Discussion

Medical Intervention and Suicide Risk

Dr. Hendin: Dr. Wyatt, how do the baseline data on suicide rates in schizophrenia prior to the availability of clozapine compare with current data? Are your reservations about the Walker et al. study *[Walker AM, Lanza LL, Arellano F, et al. Epidemiology 1997;8:671–677]* related to the fact that we have no data to compare it with?

Dr. Wyatt: Those schizophrenia patients who take clozapine comprise a specialized group; they are treatment refractory. I do not know whether one can extrapolate from within group studies to a general population. I have seen that patients who have responded to clozapine have had a reasonably high risk of suicide as they have started to improve.

Dr. Angst: The issue of the relationship between suicidal ideation, attempt, and completion is complex, as shown by the presentation of John Mann at this meeting. The study of maprotiline by Rouillon et al. *[Rouillon F, Lejoyeux M, Filteau MJ, In: Montgomery SA, Rouillon F, eds. Long-Term Treatment of Depression. Chichester, England: John Wiley & Sons; 1992:81–111]* showed an increase of suicide attempts in patients taking maprotiline compared with those taking placebo. In this case, it is interesting that instances of suicide ideation declined among these patients as a group, so the suicide item on the Hamilton Rating Scale for Depression improved, in spite of the fact that suicide attempts in this population increased. We do not know, of course, whether 1 group contained patients with more special risks than another.

Dr. Müller-Oerlinghausen: Insofar as the groups were not matched, interpretation of these data is impossible. It should be emphasized that the suicide attempts occurred only in the patients who had relapsed; otherwise efficacy was as good as among nonsuicidal depressed patients.

Dr. Baldessarini: Dr. Müller-Oerlinghausen, what is your best clinical understanding about choices between types of antidepressants as they relate to people who are or are not at high risk for suicide?

Dr. Müller-Oerlinghausen: This issue is quite controversial. Attitudes may differ slightly from country to country, from medical school to medical school; they may even be subject to the local influence of manufacturers. We still adhere, as do many of our colleagues in Germany, to the somewhat old-fashioned idea that sedative antidepressants are the best choice for acutely suicidal patients. There may be good reason to treat a patient with a serotonin selective reuptake inhibitor (SSRI), but we should always be aware of possible activating side effects whether prescribing an SSRI or a tricyclic antidepressant (TCA). We should clearly avoid prescribing activating drugs.

Dr. Baldessarini: Treatment or medication that induces agitation, restlessness, or sleeplessness, for example, should be avoided in suicidal patients.

Dr. Lenox: Dr. Sackeim, you have looked at the effects of lithium plus nortriptyline in suicidal patients. Did you examine the effects of lithium alone in that population?

Dr. Sackeim: No, and I am skeptical about the value of lithium alone in this patient population. Coppen et al. *[Coppen A, Abou-Saleh MT, Milln P, et al. Br J Psychiatry 1981;139;284–287]* did a small study comparing the effects of lithium versus placebo a number of years ago. During the first 6 months after electroconvulsive therapy (ECT), lithium had no effect on suicidal patients, although there was a protective effect over a longer period.

Dr. Baldessarini: In the old literature dealing with patients with unipolar depression, the outcome with patients taking lithium alone is considerably worse than for patients taking a TCA alone. The combination of lithium plus a TCA is consistently superior in that literature as well. Dr. Sackeim, in the Iowa studies, Avery and Winokur *[Avery D, Winokur G. Arch Gen Psychiatry 1976;33: 1029–1037]* found that suicidal patients tended to receive gentler treatment if they were also medically infirm, contaminating conclusions about morbidity and mortality as a function of adequate treatment. Is that not part of the problem?

Dr. Sackeim: Yes, but the patients who have significant medical comorbidity, particularly cardiovascular disease, were in the period up until the 1990s much more likely to be treated with ECT, so typically a medically sicker population was being assessed. If prior studies showed an impact on reduction of mortality rates in patients treated with ECT, we would have to ask why a very short-term treatment like ECT is associated with fewer incidents of cardiovascular death and fewer accidents over 3 or 4 years.

Dr. Baldessarini: While we focus on suicide, we should remember that serious psychiatric disorders have mortality risk independent of suicide, particularly from cardiovascular and pulmonary disease as well as other causes. This fact is very striking in the bipolar literature; it may also be the case with depression and schizophrenia. We must keep overall mortality rates in mind.

Dr. DePaulo: Data reported this morning indicated that patients with bipolar disorder are mostly in the depressed state when they attempt or commit suicide. Bipolar patients naturally spend more time in the depressed state

than in the manic or the mixed state. Do we have data to indicate risk factors based on how long the patient has been in a depressed state? We have asserted that mixed states are more dangerous than manic states, but the data presented here indicate otherwise.

