

Suicidality and Substance Abuse in Affective Disorders

Joseph F. Goldberg, M.D.; Tara M. Singer, M.A.;
and Jessica L. Garno, M.A.

The relationship between suicidality and substance abuse has long been recognized, although studies have only fairly recently begun to identify factors that may help clarify how alcohol or other drug abuse increases the susceptibility to suicidal behavior in vulnerable populations. In particular, alcohol and other psychoactive substance misuse has been linked with mood destabilization and the induction of manic or depressive episodes in affectively ill individuals, while also demarcating groups with heightened tendencies toward impulsivity, aggression, and sensitivity to interpersonal loss. Serotonergic mechanisms have been implicated in each of these clinical settings, along with possible dysregulation of other neurotransmitter systems. Psychosocial aspects of alcohol or drug abuse relevant to suicide may involve a heightened sensitivity to interpersonal loss, poor coping skills in response to adverse life events, and affective dysregulation induced by circadian and psychosocial stresses. Consequently, self-destructive behaviors with relatively little premeditation may arise during periods of increased stress, intoxication, depression, or other psychopathology. Early detection of substance abuse followed by appropriate pharmacologic and/or psychotherapeutic interventions may greatly help to minimize the formation of complex comorbid psychiatric conditions and reduce the potential for suicidal acts among high-risk populations.

(*J Clin Psychiatry* 2001;62[suppl 25]:35-43)

While numerous factors have historically been associated with suicidal behavior, alcohol abuse and drug abuse have repeatedly been identified as among the most robust predictors of both attempted and completed suicide. Alcohol and/or drug abuse is associated with more

than half of reported suicides in the United States and abroad.^{1,2} Current data suggest a 5- to 10-fold increase in risk for attempting suicide among alcohol abusers as compared to nonabusers, above and beyond the effects of psychiatric comorbidity.^{3,4} Research efforts have extensively sought to clarify links between alcohol/substance abuse and suicidality, leading to the recognition of factors such as depression, impulsivity, serotonergic dysfunction, and genetic components as potent contributors. Yet, despite such clinical profiling, the actual positive predictive value of any individual risk factor or even constellations of risk factors appears relatively low.⁵ Suicide prediction remains a tremendously elusive endeavor. Nevertheless, it is clear that a greater awareness and understanding about the role of alcohol and other drug abuse in suicidality may help clinicians to better recognize vulnerabilities and anticipate likely outcomes. It may also help clinicians to identify and directly treat those factors that pose the greatest risk for suicide.

This article will summarize and integrate current research findings regarding alcohol or other substance abuse and suicidality from several perspectives, including clinical phenomenology and comorbidity, hereditary diatheses, and neurotransmitter dysfunction. A distillation of these corollaries to suicidality and substance misuse is presented in Table 1. Finally, we will consider ways in which these findings may help to inform treatment decisions relative to suicide risk among affectively ill patients with comorbid substance use disorders.

From the Bipolar Disorders Research Clinic, Payne Whitney Clinic-New York Presbyterian Hospital, New York (all authors); the Department of Psychiatry, Weill Medical College of Cornell University, New York (Dr. Goldberg); Lenox Hill Hospital and the Department of Psychology, New York University, New York (Ms. Singer); and the Department of Psychology, Long Island University and Montefiore Medical Center, Bronx, N.Y. (Dr. Garno).

Presented at the symposium "Suicide Prevention Intervention," which was held October 24, 2000, in Boston, Mass., and supported through an unrestricted educational grant from Solvay Pharmaceuticals.

Supported, in part, by research grants from the American Foundation for Suicide Prevention, the Alcoholic Beverage Medical Research Foundation, a National Alliance for Research on Schizophrenia and Depression (NARSAD) Young Investigator Award, the Nancy Pritzker Foundation, and from a fund established in the New York Community Trust by DeWitt Wallace.

Financial disclosure: Dr. Goldberg has been a consultant for Eli Lilly, Janssen, Abbott, and GlaxoSmithKline; has received grant/research support from Abbott, Eli Lilly, Janssen, GlaxoSmithKline, Shire, R.W. Johnson, Pharmacia, Forest, Novartis, AstraZeneca, Wyeth-Ayerst, and Bristol-Myers Squibb; has received honoraria from Eli Lilly, Janssen, Abbott, and GlaxoSmithKline; and is on the speakers/advisory board for Abbott, Eli Lilly, GlaxoSmithKline, and Janssen.

Reprint requests to: Joseph F. Goldberg, M.D., Payne Whitney Clinic, 525 E. 68th St., New York, NY 10021 (e-mail: JFGoldbe@mail.med.cornell.edu).

Table 1. Corollaries of Suicidality and Substance Use Disorders in Affectively Ill Patients

Dimension	Comment
Depression	Extent and severity of depression may be associated with suicide ⁶ ; superimposed alcohol/drug abuse further increases suicide risk ^{9,20}
Bipolarity	High risk for comorbid alcohol or drug abuse in bipolar patients ¹¹ ; substance abuse linked with mixed states ^{12,19,21} ; substance misuse and mixed states both may confer heightened risk for suicide attempts ¹⁹ and completions, ¹⁶ potentially via demoralization and hopelessness ²⁶
Impulsivity	High impulsivity/low premeditation and intent often characterize suicide attempts among individuals with alcohol dependence, ^{34,35} although high-lethality methods may be common ¹⁰
Aggression	High aggression differentiates bipolar suicide attempters from nonattempters ²² ; violence may be associated with suicidality among male alcoholics ³⁹
Family history	Familial suicide risk may be higher in mood disorder patients when substance misuse coexists ⁶⁶ ; family history of alcoholism may be associated with suicidal behavior in probands ^{62,63}
Interpersonal/ psychosocial	Interpersonal loss and negative reactions to life stresses may trigger drinking behavior and impulsive self-harm, especially during intoxication ¹⁰³⁻¹⁰⁵

ALCOHOLISM, DEPRESSION, AND SUICIDALITY

It is by now widely recognized that alcohol abuse and/or other drug abuse is highly prevalent among individuals with severe forms of major affective illness. Tondo and colleagues⁶ identified a significant association between substance abuse and suicidality among those with predominantly depressive or dysphoric (rather than predominantly manic) affective disorders, highlighting the importance of depression as a driving force behind suicide attempts, particularly with coexistent substance abuse. This is consistent with studies reporting that depressed alcoholics are more often suicidal than depressed non-alcoholics.^{7,8} However, alcohol or drug abuse among depressed patients has also been associated with suicidal ideation above and beyond the contribution of depressed mood.⁹ In addition, suicide attempts of high medical lethality may also be more common in mood disorders that involve substance misuse.¹⁰ These findings suggest that the presence of substance abuse may increase suicide risk independent of the severity of depression and may result in more medically dangerous attempts.

