Letters to the Editor

Treatment of Corticosteroid-Induced Mood Changes With Olanzapine

TO THE EDITOR: We report a case of severe mood changes during corticosteroid therapy that was successfully treated with the atypical antipsychotic olanzapine.

Ms. A was a 21-year-old woman with no personal or family history of mood disorders who, at presentation, had received 3 months of prednisolone therapy (30 mg/day) for severe asthma. Other medications in her regimen included inhaled steroids and β-agonists. A psychiatric consultation was requested by her allergist.

Ms. A reported a depressed mood, mood swings, crying spells two to three times daily, suicidal ideation, anxiety, and insomnia beginning within days of starting chronic corticosteroid therapy. She had rapid speech and prominent affective lability ranging from smiles to tears during the interview. Her scores on the 28-item Hamilton Depression Rating Scale, Young Mania Scale, and Brief Psychiatric Rating Scale (18-item, 1–7 scale) were 33, 9, and 31, respectively.

A regimen of olanzapine, 2.5 mg at night, was started. Three weeks later, Ms. A reported the "medicine really, really helped." The crying spells had decreased to about one each week, while mood swings and suicidal ideation had subsided. The only side effect was mild sedation at bedtime, which she felt improved her sleep. During the interview, her affect was stable and euthymic. Her Hamilton rating scale, Young Mania Scale, and Brief Psychiatric Rating Scale scores decreased to 3, 0, and 19, respectively. After 5 months of olanzapine therapy, she remained free of mood symptoms, despite the continuing use of corticosteroids, and was tolerating the medication well.

Olanzapine is an atypical antipsychotic that, unlike conventional neuroleptics, binds rather nonselectively to dopamine (D_1, D_2, D_3, D_4, D_5) receptors and acts as an antagonist with serotonin ($5\text{-}HT_{2A}$, $5\text{-}HT_{2B}$, $5\text{-}HT_{2C}$, $5\text{-}HT_6$) receptor subtypes (1). Side effects include somnolence and, like corticosteroids, weight gain. Some data suggest that olanzapine has mood-stabilizing properties in bipolar patients (2). Ms. A had a substantial improvement in mood symptoms with the addition of olanzapine, and the medication was well tolerated.

The results of Ms. A's pulmonary function tests were essentially unchanged on the first and second visits, suggesting that the improvement in mood was not secondary to improvement in asthma symptoms. No other medication changes had occurred.

Corticosteroids are frequently prescribed medications. Mania, depression, mood lability, and psychosis are not uncommon side effects (3). Very limited data suggest that lithium, neuroleptics, and ECT may be effective treatments (3). Our experience suggests that olanzapine may also reduce these mood changes. Controlled trials of olanzapine in individuals with corticosteroid-induced mood changes are warranted.

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Mood Stabilization and Weight Loss With Topiramate

TO THE EDITOR: The anticonvulsants valproate and carbamazepine have gained increasing popularity in the treatment of bipolar disorder and other conditions involving affect or impulse dysregulation. As with lithium, however, a major adverse effect of these drugs is weight gain. While the newer anticonvulsants lamotrigine and gabapentin have generated interest as possible mood stabilizers, their potential for causing weight gain is unclear. In contrast, the novel anticonvulsant topiramate (1), a monosaccharide derivative, has the unique adverse effect of weight loss. To our knowledge, the thymoleptic efficacy of this drug has not been described. We report our initial experience with topiramate in two patients with mood disorders for whom weight gain had been a major problem.

Mr. A was a 37-year-old man with a 10-year history of rapid-cycling bipolar disorder, including two episodes of manic psychosis and at least five episodes of severe melancholia. For 10 months, he had presented with primarily depressive features, including hopelessness and psychomotor slowing, although with continuing grandiosity. His condition was complicated by obesity, with a weight of 245 lb. He was on a maintenance dose of valproate, 2500 mg/day; bupropion, 300 mg/day; and olanzapine, 10 mg/day. A 4-month trial of levothyroxine, 0.1 mg/day, yielded no weight change. Valproate was discontinued, and a dose of topiramate was titrated to 200 mg/day. In the next 3 months, Mr. A lost 25 lb. He initially reported no change in food consumption but subsequently described a greater motivation to exercise. His mood remained stable, with improved depressive symptoms and no emergence of anxiety.

Ms. B was a 33-year-old woman with a long history of recurrent major depression complicated by marked mood lability and impulsivity. She was also obese, with a weight of 226 lb. She was demoralized by failed attempts to lose weight, despite dieting and exercise. Her mood had stabilized after many psychotropic trials on a regimen of val-

proate, 2000 mg/day, and bupropion, 450 mg/day. She requested appetite suppressants, but a past history of substance abuse contraindicated stimulants. She was given a dose of levothyroxine, 0.1 mg/day, with no effect. One month later, her dose of valproate was discontinued and a dose of topiramate was titrated to 300 mg/day. Within 2 months, she lost 15 lb. However, she became increasingly irritable, depressed, and anxious. Topiramate was discontinued and replaced with a regimen of gabapentin, 1500 mg/day; fluoxetine, 40 mg/day; and clonazepam, 2 mg/day. Her anxiety and irritability were markedly reduced, but she regained 8 lb. within 2 weeks.

In these patients, the substitution of topiramate for valproate resulted in significant weight loss. Mr. A, with bipolar disorder, experienced no loss of thymoleptic efficacy; Ms. B, with unipolar depression and impulsivity, experienced increasing depression and anxiety. Anxiety has been reported as an adverse effect of topiramate (1). Like other thymoleptic anticonvulsants, topiramate has significant effects on γ-aminobytyric acid function (2), but the mechanism of its effects on weight is unknown. Further study should clarify topiramate's utility in treating mood disorders.

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Testosterone-Patch-Induced Psychotic Mania

TO THE EDITOR: With the introduction of new antiviral agents, longevity has increased for many AIDS patients, along with the potential for AIDS wasting syndrome. Suggested remedies for this syndrome have included growth hormone, marijuana, appetite stimulants, ketotifen, exercise, anabolic steroids, and most recently, the testosterone patch. The effects of anabolic steroids on behavior have long been recognized and include mood lability, irritability, euphoria, insomnia, aggression, and sometimes delusions or hallucinations. Reports of behavioral effects of exogenous testosterone are limited and inconsistent (1). One study of intramuscular testosterone for male sexual dysfunction found irritability and uncharacteristic assertiveness in some patients (2), but there are no documented behavioral side effects of the testosterone patch. We report the first case of psychotic mania associated with testosterone patch administration.

Mr. A, a 28-year-old Caucasian man with AIDS, came to the emergency department after 2 weeks of worsening mania with an elevated mood, increased energy, decreased sleep, increased activity, racing thoughts, grandiose delusions, and auditory hallucinations. Approximately 1 month earlier, he was prescribed the testosterone patch for a 20-lb weight loss occurring over the previous 2 years. Mr. A had a history of bipolar II disorder (DSM-IV) but had never previously become psychotic or required hospitalization. A medical workup excluded infection or other AIDS-related processes as the cause of his psychosis. He was started on a regimen of divalproex, 500 mg/b.i.d., and his usual anti-AIDS regimen was continued, except for the testosterone patch. By day three, his sleep and energy had improved, but his psychosis and racing thoughts persisted. A regimen of risperidone, 4 mg at bedtime, was added with good results. Because he had a history of idiopathic thrombocytopenic purpura, his dose of divalproex was discontinued on the fourth day when his platelet count dropped from 100,000 to 65,000. Although Mr. A refused to take another mood stabilizer, he remained much improved and was discharged on a regimen of risperidone monotherapy.

Although we cannot definitively rule out other etiologies for Mr. A's psychosis, this case suggests that administration of even low-dose steroids, such as the testosterone patch, may precipitate psychosis in susceptible individuals. As physicians treat an increasing number of patients with AIDS, it is important that they be aware of this potential danger and exercise caution in the treatment of patients prescribed testosterone for AIDS wasting, particularly patients with histories suggesting a predisposition to mania or psychosis. This includes individuals with histories of bipolar disorder or psychosis or individuals with a first-degree family history of these disorders.

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Prolonged QT Interval After Trazodone Overdose

TO THE EDITOR: It is well recognized that tricyclic antidepressants, particularly in an overdose, may cause a variety of cardiac effects including QT interval prolongation on ECG (1). Newer antidepressants, including trazodone, have been associated with few cardiac side effects. The manufacturer of trazodone has received no reports of QT interval prolongation associated with trazodone at therapeutic doses or in overdose (personal communication, Mark Forest, Pharm.D., Bristol-Myers Squibb, Sept. 17, 1997). Trazodone has very rarely been associated with ventricular tachycardia (2), and there is one case report of QT prolongation and polymorphous ventricular tachycardia associated with trazodone in combination with the antiarrhythmic amiodarone (3). I report here the case of a patient who experienced significant QT prolongation after a trazodone overdose without arrhythmia or other adverse consequences.

Ms. A, a 29-year-old married woman, took an overdose of 60 units (50 mg each) of trazodone at about 9:00 p.m. and went to bed. Her normal medication regimen was fluoxetine, 40 mg every morning; trazodone, 50 mg every evening; and diazepam, 10 mg/t.i.d. as needed. She denied ingesting any other substance besides trazodone. She came to the emergency room the following morning with seda-

tion, dizziness, and nausea. An ECG at 9:00 a.m. (12 hours after the overdose) showed sinus bradycardia (57 beats per minute), normal P-R (164 msec) and QRS (96 msec) intervals, but a prolonged corrected QT interval (607 msec) and nonspecific T-wave changes. She was treated with gastric lavage and charcoal. Cardiac monitoring over the next 30 hours showed no significant arrhythmias. An ECG given 26 hours after the overdose showed a less prolonged, corrected QT (486 msec) and the same nonspecific T-wave changes. An ECG given 3 days after the overdose showed a corrected QT of 429 msec and nonspecific T-wave changes. No pre-overdose ECG was available for comparison. Ms. A had no personal or family history of cardiac disease, syncope, or sudden death. She was taking no medication other than the psychotropic drugs. A toxicology screen was positive only for antidepressants and benzodiazepines.

