axis II are two of the most notable contributions of American psychiatry. As a result, the concept of borderline syndrome has been evolving, defined, and refined. A great deal of heterogeneity has been noted within the syndrome. Hurt and Clarkin (2) have identified three subclusters based on eight DSM-III criteria of borderline personality disorder. In our clinical experience, Hurt and Clarkin's affective subcluster, characterized by intense inappropriate anger and affective instability, is a bipolar disorder look-alike.

Dr. Gunderson also talked about the factors that may obscure borderline personality disorder. In our experience, comorbidities such as posttraumatic stress disorder, panic disorder, dissociative disorder, eating disorder, cyclothymia, somatization disorder, dependent personality, substance dependence, and depressive disorders can lead to underdiagnosis of borderline personality disorder. We share the concern of Dr. Gunderson about the ever-widening use of an affective disorder diagnosis. We believe that after the landmark trans-Atlantic study (3), the diagnostic pendulum has swung to the other extreme; in the past schizophrenia was overdiagnosed in the United States and now the same appears the case with bipolar disorder. When both bipolar disorder and borderline personality disorder are listed among the differential diagnoses, the former typically preempts the diagnosis. In 1896, Kraepelin worked very hard to differentiate manic depressive insanity (now bipolar disorder) from dementia praecox (now schizophrenia). However, a century later, the concept of manic depressive illness once again faces the threat of dilution. Because of the tremendous therapeutic implications, as outlined by Dr. Gunderson, it is imperative that we always consider borderline personality disorder in the differential diagnosis of bipolar disorder. We always remind ourselves that what glitters is not always gold and if the only tool we have is a hammer (pharmacotherapy) we will see only nails (bipolar disorder).

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Drs. Gunderson and Bolton Reply

TO THE EDITOR: Dr. Feiner asserts that our patient should have retained the diagnosis of bipolar disorder and that our diagnosis of borderline personality disorder was based on the observation that the patient was unresponsive to numerous trials of medication. He goes on to suggest that the patient may have had a form of "subclinical epilepsy," for which further medication trials were warranted.

We agree with Dr. Feiner that combining antidepressants with antiepileptic drugs is worthy of trial. However, since these medications can decrease symptoms of borderline personality disorder (1–3), and subclinical neurological problems are common in these patients (4–6), responsiveness to this combination should not be thought to be indicative of bipolar disorder. More importantly, we want to emphasize that we did not and would not use the borderline or other personality disorder diagnosis only if and when all other axis I diagnoses were excluded. Our diagnosis of borderline personality disorder began with the observation that the patient met all nine DSM-IV criteria for borderline personality disorder. In addition to minimal medication responsiveness, the clinical course was marked by the regressive use of hospitals, splits in object relationships, intense attachments, fears of abandonment, and feelings of emptiness that are prototypic for this disorder.

By emphasizing further trials of pharmacotherapy and dismissing the diagnosis of borderline personality disorder, Dr. Feiner furthers the very split between biologic and dynamic treatment modalities that he decries. We believe that patients with either or both diagnoses are in some sense "fighting to survive" and should have treatment that joins the benefits of carefully selected psychosocial modalities with those from medications. The primary problem with Dr. Feiner's emphasis remains the danger of disproportionately hinging the patients' hopes to a modality that will be modestly helpful at best while unwittingly discouraging the patients' sense that they can, and may need to, actively try to change themselves. We borrow from Drs. Prakash and Roback's letter by suggesting that Dr. Feiner risks seeing only nails (i.e., bipolar disorder) if he entrusts his therapeutics too exclusively to his hammer (i.e., medication).

From the array of issues on which Drs. Prakash and Roback thoughtfully commented, we will highlight a few that we particularly appreciated. We agree that psychosocial treatments are anything but homogeneous in their implementation and that the assertion of "treatment resistance" can cover a wide range of causes, the correction of which lies only in knowing the specific details of what transpired within the relevant "therapeutic" relationships. Despite advances in manualizing psychosocial therapies, the use of multiple modalities and the uniqueness of treatment settings, styles, and resources assure that we remain a long way from offering standardized psychosocial regimens to patients.