These concerns are particularly salient for individuals suffering from bipolar disorder since epidemiologic studies suggest that the likelihood of a lifetime comorbid diagnosis of substance abuse or dependence is higher in bipolar illness than any other Axis I disorder.¹¹ Hence, the majority of patients with bipolar disorder are likely to manifest

signs of alcohol or other drug abuse at some point in their lives. In addition, alcohol abuse and other drug abuse have been frequently associated with the propensity to develop mixed states in bipolar disorder.¹²⁻¹⁵ Mixed states, in turn, have been shown to increase the likelihood of suicidality among bipolar patients.¹⁶⁻¹⁹

Research by our group found that a history of alcohol or other drug abuse was associated with an increased risk for suicidality and mixed states, both cross-sectionally and longitudinally.¹⁹ Furthermore, we observed that the presence of alcohol abuse or dependence led to an approximate 4-fold increased risk for suicidality above and beyond the effects of mixed states or dysphoric manias.²⁰ In a related study, Keller and colleagues²¹ found that drug abuse comorbidity accounted for a greater proportion of poor outcome among mixed manic patients than the presence of mixed states per se. This is consistent with the findings discussed above for unipolar depressive disorders and suggests that alcohol and substance abuse may have a strong, independent effect on suicidality above and beyond the contribution of mood state. Nonetheless, it should be noted that one recent study reported no increased association between substance abuse/dependence and a history of suicide attempts in a cohort of bipolar patients with or without lifetime suicide attempts.²² However, these authors noted that because comorbid substance abuse/dependence was evident in the majority of their study sample, the high baseline comorbidity rate may have precluded detection of statistical differences in suicide risk as compared to bipolar patients without comorbid substance abuse.

Other authors have also observed an important connection between substance abuse and poor psychosocial outcome or illness course.²³⁻²⁵ It may be that alcohol or substance abuse leads to a greater decline in functioning and an increase in the severity of the illness. These consequences, in turn, may lead to a greater sense of hopelessness and an increased vulnerability to suicide. Similarly, the passage of multiple affective episodes may worsen prognosis and diminish the likelihood of treatment responsiveness in general, potentially heightening the risk for demoralization and hopelessness as further contributors to suicide risk.²⁶

The onset of substance abuse relative to initial manifestations of affective disorder bears on theories about longitudinal suicide risk. Some authors have observed that substance abuse may often precede the development of a first episode of mania by several years or longer.²⁷ Other investigators have noted that among both adult and adolescent suicide victims, alcohol abuse and other drug abuse often arise years before death,^{28,29} suggesting that substance misuse may exert a chronic influence on the longitudinal development of suicide risk.

There is some evidence that the complex relationship between suicidality, alcohol or substance abuse, and mood

disorders may be different for men and women. In a study of suicide completion in bipolar disorder over a 12-month period, alcohol dependence was identified in 56% of 18 male victims but none of 13 female victims.¹⁶ This suggests the possibility of a strong gender difference in the role of alcoholism as a proximal risk for suicide completion. Frye and colleagues³⁰ also observed more extensive depressive morbidity among alcoholic than nonalcoholic bipolar women,³⁰ but more suicidality in alcoholic bipolar men than alcoholic bipolar women (Mark Frye, M.D., written communication, March 12, 2001). Gender differences in suicide attempts versus completions among bipolar patients may also reflect previous observations that, historically, women attempt suicide more often than men, but men appear more likely to complete suicide, perhaps in part due to their use of more lethal and/or violent methods.²

IMPULSIVITY AND AGGRESSION

Impulsivity has also been thought to play an important role in the relationship between alcohol or substance abuse and suicidality. Several studies have found higher trait impulsivity in patients with affective disorders who have attempted suicide as compared with those who have not attempted suicide,³¹⁻³³ although one recent study did not find support for this relationship.²² Other investigations have found that among affectively ill patients, violent suicide attempts are associated with greater impulsivity and lower intent than nonviolent attempts.^{34,35} High impulsivity and low intent have been noted in depressed alcoholic suicide attempters as compared to depressed nonalcoholic suicide attempters.³⁴ In addition, neurobiological studies have observed lower levels of central serotonin function among impulsive than nonimpulsive attempters, independent of aggression.³⁶

Distinct impulse-control disorders have been found in nearly 40% of individuals with alcohol dependence,³⁷ although it has been suggested that impulsivity among alcoholics may more often reflect sensation-seeking traits rather than aggressive or self-destructive tendencies.³⁸ However, at least among males with alcohol dependence, impulsivity and violent behavior have been shown to co-occur frequently.³⁹ This relationship may not be as strong in women who misuse alcohol.⁴⁰ High impulsivity levels have also been associated with greater relapse among polysubstance abusers who attend self-help groups.⁴¹

Although impulsivity has been separately linked to both suicidality and substance abuse, there have been few studies examining the relationship between these 3 factors. One such study found that substance abuse comorbidity and suicidality were both highly prevalent among individuals with borderline personality disorder.⁴² Interestingly, another study found that high impulsivity was the sole factor associated with number of lifetime suicide at-

tempts after controlling for depression and substance abuse in borderline personality disorder.⁴³ This finding suggests that impulsivity may have an independent relationship with suicidality, yet still represent a corollary to other forms of psychopathology.

Beck and colleagues³ found that hospitalized suicide attempters with coexistent alcoholism were 5 times more likely to eventually commit suicide as compared to those without alcoholism. The only other predictor of eventual suicide completions in that cohort was the number of precautions taken to prevent intervention at the index attempt. This suggests that those individuals who were less impulsive and more premeditated in their planning were more likely to eventually complete suicide. A possible implication of these findings is that high impulsivity may be a more robust predictor of suicide attempts than completions. However, to the extent that pathways to suicide completion may differ from pathways to attempts only, impulsivity may hold greater significance for attempts involving low intent. In fact, Rossow and colleagues⁴ observed that alcohol abuse conferred a higher risk for suicide attempts than completions, potentially reflecting a greater degree of impulsivity, intoxication, and low intent in suicide attempters versus completers.