Ms. A experienced an asymptomatic but significant increase in her corrected QT interval. Trazodone appears to have been the cause, given the temporal relationship to the overdose, the absence of other drugs known to prolong the QT interval, and no history to suggest a familial long QT syndrome or cardiac disease.

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Hyperglycemia and Olanzapine

TO THE EDITOR: Olanzapine is an atypical antipsychotic agent that has been widely prescribed in the United States since October 1996. This drug is structurally similar to clozapine. While clozapine has been associated with hyperglycemia (1, 2), including a series of case reports from our institution (3), to the best of our knowledge, there have been no published reports of olanzapine-associated hyperglycemia. We report this case of an adverse drug reaction in a diabetic patient.

Mr. A, a 45-year-old black man who was previously high functioning and had a 4-year history of diet-controlled diabetes and hypertension, presented to the psychiatry service in January and was diagnosed with major depressive disorder with psychotic features ruled out.

Medically, his diabetes was well controlled, with a glycosalated hemoglobin of 7.4% on a dose of 5 mg/day of glyburide. His systolic and diastolic blood pressure averaged 136 and 80 mg Hg, respectively, on a regimen of extended-release nifedipine, 30 mg/day.

After a trial of nefazadone failed, he was switched to fluoxetine, titrated to a dose of 60 mg/day. Shortly thereafter, he experienced auditory hallucinations; haloperidol, 4 mg/day, and thioridazine, 50 mg/day, were added, but he developed severe parkinsonian symptoms and was switched to olanzapine, 10 mg/day, in May. Within 24 hours after the initiation of olanzapine, he came to the emergency room at the Veterans Administration hospital with three-plus pitting edema and profound weight gain. An echocardiogram was completed that day, and results were found to be within normal limits.

At his May medical clinic appointment, his weight was documented at a 25% increase since his last appointment. His blood sugar readings were now 180–260 mg/dl; his dose of glyburide was increased to 5 mg twice daily, and his medical workup continued.

This included a CT scan of the abdomen to rule out inferior vena caval compression and tests of urine protein and serology to exclude nephrotic syndrome, acute hepatitis, low albumin state, or acute renal insufficiency. None of these test results revealed significant findings. There were no concurrent infectious processes, his dietary regimen was unchanged, and there was no alcohol or drug use.

Later that same month, his glucose ranges were 300–400 mg/dl; his dose of glyburide was increased to 10 mg twice daily, and a diuretic was added. His glucose levels continued to range higher: 380 to 500 mg/dl per home glucometer and 303 mg/dl serum. An endocrinology consultation was obtained, and normal pressure hydrocephalus insulin was begun at 10 units twice daily and titrated to 45 units twice daily, plus regular insulin coverage with a sliding scale; this had little effect on his hyperglycemia. Mr. A reported polyuria, polydipsia, and blurred vision during this time.

Other complications included a persistent *candidal balanitis*, requiring fluconazole therapy, and a significant increase in his lipid profile. His cholesterol increased 85 points to 325 mg/dl, and his triglycerides were 2,337 mg/dl.

After 3 months, Mr. A was counseled of his option to discontinue the olanzapine, knowing that his mental health would be affected after finally achieving good control. He decided to discontinue it. Within 1 week, his blood sugar returned to normal (85–155 mg/dl); all insulin was discontinued, and his dose of glyburide was decreased to 5 mg twice daily. His weight decreased by 15 lb. He did well medically, without any episodes of hyperglycemia.

We believe this case demonstrates that olanzapine can severely exacerbate diabetic control and recommend that physicians carefully monitor the blood sugar of diabetic patients on this medication or in those predisposed to diabetes.

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Mania Onset While Using Dehydroepiandrosterone

TO THE EDITOR: Steroids are widely recognized as inducing changes in mood, including depression, euphoria, and psychosis with manic symptoms (1). Dehydroepiandrosterone (DHEA) is an adrenal steroid that is transformed into various compounds in many bodily tissues, including skin, muscle, brain, and reproductive organs (2). Adrenal production and serum concentration of DHEA are known to peak between ages 25 and 30 years and thereafter decrease with age. DHEA is widely available over the counter as a dietary supplement and has been widely touted as a fountain of youth and a sexual tonic and promoted for a variety of ills (3). We report a case of severe mania occurring during the use of oral DHEA.

Dr. A, a 51-year-old married man, required involuntary hospitalization because of grandiose delusions, expansive and irritable mood, and extreme psychomotor agitation in May. In January, he had begun taking DHEA, 50 mg daily, to increase his energy level. In retrospect, he denied experiencing depressive symptoms at that time. He was also taking multivitamins and a beef liver extract tablet. Within days of starting to take DHEA, he noted increased energy and a sense of drive. Within 2 weeks, his wife noted gradually worsening psychomotor acceleration, insomnia, irritability, and grandiosity. About a week before hospitalization, he decreased his dose of DHEA to 25 mg/day because of his wife's concern about his irrational and hyperactive behavior. He had no history of prior mania, depression, or psychiatric treatment. However, his baseline mood status may have been mildly hypomanic, with a high level of energy and drive that had contributed to his professional success. His mother's half sister had been repeatedly hospitalized for depression, but the family history was otherwise negative for psychiatric disorder, alcoholism, and suicide.

The severity of his psychosis necessitated the appointment of a temporary personal guardian with power of attorney. In the hospital, he responded slowly but well to a combination of haloperidol, 10 mg/day, and divalproex, 1500 mg/day, with serum levels of 81.3 ng/ml. Dr. A's symptoms disappeared completely over several weeks. As his condition improved, he became increasingly insightful into the extent of his illness and experienced transient mild depressive symptoms in response to feelings of humiliation related to his acute mental illness. Haloperidol treatment was tapered and discontinued without recurrence of psychosis or insomnia, while Dr. A continued receiving divalproex. Four months after his hospitalization, he was symptom free, and he remained well on divalproex monotherapy.

The effect of orally administered DHEA depends on many factors, including serum levels of DHEA and the metabolic status of the body. In most tissues, DHEA is thought to exert antiglucocorticoid effects. DHEA is produced in the central nervous system as well as the human adrenals and is present in the brain, concentrated in limbic regions, in levels much higher than other steroids. DHEA has been postulated to function as an excitatory neuroregulator, antagonizing γ-aminobytyric acid transmission (4). Although it appears possible that Dr. A may have had a bipolar diathesis, oral DHEA may have played a role in the induction of his acute manic episode. Further research is needed to determine the mood effects of DHEA, including its potential risk for patients with bipolar disorder.

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Schizophreniform Disorder: Exception Proves the Rule

TO THE EDITOR: Schizophreniform disorder refers to schizophrenia-like psychoses with a duration of less than 6 months. The validity of this condition as a distinct diagnostic entity has been questioned (1). This may be at least in part because of the variability in how we define this disorder. In DSM-IV, a provisional diagnosis of schizophreniform disorder can be made when an episode lasts for less than 6 months. Alternatively, schizophreniform disorder is diagnosed as "definite"—i.e., without the "provisional" qualification—when a patient with an episode of schizophrenia-like illness has "recovered" within 1 to 6 months (DSM-IV). The recovery required to make the diagnosis is not adequately defined. The following case emphasizes the need for clarification.

As part of an ongoing prospective follow-up study of patients with first-episode psychotic disorders, we have been conducting longitudinal reevaluations of diagnoses. Among 115 such patients, 15 met an initial (4-week assessment) diagnosis of schizophreniform disorder—provisional. Upon reevaluation at 6 months, 14 patients were rediagnosed with schizophrenia on the basis of their fulfilling the duration criteria of 6 or more months of illness (including prodromal, active, and residual phases).

The one exception was Ms. A, a 37-year-old single Caucasian woman who was a college graduate and worked as a nutritional therapist. She was admitted for a 2-week history of auditory hallucinations, referential and persecutory delusions, anxiety, sleeplessness, and agitation. Following treatment with risperidone (up to 4 mg per day), she gradually improved. She continued to experience mild ideas of reference for 2 to 3 months; then her symptoms completely subsided. She returned to full-time work and functioned well without any symptoms while on a low dose (2 mg) of risperidone. Two years later, she enrolled in a study of gradual medication withdrawal under close supervision. Auditory hallucinations returned within a week after her last dose of risperidone. Upon reinstitution of her medication, her symptoms gradually improved over the following month.

Ms. A had clearly met DSM-IV criteria for schizophreniform disorder. This diagnosis would have continued to be our best estimate had she not had a trial of medication dis-

continuation. Thus, hers was not a "true" recovery, and the possibility of persistence of the illness, or the vulnerability for reemergence of symptoms, was only uncovered by the attempt to discontinue medication. We suggest that a diagnosis of "schizophreniform—provisional" should only be changed to schizophreniform without qualification if a patient is asymptomatic without ongoing treatment for psychotic symptoms. How long after discontinuation of medication should one assign a diagnosis of schizophreniform without qualification? Only prospective studies in which antipsychotic medication-free remission is observed will address that question.

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Gabapentin-Induced Ejaculatory Failure and Anorgasmia

TO THE EDITOR: Psychotropic drugs are well known to affect sexual functioning (1) and may contribute to patient noncompliance. The serotonin reuptake antagonist antidepressants are particularly known for their effects on orgasm (2–4). Much less is known about the adverse sexual effects of anticonvulsants, although one case report suggests that carbamazepine may cause ejaculatory failure (5). We report a case of ejaculatory failure and anorgasmia associated with gabapentin.