We especially like the attention Drs. Prakash and Roback give to the biases clinicians can bring to bear on their use of particular diagnoses—biases related to therapeutic optimism, to a patient's likability, and even to a patient's achievement status. Here we would note that the diagnosis of borderline personality disorder is often assigned pejoratively to patients that clinicians find difficult to treat (or don't like). In contrast, patients or their families can welcome the borderline personality disorder diagnosis when it is recognizable, accurately reflects what they have experienced, and prepares them for what to expect. For patients like the one we presented, offering only a therapeutically optimistic axis I diagnosis, while ignoring the axis II condition, does not do anyone a favor.

A final comment, responsive to both letters, is to underscore that we did not mean to suggest that patients are very satisfactorily captured by either a bipolar or borderline diagnosis. Rather we see a need to develop these diagnoses to reflect both neurobiological dispositions, for which drugs may have more predictable benefits, and characterological dysfunctions, for which more specific psychosocial therapies are indicated.

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ADHD and Maternal Smoking During Pregnancy

TO THE EDITOR: Sharon Milberger, Sc.D., and colleagues (1) found an association between smoking by mothers during pregnancy and attention deficit hyperactivity disorder and lower IQ in their children that could not be attributed to socioeconomic status, parental attention deficit hyperactivity disorder, or parental IQ. However, the results of their study would have been more conclusive if other confounding variables had been controlled. Mood and other substance-related disorders may indeed be more common in individuals who smoke, and heavy smoking during pregnancy may indicate a strong nicotine dependence. So it would have been necessary to evaluate alcohol use during pregnancy, since alcohol abuse by mothers has been associated with hyperactivity, inattention, and lower IQ in the offspring despite no signs of fetal alcohol syndrome (2). Given the relationship between smoking and depression, and the association between postpartum depression and lower IQ in children (3), it would have been important to assess antecedents of maternal depression.

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Dr. Milberger and Colleagues Reply

TO THE EDITOR: We appreciate the comments from Drs. Chabrol and Peresson regarding two potential confounding variables (maternal alcohol use during pregnancy and maternal depression) that could account for the association that we observed between maternal smoking during pregnancy and attention deficit hyperactivity disorder and lower IQ in their children. From the studies that Drs. Chabrol and Peresson cite, as well as our own work (1) and that of others (2), we agree that it is necessary to control for maternal alcohol use during pregnancy and maternal depression when looking at these associations. Consequently, we reran our analyses by adding maternal alcohol use during pregnancy and maternal depression into the multivariate models. This reanalysis revealed that the association between maternal smoking during pregnancy

and attention deficit hyperactivity disorder status and IQ in the children remained unchanged after these two additional variables were controlled (i.e., there was still a significant association between maternal smoking and attention deficit hyperactivity disorder and a nearly significant association between maternal smoking and IQ).

We thank Drs. Chabrol and Peresson for bringing these two important variables to our attention. The inclusion of these variables in the analysis further highlights the robustness of the association between maternal smoking during pregnancy and attention deficit hyperactivity disorder and lower IQ in the offspring.

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SHARON MILBERGER, SC.D.
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On an Engaging Patient With Paranoid Schizophrenia

TO THE EDITOR: Dr. Sobel and colleagues (1) are mistaken in thinking that a patient who fits diagnostic criteria for paranoid schizophrenia but is "engaging and relates well to others" is unusual. They would be able to meet many such patients if they were to visit our rehabilitation service in a socially deprived part of London. Since this would involve rather a long journey, I suggest instead that they develop settings in which they will get to know their own patients better as people. Theorizing about diagnosis must inevitably go astray if not based on this foundation.

I am sure that they will find it as rewarding an experience as I have (2). They may care to ponder the prejudices and preconceptions that have led to the grievous underestimation of the capacity for human feelings and fellowship in patients with schizophrenia, an underestimation that has unfortunately continued largely unexamined from the institutional to the community care era (3).

I hope that the experience will also stimulate the authors' own capacities for relating to others so that they will appreciate the courage and resilience with which many of these patients cope with terrible life circumstances, catastrophic illness, and stigmatization by the public—as well as by physicians. Perhaps then they will reconsider their inaccurate and, I am sure unintentionally, patronizing equation of their patient's coping attempts with the behavior of a 9- or 10-year-old child.

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TO THE EDITOR: In the discussion of the case of interpersonal relatedness and paranoid schizophrenia, Dr. Cancro appears to have misstated Schneider's assessment of first-rank symptoms and to have incorrectly suggested that Kraepelin "would not call our patient schizophrenic." As the works of Kraepelin and Schneider arguably constitute a substantial part of the foundation of modern psychiatry, corrections may be in order.