Collectively, the current literature suggests that impulsivity plays a role in both suicidality and substance abuse. High levels of impulsivity and substance abuse may render individuals particularly vulnerable to suicide attempts or spontaneous or impulsive self-destructive behaviors. In contrast, a greater degree of premeditation associated with suicidality may be a stronger predictor of suicide completion. However, further longitudinal research is needed to clarify these dimensions in groups at high suicide risk.

Hostility and aggression are often linked conceptually with impulsivity based on observations involving forensic populations⁴⁴ as well as in clinical populations of individuals with affective and/or psychotic disorders, personality disorders, and other psychiatric conditions.^{45,46} Convergent data from both preclinical and clinical studies demonstrate abnormalities of central serotonin function across a range of conditions that involve features of depression, alcohol dependence, aggression, impulsivity, and suicidality.⁴⁷ Impulsivity and aggression may also be synergistic factors for some suicide attempters.⁴⁸

It is noteworthy that the distinct connection between impulsivity and aggression relative to suicidality has itself received surprisingly little study. In bipolar disorder, Oquendo et al.²² found that aggression-hostility scale scores were significantly higher among ever- versus never-suicidal bipolar patients, but measures of trait impulsivity failed to differentiate suicide attempters from nonattempters. In addition, Stanley and colleagues⁴⁹ reported that among never-suicidal patients, aggressive behavior was related to low central serotonin function independent of features related to impulsivity.

It is possible that the link between impulsivity and aggression differs among alcohol-dependent versus non-dependent individuals. For example, some authors have suggested that an association between serotonergic abnormalities and alcoholism may be strongest in type II/antisocial alcoholism,⁵⁰⁻⁵³ perhaps more so than in alcoholism without antisocial features. Neuropharmacologic aspects of suicidality and alcoholism (including serotonin and other neurotransmitter systems) are discussed further below.

NONAFFECTIVE MANIFESTATIONS OF PSYCHOPATHOLOGY

Anxiety—particularly panic attacks—has been described by some authors as markedly elevating the risk for suicide attempts, independent of the impact of coexistent depression or drug abuse.^{54,55} Primarily alcohol-dependent patients who attempt suicide have been shown to have greater levels of panic disorder, phobic disorders, and generalized anxiety disorder as compared to alcohol-dependent nonattempters.⁵⁶

Psychosis has also been identified in some investigations as an independent risk factor for suicide, and psychological autopsy studies have suggested that nearly 20% of suicide victims may be psychotic at the time of suicide.⁵⁷ Lifetime comorbid substance abuse has been reported to occur in as many as 40% of individuals with schizophrenia and may show a significant association with suicidal ideation independent of positive, negative, or depressive symptoms.^{58,59} Multifactorial models of suicide completions have observed that psychosis in itself may not differentiate suicide attempters from nonattempters,⁶⁰ suggesting that psychosis—like depression—may contribute to the diathesis upon which additional stressors and clinical factors may precipitate suicidal behavior.

Further insights regarding the relationship between suicidality and alcoholism across psychiatric diagnoses may derive from considering in greater detail the family-genetic and neuropharmacologic mechanisms that appear common to both clinical situations.

HEREDITARY LINKS

A number of contemporary studies indicate that suicidal behavior may cluster within certain families.⁶¹ The potential role of drug abuse (particularly alcohol) in mediating this risk is suggested by several reports. Family histories of alcohol^{62,63} or other drug dependence⁶⁴ have been associated with an increased likelihood of suicidal behavior among adults and adolescents who present for psychiatric treatment. Alcohol-dependent patients who have ever made a suicide attempt appear significantly more likely than those without prior suicide attempts to have a family history of completed suicide.⁶⁵ Among bipolar patients, at-

tempted suicide in both probands and relatives may be especially likely when alcohol dependence is also present.⁶⁶ These findings suggest that genetics may provide a diathesis for suicidality both directly and indirectly through correlated vulnerabilities.

As a complex behavioral phenomenon, it would seem highly unlikely that suicide arises as the result of variation at any individual genetic locus. However, the collective impact of multiple genes, each of small effect, may together confer a heightened susceptibility to suicide-related behaviors. For example, concordance between monozygotic twin pairs has been demonstrated in temperamental or behavioral features such as irritability or aggression,⁶⁷ suggesting the possibility that psychological as well as affective and other biological factors might constitute the essence of a genetic predisposition toward behaviors linked to suicidality.⁶¹

Some authors have noted that, at least in the case of bipolar disorder, clinical phenomena such as suicidal behavior and alcoholism may each contribute to the designation of illness subtypes²⁶; as such, alcohol comorbidity and suicidality may together represent distinct subgroupings of bipolar illness that constitute bona fide phenotypes.⁶⁸ Much the same way some clinicians regard lithium responsiveness as an external marker for refining more genetically homogeneous subgroups,⁶⁹ bipolar disorder with comorbid alcoholism might also represent an illness subclassification for which genetic contributors may be especially salient. To the extent that alcohol dependence and suicide risk share a heightened co-occurrence across generations of bipolar pedigrees,⁶⁶ the exploration of other possible phenotypes linked to alcoholism may shed further light both on the nosology of bipolar subtypes and on the definition of bipolar groups at highest suicide risk.

NEUROTRANSMITTER SYSTEMS IN ALCOHOLISM AND SUICIDE

Serotonin Dysfunction

As noted earlier, serotonergic dysfunction has been thought to play a role in the pathophysiologies of impulsivity, aggression, alcohol dependence, suicide, and affective disorders and may suggest a common neurochemical connection among these factors.⁷⁰ In alcohol-abuse patients, functional neuroimaging studies of brain stem serotonin function indicate low levels of serotonin transporter (5-HTT) activity or brain stem serotonin blood flow and glucose metabolism.^{53,71} Decreased 5-HTT binding has also been associated with alcohol intoxication and aggression.⁷² In addition, impulsive, violent alcoholics have been observed to show low cerebrospinal fluid levels of the serotonin metabolite 5-HIAA.⁷³⁻⁷⁵ Similarly, there is some evidence that suicide completers have locally reduced 5-HTT binding in the ventral prefrontal cortex as compared to nonsuicides.⁷⁶