Dr. Baldessarini: True. This is a difficult question. Preliminary raw data indicate that most people attempt suicide when depressed, a fact that is hardly surprising.

Dr. Angst: We lack good data, but it makes sense to assert that any change in state constitutes a critical period for the bipolar patient who has to adapt to these changes. During stable periods of an episode, chronic or acute, the bipolar patient is at lower risk for suicide than during periods of rapid change, for instance, at the beginning of the episode or when the episode is resolving, and at the same time the condition becomes very unstable. We can hypothesize that the gradient of the deterioration is a critical parameter.

Dr. Baldessarini: Our data indicate that there are probably more patients in manic episodes per unit time than there are in depressive episodes. Depressions, though fewer, tend to be longer in duration, however, so patients spend more time in depressive states. Bipolar detection is the critical next step in therapeutics.

Dr. Goodwin: Pay attention to the patient with highly recurrent unipolar disorder. Schou *[Schou M. Arch Gen Psychiatry 1979;36:849–851]* found, in a review of the Danish and U.K. data concerning TCA versus lithium prophylaxis, that patients with unipolar depression treated with TCAs experienced an episode of depression within 24 months, the same cycle frequency (roughly 12 to 24 months) as the patients with bipolar disorder had. Among that group of patients with unipolar depression, the relapse rate in the group of patients taking TCAs was 50% higher than the relapse rate in the group of patients taking lithium. The relapse rate for patients taking lithium was 20% in the group of bipolar disorder patients and 22% in the group with recurrent unipolar depression.

Dr. Baldessarini: A question asked at least since Kraepelin's time is whether there is truly a distinction between patients with bipolar disorder and with unipolar depression or whether there are some intermediate syndromes that overlap and may resemble bipolar disorder. Modern concepts of bipolar II disorder have helped, but there are probably still patients with highly recurring unipolar depression who may respond to the same drugs as patients with bipolar disorder.

Participant: Does the income of patients relate to the political problems of using ECT in public settings?

Dr. Sackeim: Yes. The irony is that the Olson et al. paper *[Olson M, Marcus S, Sackeim HA, et al. Am J Psychiatry 1998;155:22–29]* in the American Journal of Psychiatry documents that if a patient receives either ECT or treatment with drugs for recurrent depression from the start of hospitalization for the first 5 days, hospitalization costs are considerably lower with ECT, and the length of stay is shorter. That effect escalates with the severity of depression, with patients who are psychotically depressed particularly demonstrating a more rapid response than less severely depressed patients. ECT saves money, but only the richest patients receive it.

Dr. Baldessarini: Dr. Müller-Oerlinghausen, the older antidepressants are more lethal than most of the modern antidepressants in acute overdose. Does the use of safer drugs affect the suicide rate among depressed patients? A British study *[Freemantle N, House A, Song F, et al. BMJ 1994;309:249–253]* indicates that only the method and not the suicide rate changes as a result of using safer drugs. Are those findings accurate?

Dr. Müller-Oerlinghausen: This issue remains an open question. Some solid data indicate that safer antidepressants have no special benefit in reducing the suicide rate *[Müller-Oerlinghausen B, Berghöfer A. J Clin Psychiatry 1999;60(suppl 2):94–99]*. So many confounding factors affect the suicide rate that it is nearly impossible to isolate the result of antidepressant treatment. Still, we have the experience of Dr. Rutz *[Rutz W, Knorring L von, Walinder J. Acta Pscychiatr Scand 1989;80:151–154]*, who showed that, when doctors are educated appropriately, suicide rates decrease. We have also performed some calculations to estimate the number of lives per year saved by prescribing lithium appropriately in Germany *[Ahrens B, Müller-Oerlinghausen B. In: Müller-Oerlinghausen B, Greil W, Berghöfer B, eds. Die Lithium therapie. 2nd ed. Berlin: Springer-Verlag; 1997: 262–277]*. If our data prove generalizable, 200 people a year might be saved. In single actions, one can demonstrate the impact of better training or better treatment on a specific population, but there is no basis on which to judge if these results can be generalized. In Sweden, the impact of training lasted just 1 year.

Dr. Sackeim: Some very provocative new data on developmental shifts in responsiveness to serotonin reuptake inhibitors and relatively serotonergic drugs have been reported. It is suggested that people lose responsivity to SSRIs as they age. Elderly men are at the greatest risk for suicide, and they are often treated with SSRIs because they are well tolerated. Unfortunately, the most tolerable of the agents may be the least effective in these patients.

Dr. Baldessarini: Conversely, it is thought that children respond poorly to TCAs while older patients do very well with them.