Mr. A was a 41-year-old man with a long history of bipolar II disorder and alcohol dependence with intermittent cocaine abuse. After completing a 4-week alcohol treatment program, he developed mild hypomania. He had no medical problems and no history of sexual dysfunction. Gabapentin treatment was initiated for hypomania at 300 mg per day and gradually titrated to 600 mg 3 times per day over 1 month. While taking 300 mg of gabapentin 3 times per day, he noticed orgasm was more difficult to attain. Neither libido nor erection was affected. Gabapentin reduced his hypomania, but as the dose increased, he found ejaculation and orgasm increasingly difficult to achieve. He could have intercourse with a normal erection for 20 minutes but could not ejaculate. At times he attained a sense of incomplete orgasm sensation but did not ejaculate. There was no retrograde ejaculation. Mr. A took gabapentin for 4 months and eventually stopped the medication because of his inability to ejaculate. During this time, he remained abstinent from alcohol, and the results of three urine drug screens for cocaine and marijuana were negative. He denied using other illicit or over-the-counter drugs. One week after stopping the gabapentin dose, he reported the return of his usual orgasm and ejaculation abilities.

This case demonstrates a clear on/off phenomenon of anorgasmia related to gabapentin, which may be dose related. The frequency of this adverse effect is unknown, although sexual side effects were reported as uncommon in clinical trials when epilepsy was treated. It is unknown if gabapentin might affect other areas of sexual functioning, although, in this man, it did not. The mechanism of action of gabapentin is unknown, and the effects on ejaculation or other aspects of sexual function are also unknown. As gabapentin becomes more commonly used in psychiatric practice, the frequency of this adverse effect may become more apparent.

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Severe Vasculitis After Therapy With Diazepam

TO THE EDITOR: Diazepam is a benzodiazepine prescribed worldwide. In respect to its posology and indications, the drug is generally well tolerated. Hypersensitivity manifestations are very rare and of mild severity (1). The causative role of the drug in one case of allergic interstitial nephritis has been previously described (2). We have recently seen a patient who experienced bullous vasculitis, fever, and neutrophilia after therapy with diazepam.

Ms. A, a 50-year-old woman, was referred to our hospital for chronic depression or dysthymic disorder with alcohol dependence. There was no history of drug allergy. She was given 100 mg of thioridazine orally once a day and 10 mg of diazepam four times a day. After 2 days, she noticed an erythematous eruption on her ankles. Thioridazine treatment was first discontinued. As the eruption became more erythematous and affected both extremities and flanks within a few hours, methylprednisolone was administered at a dose of 80 mg daily. The next day, the eruption progressively became bullous, and Ms. A's condition worsened. She felt ill and had pyrexia at 39.4°C. Urea and creatinine levels stayed within normal limits. The results of blood cultures were negative. A skin biopsy revealed bullous vasculitis with numerous eosinophils within the dermis. Diazepam therapy was then discontinued, which led to the resolution of pyrexia and the progressive healing of the cutaneous lesions. Postinflammatory ulcers persisted on both ankles for 2 months. The results of a lymphocyte blast transformation test was positive for diazepam.

Cutaneous side effects of diazepam are very rare and of mild severity (1). To our knowledge, severe vasculitis from diazepam has not been previously reported. The imputability of the drug is strongly supported by the improvement of Ms. A's condition after the discontinuation of diazepam and blas-

togenesis after in vitro exposure of her lymphocytes to the drug. We suggest that psychiatrists be aware of this potential side effect and allow prompt withdrawal of the drug.

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Allergic Reactions From Injectable Methadone

TO THE EDITOR: Oral or injectable methadone is widely used in the treatment of opiate dependence. There are several side effects caused by methadone therapy, the most commonly reported being nausea, vomiting, dizziness, mental clouding, and pruritus. There have also been a variety of skin lesions associated with intravenous opiate treatment. The following report suggests that local urticarial reactions may be quite frequently caused by intravenous methadone use.

Five out of 20 patients participating in an injectable methadone research program, with a mean dose of 70 mg (SD= 20) and a mean frequency of 5.1 injections/week (SD=0.7), developed red skin lesions and pain in the forearm and arm during and after intravenous methadone injection under clinical supervision. The patients showed slightly raised round red lesions with an annular border, some measuring up to 3 inches in diameter. The lesions were always proximal to the injection site but did not reappear after each injection. Occasionally, the lesions overlaid the veins along several dozen inches, sometimes with a lesion-free segment and other times continuously. Because most of the injections are administered to the arm or hand, most of the lesions were located on the arm. The lesions were associated with pain along the relevant vein and disappeared within 10 minutes to 2 hours after injection.

To our knowledge, this is the first report of localized urticaria associated with intravenous methadone use. Methadone can, as do other opiates, induce release of histamine by degranulation of mast cells by a nonspecific mechanism (1–3). It remains to be established whether prophylactic treatment with antihistimine type-1 receptor antagonists can alleviate pruritus or urticaria. As demonstrated by this report, local urticarial reactions to intravenous methadone can be frequent. These reactions can be considered a severe side effect, but in the context of severe opiate addiction, this manifestation, with transient localized pain, was not an exclusion criterion. In this study, in which written informed consent was obtained, subjects with allergic manifestation could be switched to an oral preparation. We observed, however, that this change in method lasted not more than 3 days before patients returned to intravenous administration. Nevertheless, this type of reaction may represent a risk factor for lower participation in intravenous methadone programs and higher illicit opiate use.

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Clozapine and Paroxetine in the Treatment of Schizophrenia With Obsessive-Compulsive Features

TO THE EDITOR: Patients whose schizophrenia is characterized by marked obsessive-compulsive features can be difficult to treat successfully and often require a combination treatment (1). If the psychosis in such patients does not respond to a neuroleptic and they are treated with clozapine alone, their obsessions may not improve, and some reports suggest that they may worsen (2). We report a patient with schizophrenia with obsessive-compulsive features who was resistant to multiple pharmacological trials of various antipsychotic and anti-obsessive-compulsive regimens but responded to a combination of clozapine and paroxetine.

Mr. A, a 32-year-old man with schizophrenia whose psychosis had not responded to treatment for the past 4 years, was admitted to our unit for evaluation and management. He was quite delusional but also had prominent negative symptoms. In addition to these classic features, he had disabling obsessive-compulsive symptoms such as the need to repeat his steps and continually retrace every public transit ride he took. His obsessive-compulsive symptoms prevented him from functioning independently, even though he was an intelligent and well-informed college graduate. Previous lengthy trials of perphenazine and risperidone (targeting the psychosis) as well as sertraline (targeting the obsessive-compulsive symptoms) were unsuccessful in controlling Mr. A's psychotic and obsessive-compulsive symptoms, respectively. When he came to our unit, he was weaned off of his medication and underwent a 2-week drug washout period. During this time, he remained psychotic with nearly constant obsessive-compulsive symptoms, such as picking at his clothes, and resistance to outings off the unit because of his "need" to undertake various rituals and tasks while off the ward. At the end of this 2-week period, clozapine was started and slowly titrated up to a level of 200 mg per day. After treatment with clozapine for 1 month, there was improvement in some of the "positive" psychotic symptoms (delusions), but there was mild worsening of others (hostility, grandiosity) as rated by clinical team members' subjective impressions. However, while he was receiving clozapine, there was no improvement in his obsessive-compulsive symptoms; rather, the treatment team felt that there was an accentuation of his obsessions during this time. Paroxetine was then added to the clozapine regimen, and a dose of 30 mg per day was reached by 2 weeks. The paroxetine was well tolerated, and blood levels of clozapine remained stable (in the range of 150 ng/ml) during paroxetine treatment. The addition of paroxetine resulted in a significant reduction in obsessive-compulsive symptoms (over a period of 14 weeks), as demonstrated by a decrease in his to-

tal Yale-Brown Obsessive Compulsive Scale score from 30 to 15 and in his Yale-Brown obsessional subscale score from 16 to 9. During this same period, his positive symptoms (rated on the Brief Psychiatric Rating Scale) declined by 40%. After 14 weeks on the combined treatment of clozapine and paroxetine, his Clinical Global Impression scale score, which had been 6 (severely ill) before the initiation of clozapine, fell to 3 (mildly ill).

With this severely ill patient with treatment-refractory schizophrenia and obsessive-compulsive symptoms, a combination of clozapine and the selective serotonin reuptake inhibitor paroxetine resulted in significant clinical improvement in both psychotic and obsessive-compulsive symptoms. While paroxetine has been reported by some to increase clozapine levels (3), in Mr. A, this did not happen. However, because paroxetine is largely metabolized by the cytochrome P450 IID6 (CYPIID6) enzyme (4) and clozapine is predominantly metabolized by the CYPIA2 and partly by the CYPIIIA enzymes (5), perhaps the lack of increase in his clozapine blood level should not be that surprising. Moreover, we have reported previously on another case (6) in which paroxetine was added to clozapine without affecting blood levels of clozapine. Nonetheless, given the potential interaction, until more data are collected, clozapine levels should be monitored closely during initial phases of paroxetine therapy. In addition, prospective studies are required to fully assess the optimal pharmacological management of patients who have treatment-refractory psychosis with obsessive-compulsive features.

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Distinguishing Change in Primary and Secondary Negative Symptoms

TO THE EDITOR: Clozapine, the prototype of atypical antipsychotics, has been noted to have a number of unique clinical features, including the improvement of negative symptoms, when compared with conventional neuroleptics (1). Subsequent studies with other novel neuroleptics also suggest clozapine's superior efficacy in this particular respect (2, 3).

Such claims are tempered by the argument that there is a distinction between primary, or deficit, and secondary negative symptoms (4). Specifically, it is suggested that the former may reflect more enduring psychopathological changes and are therefore less amenable to change, whereas the latter relate to state phenomena such as depression, extrapyramidal symptoms, or environmental deprivation.