Molecular genetic studies have begun to identify the impact of specific aspects of the serotonin system on suicidality, impulsivity, and substance abuse. For example, the presence of a low activity polymorphic variant of the promoter region for the serotonin transporter has been linked with alcoholics as compared with controls.⁷⁷ Individuals who are polymorphic for this short variant of the 5-HTT promoter may also have a heightened risk for suicide attempts, particularly attempts that were repetitive and severe⁷⁸ or violent.⁷⁹ Low turnover of tryptophan hydroxylase (TPH), the rate-limiting enzyme in the synthesis of serotonin, has been associated with poor impulse control, and a polymorphic variant of the TPH gene has been associated with suicidality.⁸⁰ These findings suggest that the serotonin system may play an important role in the modulation of many factors related to suicidality. Lower levels of serotonin may be associated with alcoholism, impulsivity, and suicidality. However, possible causal links between these phenomena have not, as yet, been determined, nor have the implications of such a complex interconnection of factors been fully described.

Other Neurotransmitter Dysfunction

Possible noradrenergic dysfunction among alcoholics and among suicidal patients has been preliminarily reported. Abnormal, age-inappropriate loss of locus ceruleus neurons has been described in both suicide victims and alcoholics as compared to nonpsychiatric controls,⁸¹ although cell loss appears especially marked in alcoholic suicide victims.⁸¹ Impulsivity and sensation-seeking both appear associated with increased noradrenergic function, but links to aggression and suicide are less clear.^{82,83}

A direct contribution of dopamine dysfunction to suicidality and/or alcoholism has not been demonstrated, although dysregulation of the dopamine reward pathway could play a role in the genesis of high-risk behaviors that ultimately may lead to increased risk for dangerousness or self-harm. Diminished dopaminergic function, as evidenced by blunted growth hormone response to apomorphine, may also be a residual marker of alcohol dependence.⁸⁴

Excitatory neurotransmitters (e.g., glutamate and aspartate) and inhibitory neurotransmitters (e.g., γ -amino-butyric acid [GABA]) are thought to play a central role in mood stabilization and impulsivity. Studies in alcoholism have provisionally reported increased frequencies of some GABA-system polymorphic variants among alcohol-dependent subjects versus controls.⁸⁵

While these initial observations suggest that several neurotransmitter systems may contribute to the modulation of affect, impulsivity, and substance misuse, direct associations with suicidal behavior or alcoholism remain subject to speculation. Their clinical relevance bears on issues related to neuropharmacologic treatment decisions, particularly with respect to nonserotonergic drugs that

may help to diminish the risk for impulsivity, aggression, and suicide.

Implications for Pharmacotherapy

From the foregoing, decisions about differential pharmacotherapy for clinical conditions involving alcohol or drug dependence and suicide risk may follow particular pathways. The role of serotonergic antidepressants has been shown to dramatically reduce suicidal behavior among depressed patients.⁸⁶ At the same time, selective serotonin reuptake inhibitors (SSRIs) such as fluoxetine may help to diminish alcohol symptoms as well as depressive features in depressed alcoholics with suicidality.⁸⁷ The anti-impulsivity and antiaggression properties attributed to SSRIs^{88,89} may suggest a role for their use in some depressed patients for whom both suicidality and alcoholism may be high risks.

For individuals with bipolar spectrum disorders, the use of antidepressants unopposed by mood stabilizers diverges from current best-practice recommendations in light of their risk for destabilization of mood.^{90,91} While the anti-suicide property of lithium has been well demonstrated,⁹² it is unknown whether this effect becomes attenuated in the presence of significant alcohol or other drug abuse in bipolar disorder. Preliminary studies have suggested that divalproex may also confer protection against suicidality that may be at least comparable to that of lithium.⁹³ Because anticonvulsant mood stabilizers such as divalproex may show better antimanic efficacy than lithium in the presence of comorbid alcohol or other drug abuse/dependence in bipolar illness,⁹⁴ anticonvulsant mood stabilizers may hold a clinical advantage for instances in which suicide risk may be deemed higher by virtue of dysphoric manias^{95,96} and/or substance misuse. Further controlled treatment studies are needed to affirm these provisional observations.

The role of atypical antipsychotic agents as mood stabilizers has begun to receive growing attention.^{97,98} Possible anti-suicide effects have been associated with clozapine,⁹⁹ and initial open studies support the use of atypical neuroleptics for the treatment of schizophrenic or bipolar patients with comorbid substance abuse.¹⁰⁰⁻¹⁰²

PSYCHOSOCIAL DIMENSIONS: LIFE EVENTS AND INTERPERSONAL LOSS

Several studies have reported that adverse life events or interpersonal losses may be particularly likely to trigger suicidal behaviors among individuals with alcohol abuse or dependence,¹⁰³⁻¹⁰⁷ especially among younger alcoholics who attempt suicide.^{108,109} Adolescent suicide victims with alcohol abuse/dependence also may be more vulnerable to interpersonal separations and other psychosocial stresses as compared to nonalcoholic depressed adolescent suicide victims.^{110,111} Social isolation and alcohol misuse have

also been linked with suicide among middle-aged men.¹⁰⁵ These findings suggest that the stabilization of support networks and stress reduction interventions may be an important consideration to reduce suicide risk for affectively ill substance-abusing patients.

Implications for Psychotherapy

Findings noted above regarding the impact of interpersonal loss, as well as issues related to impulse control and sensation-seeking, bear on the psychotherapeutic approach to substance-abuse patients with particular attention to suicide risk. Targeted psychotherapy approaches that address the emotional, interpersonal, cognitive, and behavioral aspects most relevant to alcoholism and suicide risk have not been fully developed. Nevertheless, components of several current distinct psychotherapy approaches bear on clinical issues in this area, particularly in regard to the regulation of affect, impulsivity, aggression, and behavioral responses to interpersonal loss.

Cognitive-behavioral therapy has often been used to treat depressive disorders and suicidality.¹¹² The focus of the treatment involves helping the patient understand how feelings of depression and hopelessness are related to urges for self-destructive behavior and how stressors and other life difficulties impact these feelings and behaviors. Patients are also taught specific stress reduction and problem-solving skills and are helped to strengthen their support networks.