The patient in question was a 33-year-old man with a 10-year history of psychosis who suffered a relapse after he stopped taking haloperidol, only to improve upon reinstitution of the medicine. Subsequently, he demonstrated the same good social relatedness that he had had before he relapsed.

Dr. Cancro noted that "Kraepelin placed great emphasis on deterioration in schizophrenia" and, given this patient's relatedness, felt that Kraepelin would not have diagnosed this patient as schizophrenic. However, I believe a close reading of Kraepelin indicates that he might well have made just such a diagnosis in this case.

In *Dementia Praecox and Paraphrenia* (1), although Kraepelin emphasized the phenomenon of deterioration in schizophrenia, he also noted that the paranoid forms of schizophrenia at first sight do not have the slightest resemblance to the other forms, and that in the paranoid form, delusions may dominate the morbid picture for years. Although he believed that disorders of emotional life would eventually appear even in paranoid schizophrenia, he also noted that improvements might be seen in schizophrenia during which delusions and hallucinations become less vivid, and the need for occupation and resuming former relationships becomes active.

In light of these thoughts, I think it is fair to say that in this case, Kraepelin might well have given a diagnosis of paranoid schizophrenia. Furthermore, I speculate that he would have strongly recommended continued medical treatment so that the patient might not experience emotional deterioration.

After reviewing Schneider's first-rank symptoms, Dr. Cancro added that Schneider "proposed these diagnostic criteria only to insist that they should not be taken as dogma." This reading of Schneider, however, may not be accurate. Although Schneider commented in *Clinical Psychopathology* (2) that his first-rank symptoms were not basic disturbances in schizophrenia, he did believe that they had special value in the diagnosis of schizophrenia. Indeed, he believed that when a first-rank symptom "is undeniably present and no basic somatic illness can be found, we may make the decisive clinical diagnosis of schizophrenia."

It is gratifying to see Kraepelin and Schneider referenced in a Clinical Case Conference. Their works, especially those of Kraepelin, remain clinically relevant. I hope that practitioners, and especially residents, will again turn to these works and give them the close reading that they deserve.

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Turkish Dissociative Identity Disorder

TO THE EDITOR: In their article on dissociative identity disorder in Turkey (1), Vedat Şar, M.D., and colleagues stated that all but one of the patients who had been diagnosed with dissociative identity disorder had been given a different diagnosis by a previous psychiatrist. The authors attributed this discrepancy to "a current lack of awareness of the subject among mental health professionals." However, another explanation should be considered. As the authors are aware, the apparently burgeoning incidence of this disorder has been attributed to iatrogenic factors. It has also been pointed out that the disorder almost always emerges from, rather than precedes, a diagnostic interview. Therefore, it is possible that the patients in their study had not been misdiagnosed by their previous psychiatrists but that dissociative identity disorder appeared only as a consequence of the diagnostic interview conducted by the authors.

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Dr. Şar and Colleagues Reply

TO THE EDITOR: Dr. Chodoff claims that dissociative identity disorder may be an artifact of diagnostic interview and mentions that only one of our patients had been previously diagnosed with dissociative identity disorder. However, there is no evidence that genuine dissociative identity disorder can be created by any intervention. We do not agree that "the disorder almost always emerges from, rather than precedes, a diagnostic interview." In contrast, we observed that the characteristic features of the disorder always preceded the diagnostic interview. A review of the patients' charts reveals that features that would suggest a chronic, complex dissociative disorder were already evident even many years earlier. It was clear that the psychiatrists concerned never considered this category as a diagnostic probability. Relatives of the patients reported behavior attributable to alter activities of which the patient was amnesic; some of the relatives had even met the alters before admission. Spontaneous switches before any direct intake about dissociative experiences were observed during the first interview in some emergency cases. Indeed, most of the patients were given the diagnosis of dissociative identity disorder in the first few sessions, and the subsequent long-term follow-up further validated the diagnosis. We did not use hypnosis during the diagnostic process.

As in North America and several other countries, many psychiatrists in Turkey do not gather the basic information required for the diagnosis of dissociative identity disorder. Moreover, they do not integrate it into the assessment even when a patient gives the information spontaneously. After the publication of our observations in Turkey, the situation began to change. Now we have seen referral patients who have been accurately diagnosed with dissociative identity disorder by colleagues who have never diagnosed the disorder before, some of whom had even been skeptical about this diagnosis.