Path analysis and multiple regression have been employed as statistical procedures to establish whether changes in negative symptoms with treatment reflect shifts in primary versus secondary negative symptoms. These procedures are used on the basis of the premise that a direct effect on primary symptoms can be established by controlling for, or covarying out, improvement in secondary negative symptoms. By using these techniques, it has been suggested that clozapine (5), risperidone (6), and more recently, olanzapine (7) each influence primary negative symptoms after the effects of the secondary negative symptoms are factored out.

There are several problems with such an approach. First, existing reports have not agreed on the identifiable secondary negative symptoms, with one study specifying only extrapyramidal and positive symptoms (6), whereas others have addressed these as well as depressive symptoms (5, 7). A second difficulty involves the possibility that other sources of secondary negative symptoms exist. For example, neurocognitive impairment is a common feature in schizophrenia and may be integrally related to negative symptoms (8, 9). While there are reports suggesting that novel antipsychotics are superior to conventional neuroleptics with respect to cognitive measures (10, 11), studies have not yet evaluated the potential impact that they could have on negative symptoms. Any investigation that omits variables that might contribute to secondary negative symptoms risks the possibility of erroneously attributing these changes to an influence on primary symptoms.

In light of these caveats, we must be cautious in evaluating claims that novel neuroleptics can improve true deficit symptoms. In fact, more recent work indicates that clozapine can influence secondary, but not primary, symptoms (12). The optimal approach to evaluating change in true deficit symptoms is one that employs a valid measure prospectively. Statistical procedures may be of value but only if they ensure that all possible contributing factors to secondary negative symptoms are included in the analysis.

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Progress in ECT Research

TO THE EDITOR: In his astute editorial, Carl Salzman, M.D. (1), calls attention to the continuing ambivalence of the field toward ECT and the resulting lag in understanding of its mechanisms of action and relative efficacy and effectiveness in the treatment of depression (2). Steps to address these problems are now under way as a result of the recent programmatic reorganization of the National Institute of Mental Health (NIMH) (3, 4).

Intervention research supported by NIMH includes efficacy and effectiveness studies of all therapeutic modalities, including ECT. The benefit-risk ratio of different electrode placements and stimulus dosing (5) and predictors of response (6) are among the clinical reports published this decade from NIMH-funded studies of ECT. Readers of the *Journal* will recall that the last article (6) 3 years ago described the initial stage of an ongoing, three-site clinical trial comparing two medication regimens and placebo as maintenance treatment after a successful course of ECT, which without effective follow-up treatment has a distressingly high early relapse rate (2). Another clinical trial in four centers will examine the decades-old empirical practice of continuation ECT to prevent relapse, particularly when other strategies have failed to sustain ECT-induced remission (2, 4).

As Dr. Salzman suggests, perhaps the most important challenge facing the field is to convey to the next generation of clinical and basic investigators the necessity of enhancing research on the actions and role of ECT. To this end, NIMH grants directed at early-career investigators are enabling the entry of junior faculty into patient-centered and preclinical research with ECT.

ECT remains an essential component of the therapeutic armamentarium. Furthering our understanding of its optimal application and its mechanisms of action remains an important goal for the field, even as newer generations of pharmacological and psychosocial interventions narrow, but do not eliminate, the niche for convulsive therapy. We welcome the opportunity provided in the reorganized NIMH to contribute to the growing research base for ECT as part of our overall program development efforts.

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Psychotherapy With a Borderline Patient

TO THE EDITOR: I read with great interest the recent Clinical Case Conference by Joan Wheelis, M.D., about her psychotherapy with a borderline patient and the subsequent discussion by John G. Gunderson, M.D. (1). However, after nine pages of detailed text, I was struck by the one-paragraph dismissal of Ms. A's decision to terminate treatment when her mother became ill with leukemia. This sudden and seemingly premature termination of the discussion seemed to mirror an abrupt termination of therapy. The impending mortality of the mother and Ms. A's termination of her relationship with her therapist seem to annihilate this fragile patient's only support system. In a teaching article like this, I believe such circumstances warrant a detailed discussion of how a therapist should handle a patient's impending loss, a patient's desire to terminate therapy prematurely, and most important, an assessment and treatment of dangerousness in such circumstances with a borderline patient.

In reviewing her history, Ms. A presented with suicidality and substance abuse following the loss of an 8-year boyfriend and the recent termination with her 10-year therapist due to the therapist's geographical relocation. Her earliest memory described a destructive reaction at age 3 following the loss of exclusive parental attention when her sister was born, and her first wrist slashing was at age 16 after the breakup of an intense 4-year friendship, which led Ms. A to deteriorate drastically in her school performance. Then, just when Ms. A was beginning to explore her feelings about her mother in therapy and "important changes were occurring in that relationship," her mother acquired an apparently fatal illness.

Given such a history of dramatic, self-destructive acting out after perceived losses, a therapist should be very concerned about Ms. A's ability to tolerate the loss of her mother,

especially when she was beginning to deal with this relationship in therapy. The article merely states that Ms. A "experienced this possible loss as in direct conflict with her therapeutic task of exploring and tolerating her disappointments with her mother." It seems that the larger therapeutic task was for Ms. A to explore and tolerate her disappointments and losses in life and that the impending death of her mother provided the therapist with exactly such a situation in which to assist Ms. A in working through.

Dr. Wheelis was extremely honest in her countertransference commentary, and she appeared genuinely invested in the therapeutic relationship. I would welcome her thoughts and discussions with Ms. A when she wanted to terminate treatment because her mother was dying. Dr. Gunderson's expert advice concerning these circumstances would also be most helpful to the average therapist, who is only too often faced with a potentially lethal borderline patient who rejects the therapist at a time of increased vulnerability.

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Drs. Gunderson and Wheelis Reply

TO THE EDITOR: The letter from Linda S. Godleski, M.D., addresses issues related to working with Ms. A's mother indirectly.

Dr. Godleski suggests that the therapist should have been more resistant to Ms. A's wish to terminate their relationship, more active in helping her tolerate her fear of losing her mother, and more concerned with the prospect of Ms. A's self-destructive responses. As Ms. A struggled with her conflict of being connected with her mother and her therapist, much effort went into helping her recognize that she could and would benefit by trying to resolve her dilemma in therapy without having to sacrifice one for the other. She was frightened by the thought of her mother dying and could not, in that context, bear her newfound and valued experience of separation from her mother. Ms. A could not keep her conflict on a symbolic level, and she felt she must choose literally. In fact, we worried that we may have erred by attempting too vehemently to keep Ms. A in treatment. We hoped Ms. A could tolerate her struggles around her fear of loss (to accept her ambivalence about mother), but she could not comfortably do so within the transference. To be able to do this without acting out requires that a borderline patient have improved much more than Ms. A had. With respect to the "danger," we felt confident that Ms. A would return to therapy if she became self-destructive again.

Often errors are made, we believe, in overestimating the ability of a borderline patient to successfully navigate his or her psychopathology in the realm of the symbolic. We think that behavioral and psychoeducational techniques are successful because concrete interventions may facilitate less regressive treatments as well as develop skills that permit later structural change.

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Multiples: No Amnesia for Child Abuse

TO THE EDITOR: In a landmark study notable for its objective documentation, Dorothy Otnow Lewis, M.D., and colleagues (1) confirmed the noniatrogenic occurrence of dissociative identity disorder (formerly called multiple personality disorder) (2) and the nonimaginary nature of the history of child abuse.

The study is brilliant, but the authors misspoke in their Discussion section when they said that their subjects "had partial or total amnesia for the abuse they had experienced as children." In fact, as the authors stated in their Results section, it was only "in their usual personality states" that their subjects had such amnesia, implying that their subjects' other personality states did remember the abuse. Thus, although it might not be evident if you spoke only to the initially presenting personality state, these individuals did remember their traumatic experiences.

The reason I make an issue of the incorrectness of saying that these individuals had amnesia for their child abuse is that this erroneous idea is the basis of much of the skepticism about the disorder. It leads skeptics to erroneously conclude that the disorder involves "repressed memory," which later becomes "recovered memory." And they find it entirely implausible that anyone could forget such major experiences and then have the memories pop out decades later. So it is important to make it clear to skeptics that these individuals' alternate personality states have never forgotten the child abuse, even if their presenting personality states have. With this disorder, memories are not repressed into a Freudian unconscious but are dissociated into alternate states of consciousness (the alternate personality states). The memories are not miraculously recovered decades later but are belatedly shared by the personality states that came into existence when the abuse began and had always had these memories.

Obviously, I am not telling the authors anything they did not know. I just wanted to add a few words of clarification for skeptics.

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KENNETH A. NAKDIMEN, M.D.
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TO THE EDITOR: The intriguing article by Dorothy Otnow Lewis, M.D., et al. purports to demonstrate that there is objective evidence about childhood maltreatment and dissociative states in 12 murderers well antedating the onset of their legal problems, thus mitigating the potential for malingering.

A problem is that from this presentation it cannot be determined what data actually come from records preceding legal difficulties and clearly pertain to the issues of abuse and dissociative identity disorder and what do not.

Dr. Lewis and colleagues report that there are childhood medical, psychiatric, and foster care records that document abuse. It would serve the cause of clinical science best if there were publicly accessible records to document this report. Fortunately, the development of electronic record transfer and the Internet make this possible. Properly documented

records that protect the proband's privacy are entirely possible and can be made available by Internet access.

We urge Dr. Lewis and colleagues to consider making the extensive archival dossiers available for secondary analysis. This does not imply any doubt regarding Dr. Lewis and colleagues' honesty or professional abilities. However, the fact remains that different assessments of data are possible, and in a controversial area, fostering such assessments rather than simply reporting conclusory statements clearly advance the field. The expense and trouble may be daunting. However, once such a goal is subscribed to, funding mechanisms may come into being.

Recent technological advances would make this possible for all scientific journals. Data-dependent articles could and should make such data available for what amounts to an extended postpublication peer review. The failure to do so in the past has led to problematic reports. The suggestion that journals be held responsible for the detailed review of primary data would probably paralyze journal production. However, the public availability of such data allows for continued informed discussion. Lack of public availability engenders continued doubt about the substantive basis of the conclusions.