Dialectical behavior therapy, a modification of cognitive-behavioral treatment,¹¹³ was developed for the specific treatment of borderline personality disorder. Dialectical behavior therapy focuses on reducing suicidal behavior, substance abuse, and treatment dropout while enhancing interpersonal functioning and overall adjustment. Standard dialectical behavior therapy consists of 4 basic modes of treatment aimed to enhance motivation, foster treatment compliance, decrease life-threatening behavior, provide validation of emotional responses, and enhance the acquisition and strengthening of skills through a variety of techniques. Patients are asked to keep a diary card in which they record relevant behaviors of the preceding week (including suicidal thoughts, behaviors, and significant interpersonal interactions and mood). Therapy focuses on understanding repeated dysfunctional chains of behavior and cognitions that lead to self-destructive actions. Skills training is then used to identify and implement alternative adaptive coping strategies. A key aspect of this approach is the development of "mindfulness," or awareness in the moment.

The acquisition of self-monitoring skills in dialectical behavior therapy bears similarity to the Social Rhythm Metric technique developed by Frank and colleagues¹¹⁴ for the treatment of bipolar disorder. By recording daily the interpersonal and environmental factors that affect mood states, patients develop an enhanced capacity to recognize causal links in their behavior and ultimately generate alternative coping strategies and behaviors. It is likely that such

daily charting techniques, with subsequent review and exploration in the context of a skills-training psychotherapy, may be of value in a broader range of psychiatric conditions involving high potential impulsivity, aggression, and/or self-harm.

A modification of dialectical behavior therapy has been developed for the treatment of substance abuse in individuals with borderline personality disorder.¹¹⁵ In this model, the core dialectical behavior therapy approach was maintained with expanded use of a diary card to incorporate substance use, along with cognitive-behavioral strategies for substance abuse relapse prevention. There is an emphasis on abstinence coupled with the therapist's acceptance and nonjudgmental response to relapse.

Other authors have emphasized the role of family factors in treating and maintaining positive long-term outcomes in a variety of chronic psychiatric disorders. A number of lines of evidence suggest that problematic family relationships and communication styles may contribute importantly to relapse and diminished psychosocial functioning in schizophrenia and bipolar disorder.¹¹⁶ In all likelihood, impulsive, self-destructive behaviors that heighten suicide risk may generate similar types of negative family attitudes, behaviors, and communication styles in a range of conditions (e.g., chronic alcoholism, bipolar disorder, schizophrenia). Family-focused psychotherapies designed to reduce negative expressed emotion may be of value in a broader range of psychiatric conditions to alleviate interpersonal discord and enhance the support network of patients at risk for suicide.

CONCLUSION

In summary, substance use disorders frequently complicate the course of bipolar and unipolar affective disorders and may confer an increased susceptibility to treatment resistance, psychosocial impairment, extended morbidity, and poor functional outcome. The coalescence of substance abuse with depression, combined with impaired regulation of impulsivity and hostility-aggression, may contribute to an elevated risk for suicide attempts and completions in vulnerable populations. A range of pharmacotherapy options and specific psychotherapies has begun to emerge targeting these features, offering new opportunities for integrative treatment. Efforts to identify coexistent substance misuse and initiate early interventions may substantially help to reduce the risk of excess morbidity, complex psychopathology, and consequent suicide risk that might otherwise arise.

Drug names: clozapine (Clozaril and others), divalproex sodium (Depakote), fluoxetine (Prozac).

Disclosure of off-label usage: The authors of this article have determined that, to the best of their knowledge, clozapine and divalproex sodium are not approved by the U.S. Food and Drug Administration for the

treatment of suicide prevention, and fluoxetine is not approved for symptoms related to alcoholism.