The increasing frequency of reported cases of dissociative identity disorder seems to be a consequence of the improving diagnostic capabilities of clinicians rather than the burgeoning incidence of the disorder. Although the DSMs have provided diagnostic criteria since 1980, they do not cover all clinical features of the disorder. Knowing the DSM criteria is hardly sufficient to diagnose dissociative identity disorder without further information about the associated features of the disorder.

It is clear that there is a group of patients who fit the symptom constellation defined by the Dissociative Disorders Interview Schedule. No study has been conducted that has not confirmed the symptom profile of the disorder. We showed the consistency of this profile in a different culture, except for some of the individual criteria of borderline personality disorder that were taken into consideration as associated features of dissociative identity disorder. We believe that this exception is an expression of cultural difference.

Unfortunately, the treatment of patients whose dissociative identity disorder went undiagnosed was not managed effectively. Most of the patients reported ineffective previous treatment and particularly noted a lack of psychotherapeutic intervention. In our observation, the emergence of the research and clinical work on dissociative identity disorder in Turkey will exert a positive effect on the psychotherapeutic attitude among professionals. Clinicians should never be afraid to ask their patients questions.

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Gloria Revisited

TO THE EDITOR: The account of Gloria's despair by Anna Schwartz, M.D., and colleagues (1) was a timely reminder of how psychiatric understanding and treatment can be distorted by the paradigm of the moment. Gloria's behaviors were viewed solely as manifestations of disease that required medical treatment. Psychotherapy, added secondarily, was "supportive." The patient made poor progress because she was poorly understood; those treating her failed to appreciate how much of her behavior was a meaningful response to life events within the context of a particular personal history.

Thirty years ago, under the influence of a dominant psychoanalytic paradigm, psychiatrists would have been more likely to make the opposite mistake. Manifestations of disordered brain physiology were liable to be ascribed to unconscious motivation, while patients were enlisted in fruitless searches for the meaning of symptoms. Now, economic forces consign us to the role of technical experts whose job it is to scrutinize the patient for signs of disease and reach for the prescription pad. Neither paradigm describes the true task of the psychiatrist: to understand behavior as a product of the brain as it functions in the context of life events, personal history, and culture. We must insist upon this essential integrationist role as health care systems evolve. If we do not, there will remain no group of health professionals on whom patients can rely for help with disorders of behavior, emotion, and thought.

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Review

TO THE EDITOR: We authors and editors often wonder if book reviewers read everything in the books they review. Dr. Van den Bosch obviously is one who does. His review (1) was comprehensive and complete. For readers of the review who have not read our book, there were only 15 historical myths about rehabilitation listed by Anthony et al. in their article (2). Readers of the book, thus, missed nothing if they were looking for the myth that the "editorial generosity" shown to Dr. Talbott suggested. While *Schizophrenia 2004* may well reveal new insights into this disorder, revelation of a 16th myth will not be one of them.

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Reprints of letters to the Editor are not available.

Corrections

In "Attentional Functioning in Schizotypal Personality Disorder" by Sonia E. Lees Roitman, B.S., et al. (May 1997, pp. 655–660), there was an error in table 2 (p. 658). Superscripts *a* and *b* should have appeared after test condition d′, rather than in the headings. Planned comparisons indicated that on overall d′ (averaged across four digits and shapes), patients with schizotypal personality disorder performed significantly worse than patients with other personality disorders and normal subjects; schizophrenic patients performed significantly worse than normal subjects. (All statistics are as reported in original table 2.)

In the "Practice Guideline for the Treatment of Patients With Alzheimer's Disease and Other Dementias of Late Life" (Supplement to *The American Journal of Psychiatry*, May 1997), on p. 3, second column, first paragraph, which begins "Vitamin E may also . . . ," the third sentence should read "Thus, it might be considered alone or in combination with a cholinesterase inhibitor in the treatment of Alzheimer's disease [II]."

In the Brief Report "Meta-Analysis of Postmortem Studies of Alzheimer's Disease-Like Neuropathology in Schizophrenia" by Ross J. Baldessarini, M.D., et al. (June 1997, pp. 861–863), at the bottom of page 862, a study by E.D. Bird and F.M. Benes (1996) is referred to as having used comparison patients with affective disorder. This is incorrect; the control subjects were normal comparison subjects. The inclusion of normal control subjects is the accepted practice for postmortem studies of schizophrenia and one to which the authors have always adhered.