Also, widespread secondary analyses of these data, which agree with the authors, can be of tremendous value in overcoming a substantial level of a priori doubt. These authors should be interested in pursuing this goal. It would also help amplify the understanding of these complex issues if data were provided concerning possible neurological insult.

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Dr. Lewis and Colleagues Respond

TO THE EDITOR: The point of Kenneth A. Nakdimen, M.D., is well taken. Patients with dissociative identity disorder do have a storehouse of memories that are available to them only under certain circumstances and conditions. The patients' usual lack of conscious access to these materials, however, presents clinically as amnesia.

We agree with Donald F. Klein, M.D. In this study, as in most clinical studies, the public availability of the full archival dossiers on each subject might make a useful scientific contribution. However, the task of presenting the thousands of pages of sensitive data for open publication would be exorbitantly costly, time consuming, and hence, unrealistic. Suffice it to say that in at least nine of the 12 cases presented, hospital records, neglect petitions, police records of parental brutality, or all three stood as objective evidence of serious maltreatment antedating the crimes committed.

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Selective Serotonin Reuptake Inhibitors and Delusional Depression

TO THE EDITOR: We are writing to express our concern regarding two articles from the same center by Flavia Gatti, M.D., and colleagues (1) and Raffaella Zanardi, M.D., and colleagues (2) that concluded that selective serotonin reuptake inhibitors (SSRIs) alone are effective in the treatment of delusional depression and that "a new window has opened in the pharmacotherapy of this disorder." Although serotonin has been implicated in the pathophysiology of delusional depression (3), we do not believe that the evidence in the literature supports the use of SSRIs alone for the treatment of delusional depression at this time. Yet some authors (4) are citing these two articles as evidence to argue that SSRIs may be neuroleptics.

The double-blind comparison of sertraline and paroxetine (2) found response rates to sertraline alone higher (75%) than those observed in studies with a tricyclic antidepressant alone (40%) (5) and comparable to the rates observed with ECT (6), a triclyclic antidepressant plus an antipsychotic (5), and an SSRI plus an antipsychotic (7, 8). Is this possible? Had a control group been included in the study, the question of whether SSRIs alone are effective in delusional depression could have been answered. Without a control, it is impossible to draw conclusions.

We wonder if the patients were misdiagnosed. Did they have strictly defined major depression with psychotic features, or did some of them have body dysmorphic disorder, obsessive-compulsive disorder, or borderline personality disorder—disorders that may be characterized by depression plus delusional or near-delusional beliefs or other psychotic or psychotic-like symptoms that preliminary evidence suggests may respond to SSRIs alone (9–11)? It does not appear that a standard diagnostic instrument, such as the Structured Clinical Interview for DSM-III-R—Patient Version, was used to diagnose subjects' disorders. Finally, while the Dimensions of Delusional Experience Rating Scale has been demonstrated as reliable, to our knowledge, validity data are lacking.

The findings of Dr. Gatti and colleagues (1) and Dr. Zanardi and colleagues (2) are interesting and provocative, but given these apparent methodologic limitations and until further confirmatory data are available, we think that their results should be regarded with caution.

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Dr. Zanardi and Colleagues Reply

TO THE EDITOR: Any discussion about the use of selective serotonin reuptake inhibitors (SSRIs) in the treatment of delusional depression is welcome.

We still think that a new window has been opened in the pharmacotherapy of this disorder for the following reasons: 1) the efficacy of SSRIs in the treatment of delusional depression was recently confirmed by Sacchetti and colleagues (1), with response rates comparable to those obtained in our studies; 2) we recently found that in delusional depression, the addition of the 5-HT_{1A} blocker pindolol can accelerate the response to fluvoxamine, thus supporting the involvement of the serotonergic system in this disorder (2); and 3) there is no evidence of negative findings.

Despite the fact that some authors cite our articles as evidence to argue that SSRIs may be neuroleptics, what we can say with confidence is that SSRIs abate both mood and psychotic symptoms in delusional depression.

The lack of a placebo response in delusional depression is well documented, and it has been proposed that it might be an intrinsic characteristic of such patients (3). In our studies, the absence of a placebo group was a necessity in accordance with the guidelines of our hospital ethics committee because of the severity of illness and the risk of suicide. In all of the cited studies, the response rates to SSRIs were higher than the placebo response expected, even in subjects with nondelusional depression. Also the efficacy of SSRIs combined with antipsychotics in delusional depression has been only tested in open studies (4, 5).

The Structural Clinical Interview for DSM-III-R—Patient Version was used, but not with all patients, because of the peculiar and severe psychopathological condition of some. Anyway, diagnoses strictly followed DSM-III-R criteria and codiagnoses were excluded. The fact that preliminary evidence (as cited by the authors) suggests that patients with other disorders may respond to SSRIs alone does not mean that those with delusional depression should not be expected to respond.

We realize that the Dimensions of Delusional Experience Rating Scale may have some limitations, but a more specific and reliable scale is lacking. Notably, we use this scale in a qualitative manner (presence/absence of delusions), not quantitatively.

Even though we agree that further confirming data are needed, the high disability associated with this disorder and the heavy side effects of traditional treatments make any potentially useful innovation worthy of consideration.

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Freud's Practice of Psychoanalysis

TO THE EDITOR: I was most interested in the article on Freud's practice of analysis by David J. Lynn, M.D., and George E. Vaillant, M.D. (1). The authors convincingly argue that Freud mostly did not follow his own recommendations about the conduct of psychoanalysis. They suggest that Freud's actual behavior (at least regarding his relaxed approach toward anonymity and neutrality) was more in tune with the current approaches to self-revelation and therapy. Clearly, Freud's frequent and overt breeches of confidentiality rightly trouble them.

I would agree with Drs. Lynn and Vaillant that while Freud's openness and obvious humanity in the treatment of his patients is refreshing and may have been a major factor in the therapeutic successes he achieved (although his results seemed often quite equivocal), there are other messages we might take from these observations. First, I believe Freud's behavior highlights the danger of VIP treatment. Freud, as the developer of psychoanalysis, seems to have felt himself above the rules that he set up. When a clinician sees himself or herself as important or skilled, there is a strong inclination to take liberties with treatment. Self-assurance can produce the willingness to take helpful risks but can also evoke the fantasy that "I can do no wrong" and result in dangerous therapeutic bravado. Also, treating a VIP patient can lead a therapist to bend the rules in ways that would otherwise be uncharacteristic, often to the ultimate detriment of the patient.

Furthermore, I believe that Freud's behavior points to the dangers of practicing therapy in a setting in which there are goals or considerations extraneous to the treatment. Freud was constantly concerned with the health and vitality of his "movement." He seems to have often treated patients with some of his attention on their potential as benefactors. A good example is the discussion of Freud's treatment of Edith Jackson (1). Also since many of Freud's patients were in or closely connected to his circle, his attention seemed to also cover their personal behavior and relations. His brief treatment of Otto Rank, for example, was an attempt by Freud to

smooth out their personal and professional relations after Rank published his controversial (and ultimately prescient) work on the "birth trauma" (2) (wherein he developed the concept of separation anxiety).

I believe that these considerations continue to be quite relevant. What we might take from Freud's treatment recommendations is not a series of static, legalistic suggestions but the notion that always when treating patients our primary concern should be to keep our eyes on the patient and the treatment and not on the results of the study, the bottom line, or whatever else may distract us.

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VICTOR SCHWARTZ, M.D.
New York, N.Y.

TO THE EDITOR: There are four valuable aspects to the recent documentation by David J. Lynn, M.D., and George E. Vaillant, M.D., of Freud's frequent departures from anonymity, neutrality, and confidentiality in his clinical practice. First, it sheds an informed light on a less recognized facet of our profession's history. Second, the authors' demonstration that Freud worked in an emotionally expressive and behaviorally resilient manner is a useful corrective to the caricature of psychoanalytic technique made by the lay public and, unfortunately, even by some psychiatrists and psychoanalysts. Third, the article by Drs. Lynn and Vaillant is useful in reminding us that noninterpretive elements (e.g., warmth, support, acceptance) contribute heavily to the beneficial results of even those psychotherapies that rely on interpretive techniques. Finally, the authors' contribution is respectable because they avoid the temptation to speculate regarding Freud's reasons or motives (which could have included his pioneering and triumphant status in the field, his character, the particular era in the history of psychotherapy, etc.) regarding his departures from the techniques he officially deemed desirable.

While I regard the authors' contribution as valuable, I also discern two risks inherent in its publication. First, the material in this article can be used for Freud bashing. Finding that Freud said one thing and did another, the ever-eager critics of Freud might seek to debunk other profoundly important and valid aspects of his contributions. Second, some less responsible members of our profession might exploit Freud's licenses with technique in order to justify their own propensities toward boundary violations. This well-intentioned article might thus unwittingly contribute to professional "superego lacunae" (1) in vulnerable individuals.

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SALMAN AKHTAR, M.D.
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TO THE EDITOR: I wish to comment on the article by David J. Lynn, M.D., and George E. Vaillant, M.D. Drs. Lynn and Vaillant use historical sources to illustrate that Freud promulgated techniques of psychoanalysis that diverged from those he used with his analysands. Why do Drs. Lynn and Vaillant make this foray into the past? Since "Sigmund Freud's technical recommendations and theoretical contributions have retained an important influence in American psychiatry," it appears self-evident to the authors that psychiatrists "will benefit from an understanding of the relationship between these contributions and Freud's actual clinical experiences." Yet the contemporary reader would remain confused about the precise nature of this relevance. The study falls short where it could contribute to current psychiatric knowledge, and it settles instead for an ideological indictment of Freud's character and work.