REFERENCES

- Miller NS, Mahler JC, Gold MS. Suicide risk associated with drug and alcohol dependence. *J Addict Dis* 1991;10:49–61
- Moscicki EK. Identification of suicide risk factors using epidemiologic studies. *Psychiatr Clin North Am* 1997;20:499–517
- Beck AT, Steer RA, Trexler LD. Alcohol abuse and eventual suicide: a 5- to 10-year prospective study of alcohol-abusing suicide attempters. *J Stud Alcohol* 1989;50:202–209
- Rossov I, Romelsjo A, Leifman H. Alcohol abuse and suicidal behavior in young and middle aged men: differentiating between attempted and completed suicide. *Addiction* 1999;94:1199–1207
- Goldstein RB, Black DW, Nasrallah A, et al. The prediction of suicide: sensitivity, specificity, and predictive value of a multivariate model applied to suicide among 1906 patients with affective disorders. *Arch Gen Psychiatry* 1991;48:418–422
- Tondo L, Baldessarini RJ, Hennen J, et al. Suicide attempts in major affective disorder patients with comorbid substance use disorders. *J Clin Psychiatry* 1999;60(suppl 2):63–69
- Cornelius JR, Salloum IM, Mezzich J, et al. Disproportionate suicidality in patients with comorbid major depression and alcoholism. *Am J Psychiatry* 1995;152:358–364
- Salloum IM, Daley DC, Cornelius JR, et al. Disproportionate lethality in psychiatric patients with concurrent alcohol and cocaine abuse. *Am J Psychiatry* 1996;153:953–955
- Pages KP, Russo JE, Roy-Byrne PP, et al. Determinants of suicidal ideation: the role of substance use disorders. *J Clin Psychiatry* 1997;58:510–515
- Elliott AJ, Pages KP, Russo J, et al. A profile of medically serious suicide attempts. *J Clin Psychiatry* 1996;57:567–571
- Regier DA, Farmer ME, Rae DS, et al. Comorbidity of mental disorders with alcohol and other drug abuse: results from the Epidemiologic Catchment Area (ECA) Study. *JAMA* 1990;264:2511–2518
- Himmelhoch JM, Mulla D, Neil JF, et al. Incidence and significance of mixed affective states in a bipolar population. *Arch Gen Psychiatry* 1976;33:1062–1066
- Fogarty F, Russell JM, Newman SC, et al. Epidemiology of psychiatric disorders in Edmonton: mania. *Acta Psychiatr Scand Suppl* 1994;376:16–23
- Winokur G, Coryell W, Akiskal HS, et al. Alcoholism in manic-depressive (bipolar) illness: familial illness, course of illness, and the primary-secondary distinction. *Am J Psychiatry* 1995;152:365–372
- Verdoux H, Mury M, Besancon G, et al. Comparative study of substance dependence comorbidity in bipolar, schizophrenic, and schizoaffective disorders. *Encephale* 1996;22:95–101
- Isometsä ET, Henriksson MM, Aro HM, et al. Suicide in bipolar disorder in Finland. *Am J Psychiatry* 1994;151:1020–1024
- Dilsaver SC, Chen Y-W, Swann AC, et al. Suicidality in patients with pure and depressive mania. *Am J Psychiatry* 1994;151:1312–1315
- Strakowski SM, McElroy SL, Keck PE Jr, et al. Suicidality among patients with mixed and manic bipolar disorder. *Am J Psychiatry* 1996;153:674–676
- Goldberg JF, Garno JL, Leon AC, et al. Association of recurrent suicidal ideation with nonremission from acute mixed mania. *Am J Psychiatry* 1998;155:1753–1755
- Goldberg JF, Garno JL, Leon AC, et al. Correlates of suicidal ideation in dysphoric mania. *J Affect Disord* 1999;56:75–81
- Keller MB, Lavori PW, Coryell W, et al. Differential outcome of pure manic, mixed/cycling, and pure depressive episodes in patients with bipolar illness. *JAMA* 1986;255:3138–3142
- Oquendo MA, Waternaux C, Brodsky B, et al. Suicidal behavior in bipolar mood disorder: clinical characteristics of attempters and nonattempters. *J Affect Disord* 2000;59:107–117
- Tohen M, Waternaux CM, Tsuang MT, et al. Four-year follow-up of 24 first episode manic patients. *J Affect Disord* 1990;19:79–86
- O'Connell RA, Mayo JA, Flatow L, et al. Outcome of bipolar disorder on long-term treatment with lithium. *Br J Psychiatry* 1991;159:123–129
- Feinman JA, Dunner DL. The effect of alcohol and substance abuse on the course of bipolar disorder. *J Affect Disord* 1996;37:43–49
- Goldberg JF. Bipolar disorder with comorbid substance abuse: diagnosis, prognosis, and treatment. *J Psychiatr Pract* 2001;7:109–122
- Strakowski SM, Sax KW, McElroy SL, et al. The effects of antecedent substance abuse on the development of first-episode psychotic mania. *J Psychiatr Res* 1996;30:59–68
- Fowler RC, Rich CL, Young D. San Diego Suicide Study, 2: substance abuse in young cases. *Arch Gen Psychiatry* 1986;43:962–965
- Runeson B. Psychoactive substance use disorder in youth suicide. *Alcohol Alcohol* 1990;25:561–568
- Frye M, Altshuler LL, Denicoff KD, et al. Gender differences in bipolar disorder alcohol abuse comorbidity [abstract]. *Acta Neuropsychiatr* 2000;12:159
- Apter A, Plutchik R, van Praag HM. Anxiety, impulsivity and depressed mood in relation to suicidal and violent behavior. *Acta Psychiatr Scand* 1993;87:1–5
- McKeown RE, Garrison CZ, Cuffe SP, et al. Incidence and predictors of suicidal behaviors in a longitudinal sample of young adolescents. *J Am Acad Child Adolesc Psychiatry* 1998;37:612–619
- Corruble E, Damy C, Guelfi JD. Impulsivity: a relevant dimension in depression regarding suicide attempts? *J Affect Disord* 1999;53:211–215
- Nielsen AS, Stenager E, Brahe UB. Attempted suicide, suicidal intent, and alcohol. *Crisis* 1993;14:32–38
- Suominen K, Isometsä E, Henriksson M, et al. Hopelessness, impulsiveness and intent among suicide attempters with major depression, alcohol dependence, or both. *Acta Psychiatr Scand* 1997;96:142–149
- Cremniter D, Jamain S, Kollenbach K, et al. CSF 5-HIAA levels are lower in impulsive as compared to nonimpulsive violent suicide attempters and control subjects. *Biol Psychiatry* 1999;45:1572–1579
- Lejoyeux M, Feuche N, Loi S, et al. Study of impulse-control disorders among alcohol-dependent patients. *J Clin Psychiatry* 1999;60:302–305
- Lejoyeux M, Feuche N, Loi S, et al. Impulse-control disorders in alcoholics are related to sensation seeking and not to impulsivity. *Psychiatry Res* 1998;81:149–155
- Greenwald DJ, Resznikoff M, Plutchik R. Suicide risk and violence risk in alcoholics: predictors of aggressive risk. *J Nerv Ment Dis* 1994;182:3–8
- Chalmers D, Olenick NL, Stein W. Dispositional traits as risk in problem drinking. *J Subst Abuse* 1993;5:401–410
- McCown W. The effect of impulsivity and empathy on abstinence of poly-substance abusers: a prospective study. *Br J Addict* 1990;85:635–637
- Trull TJ, Sher KJ, Minks-Brown C, et al. Borderline personality disorder and substance use disorders: a review and integration. *Clin Psychol Rev* 2000;20:235–253
- Brodsky BS, Malone KM, Ellis SP, et al. Characteristics of borderline personality disorder associated with suicidal behavior. *Am J Psychiatry* 1997;154:1715–1719
- Virkkunen M, De Jong J, Bartko J, et al. Psychobiological concomitants of history of suicide attempts among violent offenders and impulsive fire setters. *Arch Gen Psychiatry* 1989;46:604–606
- Dassori AM, Mezzich JE, Keshavan M. Suicidal indicators in schizophrenia. *Acta Psychiatr Scand* 1990;81:409–413
- Grosz DE, Lipschitz DS, Eldar S, et al. Correlates of violence risk in hospitalized adolescents. *Compr Psychiatry* 1994;35:296–300
- Brown GL, Goodwin FK. Cerebrospinal fluid correlates of suicide attempts and aggression. *Ann N Y Acad Sci* 1986;487:174–188
- Horeish N, Rolnick T, Iancu I, et al. Anger, impulsivity and suicide risk. *Psychother Psychosom* 1997;66:92–96
- Stanley B, Molcho A, Stanley M, et al. Association of aggressive behavior with altered serotonergic function in patients who are not suicidal. *Am J Psychiatry* 2000;157:609–614
- Nielson DA, Goldman D, Virkkunen M, et al. Suicidality and 5-hydroxyindoleacetic acid concentration associated with a tryptophan hydroxylase polymorphism. *Arch Gen Psychiatry* 1994;51:34–38
- Lappalainen J, Long JC, Eggert M, et al. Linkage of antisocial alcoholism to the serotonin 5HT_{1B} receptor gene in 2 populations. *Arch Gen Psychiatry* 1998;55:989–994
- New AS, Gelernter J, Yovell Y, et al. Tryptophan hydroxylase genotype is associated with impulsive-aggression measures: a preliminary study. *Am J Med Genet* 1998;81:13–17
- Heinz A, Ragan P, Jones DW, et al. Reduced central serotonin transporters in alcoholism. *Am J Psychiatry* 1998;155:1544–1549
- Weissman MM, Klerman GL, Markowitz JS, et al. Suicidal ideation and suicide attempts in panic disorder and attacks. *N Engl J Med* 1989;46:984–992
- Allgulander C. Suicide and mortality patterns in anxiety neurosis and de-