Why does Freud's "sovereign readiness to disregard his own rules" matter to the readers of the *Journal* in 1998? Hypothetically, exposing that Freud never tested the ideas he promulgated could alert readers to gaps in our knowledge about psychotherapy. This investigation could encourage psychoanalytic researchers to examine more closely those elements of Freud's theories that have not been adequately studied in the clinic. Freud's experience may even give insight into how such studies could be conducted. A study like that of Drs. Lynn and Vaillant could, in fact, encourage research into psychoanalysis and elucidate where that research ought to center today. Drs. Lynn and Vaillant, though, choose not to contribute to such debates, and their historical study dressed as contemporary science fails on both counts.

In the first place, their historical reconstruction serves as an opportunity for attacks on Freud's character. Exposing Freud as, somehow, a bad researcher is problematical history. It is not clear that Freud intended his analyses to serve as trials of his recommendations, and contemporary researchers cannot hold him responsible for deviating from a protocol that he never intended to follow. Furthermore, the criteria that constitute "adequate proof" are historically based, and the standards of scientific psychiatry are not fixed but evolve. The authors would have to examine the standards of proof contemporaneous with Freud to investigate his efficacy as a researcher. He could not be expected to adhere to research habits that were codified after his time, and any indictment of his "test" on these grounds would be ahistorical. To the extent that they obscure the historical context of scientific investigations, misinterpretations of the past give a false impression of what guides psychiatric research today.

Similar anachronisms are employed when Drs. Lynn and Vaillant imply that Freud acted unethically because he was indiscreet with information from his patients' analyses on occasion without their consent. One must admit that current standards of confidentiality are not timeless, and Drs. Lynn and Vaillant cannot legitimately paint Freud as unethical because he did not adhere to our own contemporary notions of an ethical practice. Such an indictment is anachronistic and unhelpful to clinicians attempting to practice ethically in a different historical moment.

However, even granting the (ahistorical) argument that Freud was an inadequate researcher, Drs. Lynn and Vaillant could, from this vantage point, evaluate the status of current research into the utility of psychoanalytic techniques. However, to do so, they would have to mention the studies of Freud's recommendations conducted since Freud's time, for if his recommendations have been adequately tested since he outlined them, the fact that Freud himself did not test them seems hardly relevant. Instead, they hint, inappropriately, that the techniques he recommended never have been substantiated by concluding that they "deserve to be scientifically tested." Or they imply that Freud's theories have been disproven, noting that "Freud's recommendations to maintain an uncontaminated transference through anonymity

have by no means been unanimously endorsed by subsequent contributors." They do not cite a single study or current theorization of Freud's psychoanalytic techniques—in spite of the fact that an extremely cursory review of the literature from 1997 alone locates three articles on anonymity in analysis. In short, they do not allow their study of Freud to contribute to or improve our understanding of psychoanalytic technique or psychotherapy research.

This lapse, though, would not be inconsistent with the orientation of the *Journal*. The research published in the *Journal* addresses questions some distance removed from psychotherapy research or psychoanalytic theory. The 1998 and 1997 issues of the *Journal* contain no articles on psychoanalysis, no references to Freud, and only one article describing research into supportive psychotherapy for schizophrenia. The *Journal* publishes exceedingly few articles intended to further the evidentiary basis of the psychotherapies in psychiatry. Drs. Lynn and Vaillant's article is no exception, and its polemics serve to indicate that such preferences are justified when the quality of Freud's contributions is reexamined.

Therefore, it is curious but not surprising that Drs. Lynn and Vaillant find substantiation for contemporary ideas in Freud's practice. Since Freud's actual techniques "may more closely resemble the techniques that current psychotherapy research has demonstrated to be most effective," they conclude that "perhaps each outcome should be attributed more to these interactions and their qualities—warmth, support, acceptance, trust…—than to insights achieved through an interpretive exploration of the transference," which Freud himself advocated. When researchers find proof in the past for their own ideology, one can be sure that they have not removed their blinders.

Drs. Lynn and Vaillant's most consistent arguments are that Freud was unscientific and ethically dubious and that his entire corpus has been replaced by something better. The relevance of the article is all too clear: to paint psychoanalysis as a pseudoscientific fad now replaced with something more scientific. Their article constitutes a poor addition to the current debate about the place of psychoanalysis in psychiatry, and it presents little knowledge that could be helpful to contemporary practitioners. The study does not encourage relevant research into psychoanalysis; it does use ahistorical interpretations to reassure us that current research interests are justifiable in light of the past. Unfortunately, Drs. Lynn and Vaillant's past is a false construct designed to justify the preferences of the present.

ELIZABETH BROMLEY, M.D.
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Drs. Lynn and Vaillant Reply

TO THE EDITOR: We greatly appreciate the comments from Victor Schwartz, M.D. In particular, his points about pitfalls in therapy involving VIPs as clinicians or patients or involving "a setting in which there are goals or considerations extraneous to the treatment" are well taken.

We are also grateful for the kind words from Salman Akhtar, M.D., and it seems clear to us that he understood what we were trying to do. However, we take issue with the fears he expressed that people may use our article either to bash Freud or to rationalize violations of boundaries with their patients. Like Jefferson, we have faith that an educated populace will use information to act more responsibly and that people can be trusted with facts.

The letter from Elizabeth Bromley, M.D., distresses us. Either we failed badly to communicate our points, or she failed to grasp them. To begin, our article is not about Freud's character; it is about his actual methods and their relationship to the scientific status of his recommendations. Concerning confidentiality, although this feature of medical treatment is obviously not "timeless," it was a component of the Hippocratic oath, and it was also known to, and repeatedly advocated by, Freud.

Concerning the issues of anachronisms, we can see nothing ahistorical in a comparison of Freud's recommendations with his concurrent practices. It is true that we did not undertake a review of the testing of Freud's recommendations by other workers; we would welcome such a review. Our statement concerning the absence of unanimous endorsement of the necessity of anonymity cannot be refuted by individual citations from the literature, nor is it in any way equivalent to an implication that Freud's theories have been "disproven." Further, our article does not advocate any particular theory or methods of psychotherapy. It suggests one possible view of Freud's actual method. It does not thereby "find proof in the past" for any particular ideology.

Finally, Dr. Bromley seems to be raising issues beyond the content of our article by objecting to choices made by the editors of the *Journal*. Although we would not presume to take on the task of defending the *Journal*, we report that we have found it to be the most consistently relevant, informative, and reliable of the psychiatric journals.

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GEORGE E. VAILLANT, M.D.
Boston, Mass.

Mood Stabilizer Combinations for Bipolar Disorder

TO THE EDITOR: The article by Marlene P. Freeman, M.D., and Andrew L. Stoll, M.D., on combinations of mood stabilizers for treatment of bipolar disorder (1) noted the potentially dangerous interaction of lamotrigine with valproate. Unfortunately, the authors failed to mention that the risk of severe and at times fatal rashes associated with lamotrigine is much higher in the pediatric population. Readers should have been reminded of the one in 50 to one in 100 chance of life-threatening rashes associated with the use of lamotrigine in children and adolescents under 16 years. The product information monograph bears a boxed warning emphasizing that lamotrigine is not approved for use in patients below the age of 16 years.

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R. WALTER LOVELL, M.D.
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Drs. Freeman and Stoll Reply

TO THE EDITOR: We would like to thank R. Walter Lovell, M.D., for his important comments. As he indicated, the risk of serious rashes is much higher in the pediatric population than in adults. The topic of bipolar disorder in children and adolescents deserves substantial consideration, and we feel that we could not have adequately covered this information

in our article. But because Dr. Lovell drew our attention to it, we would like to discuss a few other relevant matters regarding bipolar disorder in children and adolescents.

First, diagnosis itself is generally quite challenging in this population. Presentations may be atypical, are commonly confused with other disorders, and are often seen in the context of significant comorbidity (1–3). As a result, bipolar disorder in children and adolescents is most likely underdiagnosed or inappropriately treated or both.

Mood stabilizers have not been well studied in the treatment of children and adolescents. Moreover, adequate research has not been conducted regarding combinations of mood stabilizers in children with bipolar disorder. Much of what we know about anticonvulsants in this population is based on studies of epilepsy. In addition to the increased risk of rashes with lamotrigine, other mood stabilizers may pose distinct risks in the pediatric population. For instance, valproic acid may cause a higher risk of liver failure (4) and thrombocytopenia (5) in children. Also, gabapentin has been reported to cause behavioral side effects (6, 7). Carbamazepine has been reported to be well tolerated in children (8), but cases have been reported that suggest that it may unmask a Tourette's-like syndrome (9). Lithium has been reported to be effective in the acute treatment of bipolar disorder in children (10) but has also been shown to cause frequent side effects, especially neurologic, including tremor, drowsiness, ataxia, and confusion (11).

We hope that more information becomes available regarding the safety and efficacy of mood stabilizers in children and adolescents. Many aspects of bipolar disorder in the pediatric population, including diagnosis and treatment, deserve our attention.

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MARLENE P. FREEMAN, M.D.
ANDREW L. STOLL, M.D.
Boston, Mass.

Eating Attitudes Among Black South Africans

TO THE EDITOR: Regarding the study by Daniel le Grange, Ph.D., and colleagues (1), it is pertinent to share my experience of the emerging phenomenon of eating disorders in black South Africans. While the existence of eating disorders in white South Africans is well established (2, 3), as recently as 1994 published literature on eating disorders in South Africa (4) commented on the absence of black sufferers. In 1995, the first published cases of eating disorders in black female South Africans appeared (5). I was involved in the assessment and treatment of two of the three described patient cases. To date, the number of cases I have been involved with has increased to nine. Of specific interest has been the absence of any unique features designating the sufferer as black. This suggests that within the urban setting, there is a homogenization of eating-related psychopathology across racial groups. Considering this observation within the context of cultural issues, it appears that the culture of milieu is of more relevance than that of race. Such an understanding is inferred in a recent North American study (6). Of note, however, has been the tendency of black South African sufferers to present with bulimic symptoms as part of their illnesses. These observations are similar to those of Dolan (7) in a review of cross-cultural aspects of eating disorders. A number of case reports of eating disorders in black Africans appeared in the literature in the 1980s (8–10), and it is not clear to what extent the occurrence of such conditions has changed in African countries outside South Africa. Our own preliminary research into abnormal eating attitudes among adolescent female South Africans within a private school setting (N=213) revealed that 20.7% of white respondents and 37.5% of black respondents scored above the cutoff score, denoting eating attitudes as abnormal, on the 26-item version of the Eating Attitudes Test (11). Preliminary analysis of more recent research into abnormal eating attitudes in government schools (N=1,353) revealed that 18.6% of black and white adolescents scored above the cutoff score (12). Together with the findings of le Grange et al., it is clear that within the broader South African community, eating attitudes exist that place a significant proportion of adolescents and young adults of all race groups at risk for the development of eating disorders. The conceptualization of eating disorders as racially bound within an urban setting in South Africa needs to be dispelled given that these conditions pose a potential public health risk for black South Africans.

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CHRISTOPHER P. SZABO, M.B.B.C.H., F.F.PSYCH.
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Obsessive-Compulsive Disorder With Eating Disorders

TO THE EDITOR: The effect of concomitant obsessive-compulsive disorder (OCD) on treatment success for patients with eating disorders is a significant clinical issue. Reliable data on the relationship of OCD to eating disorder treatment have been lacking until the publication of the article by Andreas Thiel, M.D., and colleagues (1). They conclude "that concomitant OCD does not indicate a significantly poorer prognosis for patients with anorexia or bulimia nervosa."

While Dr. Thiel and colleagues have made an important contribution in providing preliminary data, their conclusion may be premature. A power analysis based on Cohen (2) suggests that given Dr. Thiel and colleagues' N value of 75, their analyses all have less than a 50% chance of detecting a statistically significant—and clinically meaningful—difference of medium effect size between OCD and non-OCD patients with eating disorders and only a 10% or lower chance of detecting a difference of small effect size. Their analyses of differences in Eating Disorder Inventory scores between OCD and non-OCD groups all have less than a 1 out of 3 chance of detecting differences of medium effect size. Therefore, the N value for this study is simply too small for the results to be meaningfully analyzed by using the statistical procedures chosen by the authors.

Given the low power of Dr. Thiel and colleagues' chosen statistical procedures to find meaningful differences between the OCD and non-OCD eating disorder patients in their group, we have looked instead at the trends in their data. The trends suggest an opposite conclusion to that offered by Dr. Thiel and colleagues. For instance, 54% of the patients without OCD had recovered from their eating disorder at 30 months, but only 45% of the patients with OCD were free of symptoms. Likewise, 37% of non-OCD patients were bingeing at 30 months, compared with 52% of OCD patients. A total of 48% of non-OCD patients were vomiting, compared with 66% of OCD patients. A total of 65% of non-OCD patients were married or living with a partner, compared with only 48% of OCD patients.

Clearly, then, the trends suggest that OCD patients may indeed have a poorer treatment outcome for their eating disorder. A study with a larger N value is needed to demonstrate this possibility statistically.

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EDWARD J. CUMELLA, PH.D.
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Dr. Thiel Replies

TO THE EDITOR: My colleagues and I thank Edward J. Cumella, Ph.D., for commenting on our study, and we agree with him when he says that the statistical power is too low for detecting a difference of small effect size. However, we cannot agree with his statement that the trends in our data suggest an opposite conclusion to that offered in our discussion.

The initial results of our study regarding the prevalence of concomitant obsessive-compulsive disorder (OCD) in anorexia and bulimia nervosa, which were published 4 years ago (1), showed that the patients with an eating disorder and concomitant OCD scored significantly higher than patients with no OCD on several subscales of the Eating Disorder Inventory, indicating a higher degree of pathological attitudes about eating. These data suggest that this comorbidity was correlated with the severity of the eating disorder before treatment.

In the more recent article, we present the follow-up results of the second assessment 30 months later. Again, the patients with concomitant OCD showed a higher degree of pathology. However, analysis of variance for repeated measures revealed significant improvement over time in both groups, with and without concomitant OCD, and there were no significant group-by-time interactions. In our opinion, the results suggest a certain degree of independence between the improvement over time and the comorbidity of the eating disorder and OCD. Concomitant OCD does not indicate a significantly poorer prognosis for patients with eating disorders. Nevertheless, we share the opinion of Dr. Cumella that a study with a larger N value would be desirable.

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ANDREAS THIEL, M.D.
Innsbruck, Austria

Integration, Not Discrimination

TO THE EDITOR: Richard Balon, M.D., and colleagues (1) recently pointed out the existence of obstacles in enrolling foreign medical school graduates into residency training positions in psychiatry, probably because of discrimination on the basis of an applicant's name and medical school of grad-

uation. Was the citizenship or immigration status of the foreign applicant indicated in the letter he received, in order to make a valid comparison?

Israeli citizenship is guaranteed automatically to every Jew and his or her family, no matter the country of birth or residence, according to the Law of Return. The current wave of mass immigration from the former Soviet Union, which started in 1989, includes a disproportionately high number of physicians—280 per 1,000 immigrants—a figure that is 10 times higher than the existing proportion of physicians in Israel. The cultural, socioeconomic, and professional problems faced by immigrants become more pronounced among physicians because of the inevitable loss of status, the long requalification and licensing process, and high distress and demoralization (2).

In the field of mental health, a parallel process is taking place: an interaction between the internal vulnerability of recent immigrants and acculturation trouble has increased the number of people asking for help (3) and demanding better-trained mental health professionals speaking their languages and acquainted with their culture. Recruiting, training, and employment of immigrant doctors in order to ensure adequate diagnosis and treatment has become a serious challenge to medical services. In our state mental hospital, which is the largest in Israel and has university affiliation, foreign medical graduates presently comprise 75% of its residents, due not only to a certain shortage in the influx of local graduates into psychiatry as a postgraduate choice but to the necessity of absorbing foreign medical graduates.

As a partial solution to current problems, the Israeli Ministries of Health and Absorption, as well as nongovernmental organizations (Joint Distribution Committee, Jewish Agency), provide initial financial support and educational programs, like Balint groups and retraining courses, to improve the psychosocial skills and self-efficacy of immigrant physicians (4).

Because of this experience, we think that ensuring equal opportunities for residency training and subsequent employment of foreign medical graduates enables coping with probable discrimination between foreign and local psychiatrists, permits an adequate professional adaptation, and provides a better way to care for native and immigrant populations.

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ILYA REZNIK, M.D
DANIEL MOLDAVSKY, M.D.
Bat-Yam, Israel

"Monk" Requesting Castration

TO THE EDITOR: The Clinical Case Conference by Laura Weiss Roberts, M.D., and colleagues (1) demonstrates much of what is wrong with American psychiatry today. One of the authors, Michael Hollifield, M.D., had the great luxury of *five* sessions to evaluate the mental status of "Brother David." He apparently went about it in a cookbook fashion, checking off mental status characteristics and matching them with axis I diagnoses from DSM-IV. He ignored Brother David's lifelong pattern of anhedonia—years of agony and an array of unstable symptoms—his inability to form interpersonal relationships, and the intense loathing and fear that sexual impulses stirred up in him. His 10-year rumination about castration certainly seems to indicate pathological thought processes. During these interviews, there seemed to be a restricted affect, a peculiar concreteness of thought ("if your right hand offend thee…"), and tantalizing hints of delusional thinking ("lower existence," "rising to a higher level"). Either Brother David was clearly evasive when describing his religious group or Dr. Hollifield was reluctant to press for details. All of this made the two urologists rightly suspicious of repressed unconscious or suppressed conscious thoughts. It is astonishing that the psychiatrist decided that since Brother David was not floridly psychotic or complaining of any ego-dystonic symptoms, he was therefore making an "authentic" conscious decision. One of my colleagues wondered what Dr. Hollifield would have said had Brother David requested amputation of his right arm because he suffered from repeated impulses to punch people.

Clearly, Brother David was struggling with conflicts about gender identity, sexual drive, and overly strict primitive superego introjects. He did have a host of glaring and disruptive symptoms for many years and in fact was clinically depressed most recently. Psychodynamic concepts of drive and defense, compromise formation, shifting of defenses, externalization, and submission of one's decisions and actions to an external superego figure are all demonstrated. The nature of symptom as the resultant of drive and regressive defenses is demonstrated. The psychiatric recommendation was to allow the orchiectomy but to urge a less dramatic treatment first—i.e., pharmacotherapy. The reluctance about allowing the orchiectomy was only that it might result in unknown long-term medical and psychological "implications"—not that it was prima facie insane!

American psychiatry has lost its mind! It no longer considers the function of the mind, only of the brain, as detected by positron emission tomography scans and Hamilton Rating Scale for Depression scores. We no longer listen to the patient with analytic understanding, seeking symbolic meaning, feeling the transference and the countertransference, and using those data to aid our understanding. Where was the recommendation for psychodynamic psychotherapy? Where was the recommendation for dynamic group therapy, in view of the need for an external controlling group identity? Brother David was probably too enmeshed in his pathological "folie à 39"—please do not call it a religion—to embrace a treatment program. But we do not have to enter his psychosis with him! Someone has to remain sane.

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HENRY KAMINER, M.D.
Tenafly, N.J.

TO THE EDITOR: While the discussion of the man involved in a cult was extremely informative and well organized, I was surprised by the authors' comment that "careful observation of cult activities and extensive clinical work with cult survivors have dispelled the early belief that cults exclusively attract only psychologically damaged or psychiatrically disordered individuals." I am not taking issue with the authors' well-researched references or personal beliefs, but I do think that this statement demonstrates a widespread phenomenon in clinical psychiatry currently: the reluctance to consider character or axis II pathology as having explanatory or etiological significance in the behaviors and symptoms of our patients. I assume that "psychologically damaged or psychiatrically disordered" refers only to axis I disorders such as psychosis, mania, or severe depression that interferes with normal functioning.