- pressive neurosis. *Arch Gen Psychiatry* 1994;51:708–712
56. Roy A, Lamparski D, De Jong J, et al. Characteristics of alcoholics who attempt suicide. *Am J Psychiatry* 1990;147:761–765
 57. Robins E. Psychosis and suicide. *Biol Psychiatry* 1986;21:665–672
 58. Kamali M, Kelly L, Gervin M, et al. The prevalence of comorbid substance abuse and its influence on suicidal ideation among inpatients with schizophrenia. *Acta Psychiatr Scand* 2000;101:452–456
 59. Allebeck P, Varla A, Kristjansson E, et al. Risk factors for suicide among patients with schizophrenia. *Acta Psychiatr Scand* 1987;76:414–419
 60. Mann JJ, Watermaux C, Haas GL, et al. Toward a clinical model of suicidal behavior in psychiatric patients. *Am J Psychiatry* 1999;156:181–189
 61. Roy A, Rylander G, Sarchiapone M. Genetic studies of suicidal behavior. *Psychiatr Clin North Am* 1997;20:595–611
 62. Adams DM, Overholser JC. Suicidal behavior and history of substance abuse. *Am J Drug Alcohol Abuse* 1992;18:343–354
 63. Hesselbrock M, Hesselbrock V, Szymanski K, et al. Suicide attempts and alcoholism. *J Stud Alcohol* 1988;49:436–442
 64. Bukstein OG, Brent DA, Perper JA, et al. Risk factors for suicide among adolescents with a lifetime history of substance abuse: a case-control study. *Acta Psychiatr Scand* 1993;88:403–408
 65. Roy A. Relation of family history of suicide to suicide attempts in alcoholics. *Am J Psychiatry* 2000;157:2050–2051
 66. Potash JB, Kane HS, Chiu Y-F, et al. Attempted suicide and alcoholism in bipolar disorder: clinical and familial relationships. *Am J Psychiatry* 2000;157:2048–2050
 67. Coccaro E, Silverman J, Klar H, et al. Familial correlates of reduced central serotonergic system function in patients with personality disorders. *Arch Gen Psychiatry* 1994;51:318–324
 68. McGue M. Phenotyping alcoholism. *Alcohol Clin Exp Res* 1999;23:757–758
 69. Alda M, Grof E, Cavazzoni P, et al. Autosomal recessive inheritance of affective disorders in families of responders to lithium prophylaxis? *J Affect Disord* 1997;44:153–157
 70. Mann JJ. The neurobiology of suicide. *Nat Med* 1998;4:25–30
 71. Tiihonen J, Kuikka JT, Bergstrom KA, et al. Single-photon emission tomography imaging of monoamine transporters in impulsive violent behaviour. *Eur J Nucl Med* 1997;24:1253–1260
 72. Heinz A, Higley JD, Gorey JG, et al. In vivo association between alcohol intoxication, aggression, and serotonin transporter availability in nonhuman primates. *Am J Psychiatry* 1998;155:1023–1028
 73. Roy A, Virkkunen M, Linnoila M. Reduced central serotonin turnover in a subgroup of alcoholics? *Prog Neuropsychopharmacol Biol Psychiatry* 1987;11:173–177
 74. Roy A, Linnoila M. CSF studies on alcoholism and related behaviours. *Prog Neuropsychopharmacol Biol Psychiatry* 1989;13:505–511
 75. Virkkunen M, Goldman D, Nielsen DA, et al. Low brain serotonin turnover rate (low CSF 5-HIAA) and impulsive violence. *J Psychiatr Neurosci* 1995;20:271–275
 76. Mann JJ, Huang Y-Y, Underwood MD, et al. A serotonin transporter gene promoter polymorphism (5-HTTLPR) and prefrontal cortical binding in major depression and suicide. *Arch Gen Psychiatry* 2000;57:729–738
 77. Hallikainen T, Saito T, Lachman HM, et al. Association between low activity serotonin transporter promoter genotype and early onset alcoholism with habitual impulsive violent behavior. *Mol Psychiatry* 1999;4:385–388
 78. Gorwood P, Batel P, Ades J, et al. Serotonin transporter gene polymorphisms, alcoholism, and suicidal behavior. *Biol Psychiatry* 2000;48:259–264
 79. Bellivier F, Szöke A, Henry C, et al. Possible association between serotonin transporter gene polymorphism and violent suicidal behavior in mood disorders. *Biol Psychiatry* 2000;48:319–322
 80. Nielsen DA, Virkkunen M, Lappalainen J, et al. A tryptophan hydroxylase gene marker for suicidality and alcoholism. *Arch Gen Psychiatry* 1998;55:593–602
 81. Arango V, Underwood MD, Pauler DK, et al. Differential age-related loss of pigmented locus coeruleus neurons in suicides, alcoholics, and alcoholic suicides. *Alcohol Clin Exp Res* 1996;20:1141–1147
 82. Siever L, Trestman RL. The serotonin system and aggressive personality disorder. *Int Clin Psychopharmacol* 1993;8:33–39
 83. Roy A, Pickar D, De Jong J, et al. Suicidal behavior in depression: relationship to noradrenergic function. *Biol Psychiatry* 1989;25:341–350
 84. Detling M, Heinz A, Dufeu P, et al. Dopaminergic responsivity in alcoholism: trait, state, or residual marker? *Am J Psychiatry* 1995;152:1317–1321
 85. Sander T, Ball D, Murray R, et al. Association analysis of sequence variants of GABA(A) alpha6, beta2, and gamma2 gene cluster and alcohol dependence. *Alcohol Clin Exp Res* 1999;23:427–431
 86. Leon AC, Keller MB, Warshaw MG, et al. Prospective study of fluoxetine treatment and suicidal behavior in affectively ill subjects. *Am J Psychiatry* 1999;156:195–201
 87. Cornelius JR, Salloum IM, Cornelius MD, et al. Fluoxetine trial in suicidal depressed alcoholics. *Psychopharmacol Bull* 1993;29:195–199
 88. Coccaro EF, Kavoussi RJ, Hauger RL. Serotonin function and antiaggressive response to fluoxetine: a pilot study. *Biol Psychiatry* 1997;42:546–552
 89. Kavoussi RJ, Coccaro EF. Divalproex sodium for impulsive aggressive behavior in patients with personality disorder. *J Clin Psychiatry* 1998;59:676–680
 90. Sachs GS, Printz DJ, Kahn DA, et al. The Expert Consensus Guideline Series: Medication Treatment of Bipolar Disorder 2000. *Postgrad Med* 2000;(4, spec no.):1–104
 91. Goldberg JF. Treatment guidelines: current and future management of bipolar disorder. *J Clin Psychiatry* 2000;61(suppl 13):12–18
 92. Tondo L, Baldessarini RJ, Hennen J, et al. Lithium treatment and risk of suicidal behavior in bipolar disorder patients. *J Clin Psychiatry* 1998;59:405–414
 93. Bowden CL, Calabrese JR, Nemeroff C, et al. Effect on suicidality of divalproex, lithium, and placebo in randomized one-year maintenance treatment of bipolar disorder. *Bipolar Disord*. In press
 94. Goldberg JF, Garno JL, Leon AC, et al. A history of substance abuse complicates remission from acute mania in bipolar disorder. *J Clin Psychiatry* 1999;60:733–740
 95. Freeman TW, Clothier JL, Pazzaglia P, et al. A double-blind comparison of valproate and lithium in the treatment of acute mania. *Am J Psychiatry* 1992;149:108–111
 96. Swann AC, Bowden CL, Morris D, et al, for the Olanzapine HGEH Study Group. Depression during mania: treatment response to lithium or divalproex. *Arch Gen Psychiatry* 1997;54:37–42
 97. Tohen M, Sanger TM, McElroy SL, et al, for the Olanzapine HGEH Study Group. Olanzapine versus placebo in the treatment of acute mania. *Am J Psychiatry* 1999;156:702–709
 98. Tohen M, Jacobs TG, Grundy SL, et al, for the Olanzapine HGGW Study Group. Efficacy of olanzapine in acute bipolar mania: a double-blind, placebo-controlled study. *Arch Gen Psychiatry* 2000;57:841–849
 99. Meltzer HY, Okayli G. Reduction of suicidality during clozapine treatment of neuroleptic-resistant schizophrenia: impact on risk-benefit assessment. *Am J Psychiatry* 1995;152:183–190
 100. Green AI, Zimmet SV, Strous RD, et al. Clozapine for comorbid substance use disorder and schizophrenia: do patients with schizophrenia have a reward-deficiency syndrome that can be ameliorated by clozapine? *Harv Rev Psychiatry* 1996;6:287–296
 101. Buckley PF. Novel antipsychotic medications in the treatment of comorbid substance abuse in schizophrenia. *J Subst Abuse Treat* 1998;15:113–116
 102. Albanese MJ. Risperidone in substance abusers with bipolar disorder. Presented at the 39th annual meeting of the American College of Neuropsychopharmacology; Dec 9–14, 2000; San Juan, Puerto Rico
 103. Rich CL, Fowler RC, Fogarty LA, et al. San Diego Suicide Study, 3: relationships between diagnoses and stressors. *Arch Gen Psychiatry* 1988;45:589–592
 104. Duberstein PR, Conwell Y, Caine ED. Interpersonal stressors, substance abuse, and suicide. *J Nerv Ment Dis* 1993;181:80–85
 105. Heikkinen ME, Aro HM, Henriksson MM, et al. Differences in recent life events between alcoholic and depressive nonalcoholic suicides. *Alcohol Clin Exp Res* 1994;18:1143–1149
 106. Berglund M, Ojehagen A. The influence of alcohol drinking and alcohol use disorders on psychiatric disorders and suicidal behavior. *Alcohol Clin Exp Res* 1998;22(7, suppl):333S–345S
 107. Pirkola SP, Isometsä ET, Heikkinen ME, et al. Suicides of alcohol misusers and non-misusers in a nationwide population. *Alcohol Alcohol* 2000;35:70–75
 108. Conner KR, Duberstein PR, Conwell Y. Age-related patterns of factors associated with completed suicide in men with alcohol dependence. *Am J Addict* 1999;8:312–318
 109. Conwell Y, Rotenberg M, Caine ED. Completed suicide at age 50 and over. *J Am Geriatr Soc* 1990;38:640–644
 110. Marttunen MJ, Aro HM, Henriksson MM, et al. Psychosocial stressors more common in adolescent suicides with alcohol abuse compared with