Brother David's childhood history was elicited ("'laid back' but puncutated by occasional chaotic emotional responses from his homemaker mother") but was assumed to have no significance, since he denied that there was any problem then. We who do psychotherapy and analysis know that it is an unusual patient who comes in complaining that his or her childhood experiences have caused all sorts of difficulties in his or her life. I would guess that a closer look at Brother David's enduring coping/defense mechanisms and behavior would make clear major limitations in dealing with life's vicissitudes on the basis of ego deficits, childhood trauma, neurotic conflicts, or whatever theoretical mechanism one finds most acceptable. In any event, it need not be that he is overtly psychotic, manic, or such to request castration. All he need do is use his characteristic defense mechanisms (e.g., denial, reaction formation, and intellectualization) to determine that the cult offers him stability and structure that he can get in no other way obvious to him.

Psychopharmacologists and neuroscientists may have little need for depth psychology, but general psychiatrists and those seeing patients as consultants for other medical specialties should be able to identify the defensive styles and mechanisms of the patients they evaluate. Even more important, clinical psychiatrists should be aware of the enormous difficulties in functioning that can result from neurotic psychopathology in the absence of axis I diagnoses. I include references for further reading (1–4).

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MARCIA KAPLAN, M.D.
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Dr. Roberts Replies

TO THE EDITOR: We thank Henry Kaminer, M.D., and Marcia Kaplan, M.D., for their thoughtful responses to our Clinical Case Conference. This case was meant to be evocative. This was our aim because Brother David, his remarkable request, and his "outcome" were so compelling and distressing and he evoked so much in us. Indeed, his tale is rich with lessons about psychiatric practice, its ethics, and our culture.

We thoroughly agree with Drs. Kaminer and Kaplan that Brother David was deeply troubled, that his history was fully manifest in his everyday suffering, that his character was problematic and vulnerable, and that his defenses were maladaptive. This is especially obvious in hindsight. We agree that Brother David was guarded and evasive about his "spiritual" life, even when pressed for details. We agree that cults are not "religions." We agree that cult participation may be an indication of serious psychopathology, either axis I or II, although we are also persuaded by empirical work suggesting that the profoundly coercive techniques of cultism make every individual potentially vulnerable to their effects, particularly when undergoing significant and disruptive life changes (1). We further agree that general psychiatrists and psychiatric consultants should be highly attuned to the themes and defensive styles and mechanisms of their patients in order to understand and help them. Finally, we agree that Brother David was "probably too enmeshed" in his cult experience to participate in treatment. In fact, Dr. Hollifield sought guidance on the case from two other psychiatrists, both of whom recommended therapy for Brother David and one of whom doubted that treatment would be accepted or helpful. Brother David rejected psychotherapy.

We disagree, however, with some of the comments offered in the two letters largely because of the assumptions made by their authors. For instance, the assumption that the consultant did not appreciate or interpret the meaning of Brother David's experiences is incorrect. In fact, Drs. Kaplan and Kaminer's comments about Brother David's psychological issues derive from the story we provided. The consultant gathered details about Brother David's upbringing and psychosexual issues and, although we did not speculate beyond our understanding, included them purposefully for readers. Second, we disagree with Dr. Kaminer, who suggests that the consultant performed only a mental status examination in five sessions and asserts that he "entered" Brother David's "psychosis" by seeking to clarify his concerns and exploring alternative approaches to treating his ego-dystonic symptoms. Creating the alliance necessary to evaluate Brother David was delicate and difficult. To whatever extent it existed to allow for five full sessions with this elusive man, it was not attained through "cookbook" methods.

The point of our Clinical Case Conference really was not so much about cults, as worrisome as they are. Nor was it about one man's tragic story, as important as this was. Rather, it was about our need, as psychiatric clinicians, to remain humble and diligent in our efforts to understand, evaluate, and care for highly complex and seriously disturbed pa-

tients who may at times deceive, surprise, and befuddle us. This is at least one of the morals of the story.

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Alteration of Personality by Serotonergic Intervention

TO THE EDITOR: Since the original observation of Peter Kramer (1) that fluoxetine may change personality, various observations and statements about the influence of serotonergic antidepressants on personality have been made. Two interesting reports recently appeared in the *Journal*. First, Yevgenia Gelfin, M.D., and colleagues (2) reported that they did not observe significant effects attributable to fluoxetine on any psychological variables in 15 healthy volunteers. Then, in a double-blind study of 46 healthy volunteers, Brian Knutson, Ph.D., and colleagues (3) found that the administration of paroxetine may modulate a dimension of normal personality characterized by lower negative affect experience and higher affiliative behavior in the absence of baseline clinical depression or other psychopathology.

Any effort to explain these seemingly discrepant findings only raises more questions. First, how is a "change of personality" measured? Could the discrepancy in findings between these two studies (2, 3) be explained just by the use of different measurement tools? Second, is everyone equally affected by antidepressant treatment? According to Dr. Knutson and colleagues (3), volunteers were not equally affected. Does this mean that some may be affected and some may not be affected at all? Could this help define the biological substrate of personality? Third, would a design with the use of an active placebo help resolve the discrepancy between the two studies? Fourth, could it be that serotonergic antidepressants just help "normal" and other people tolerate stress better, as suggested by Norden (4)? Fifth, are these personality changes permanent? Neither of the two studies addresses the last issue, even though it could be easily done by repeating personality measures 1, 3, and any number of months after discontinuing the antidepressant. Maybe the authors could provide us with these data.

The only definite conclusion we can make is that we are *very* far from elucidating the alteration of personality (if any) by serotonergic antidepressants.

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RICHARD BALON, M.D.
Detroit, Mich.

Dr. Knutson and Colleagues Reply

TO THE EDITOR: We thank Richard Balon, M.D., for reemphasizing some important questions that we touched on in our report (i.e., "Is everyone equally affected by antidepressant treatment?" "Are these changes permanent?"), but we would like to clarify some of the other issues he raises. An active placebo condition might have provided useful additional data, but we should note that neither our subjects nor those of Dr. Gelfin and colleagues could reliably determine whether they had received an active or placebo compound. While the study we reported cannot address all of these issues, future studies may.

A conceptual ambiguity underlying one of the questions concerns us (i.e., "Could it be that serotonergic antidepressants just help 'normal' and other people tolerate stress better?"). This question implies that sensitivity to stress is not relevant to personality. In fact, susceptibility to stress comprises a central facet of one of the most prominent trait dimensions commonly measured by psychologists (i.e., neuroticism or negative affect) (1). This trait has clinical relevance in that it can confer vulnerability to a host of affective disorders (2). Framing personality as a unitary entity rather than as a collection of traits obscures our finding that only one aspect of personality was altered by selective serotonin reuptake inhibitor (SSRI) administration. Indeed, this selective effect led us to conclude that agents such as SSRIs might help elucidate biological substrates for some personality variables.

As Dr. Balon implies, our procedures differed from those of Dr. Gelfin and colleagues in a number of ways. These differences may have contributed to an apparent inconsistency of findings. First, we administered SSRI and placebo concurrently to different groups (by means of a double-blind procedure), rather than sequentially to the same subjects. Second, we mainly used psychometric measures developed for normal rather than clinical samples, which may have reduced our susceptibility to floor effects. Third, we also observed changes in objectively coded interpersonal behavior. Fourth, we measured plasma SSRI levels, which afforded some control for compliance or idiosyncratic malabsorption of the drug. Fifth, we tested a larger number of subjects, which may have boosted our statistical power to detect an effect.

Kramer originally observed personality changes in the patients he saw in clinical practice but not in "normal" volunteers. Although behavioral scientists can rarely make definite conclusions, we believe that we have taken the first step toward a testable hypothesis and stand by our original statement: serotonergic mechanisms may selectively modulate an aspect of personality characterized by negative affective experience.

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Premorbid Social Functioning With Schizophrenia and Bipolar Disorder

TO THE EDITOR: Recently, Mary Cannon, M.Sc., and colleagues (1) reported significantly poorer premorbid adjustment in the childhood and adolescence of schizophrenic patients and, to a lesser degree, in patients with bipolar disorder compared with healthy subjects. However, the researchers did not discuss the possible impact of different levels of expressed emotion (2) that inevitably exist in at least some schizophrenic families on the mothers' recall of their children's behavior in childhood, especially when we consider schizophrenia and bipolar disorder as long-term and chronic illnesses.

Using the Five-Minute Speech Sample (3), a brief variant of the Camberwell Family Interview (4), together with the adapted Premorbid Social Adjustment Scale (5), instead of the simple telephone interviewing that was done in the study would probably complicate the overall study procedure and the analysis of collected data a little but could undoubtedly benefit the appropriate rating of affected families and the more precise estimation of received information.

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Reprints of letters to the Editor are not available.

Correction

The article "Serial CSF Corticotropin-Releasing Hormone Levels and Adrenocortical Activity in Combat Veterans With Posttraumatic Stress Disorder" by Dewleen G. Baker, M.D., et al. (April 1999, pp. 585–588) contains two errors on page 586. In the Results section, the sentence beginning on line 8 should read: "Mean CSF CRH concentrations were lower in smokers than in nonsmokers (43.7 pg/ml, SD=13.0, versus 52.1, SD=19.2), but the difference was not significant ($F=-1.12$, $df=1, 16$, $p<0.31$)"; and the sentence beginning on line 28 should read: "Although the mean 24-hour urinary free cortisol excretion was higher in the smokers (97.5 μg/24 hours, SD=57.3) than the nonsmokers (67.4 μg/24 hours, SD=19.7), the difference was not significant ($t=-1.56$, $df=17$)."