- depressive adolescent suicides. *J Am Acad Child Adolesc Psychiatry* 1994;33:490-497
111. Pirkola SP, Marttunen MJ, Henriksson MM, et al. Alcohol-related problems among adolescent suicides in Finland. *Alcohol Alcohol* 1999;34:320-329
112. Lieberman R, Eckman T. Behavior therapy versus insight-oriented therapy for repeated suicide attempters. *Arch Gen Psychiatry* 1981;38:1126-1130
113. Linehan M, Armstrong H, Suarez A. Cognitive-behavioral treatment of chronically parasuicidal borderline patients. *Arch Gen Psychiatry* 1991; 48:1060-1064
114. Frank E, Swartz HA, Kupfer DJ. Interpersonal and social rhythm therapy: managing the chaos of bipolar disorder. *Biol Psychiatry* 2000;48:593-604
115. Linehan MM, Schmidt H III, Dimeff LA, et al. Dialectical behavior therapy for patients with borderline personality disorder and drug dependence. *Am J Addict* 1999;8:279-292
116. Miklowitz DJ, Goldstein MJ, Nuechterlein KH, et al. Family factors and the course of bipolar affective disorder. *Arch Gen Psychiatry* 1988;45:225-231

© Copyright 2001 Physicians Postgraduate Press, Inc.
One personal copy may be printed