Dementia and Bereavement: Adverse Life Experiences Complicating Depression in Later Life

Sidney Zisook, M.D., and Laura B. Dunn, M.D.

Adverse life experiences late in life, notably cognitive decline and bereavement, can precipitate depression as well as greatly complicate the recognition, course, and treatment of the depressive disorder. Cognitive decline is commonly experienced late in life, and although many adults learn to cope with this change, it may become overwhelming to an individual with depression. In patients with dementia, recognition of depression is hampered by problems patients may have reporting symptoms, and there is significant overlap of symptoms between depression and dementia. Depression is also underrecognized in individuals who have suffered a bereavement. Over time, most bereaved individuals adapt to life without their spouse, but a significant minority will experience exacerbation, onset, or persistence of depression. Clinicians can, however, be reluctant to diagnose depression in the face of such a highly disruptive life event, substituting understanding for treatment. Effective treatment of depression can also improve cognitive decline in patients with dementia and facilitate the natural grieving process in bereaved subjects. In both conditions, selective serotonin reuptake inhibitors are efficacious and well tolerated, and patients show good compliance to treatment regimens.

(Primary Care Companion J Clin Psychiatry 2000;2[suppl 5]:25–31)

Depressive syndromes occurring in the later years of life are much like those seen throughout the adult life cycle.[1–3] Unfortunately, however, decline in health status, functional abilities, or cognitive capacities or loss of loved ones all too frequently accompanies or impinges on daily life in the later years. Such losses may not only precipitate depression in vulnerable individuals,[2] but may also complicate the recognition, course, and treatment of the resultant mood disorders. This article deals with 2 of the most prevalent adverse life experiences of later life—dementia and bereavement—and discusses the recognition, clinical characteristics, and treatment of depressive syndromes that may be associated with them.

RELATIONSHIP BETWEEN DEPRESSION AND DEMENTIA

Despite the procurement of wisdom that comes with age, there is a direct relationship between advancing age and cognitive decline throughout adulthood. By the age of 55 years, if not much earlier, otherwise healthy individuals can experience increasing difficulties with such mundane tasks as recalling names, remembering where objects such as keys and wallets were just placed, and keeping track of ongoing conversations.[4] Whereas most adults cope with, and adapt to, these unfortunate concomitants of aging and may even laugh at themselves or with their friends, individuals who are depressed tend to be overwhelmed by their cognitive symptoms. Fueled by this fear, they may accentuate or magnify their cognitive difficulties. Thus, it is not uncommon for older individuals with depression to present with memory or concentration problems as their chief complaints.

The relationship between depression and cognitive deterioration is complex. By the age of 65 years, 12% to 15% of community-dwelling persons have Mini-Mental State Examination Scores of less than 24; this percentage triples by the age of 85 years.[5] Thus, depression in later life often occurs against a backdrop of deteriorating cognitive abilities. To make matters worse, depression itself may be associated with specific neurocognitive deficits (e.g., problems with attention, naming, and psychomotor speed),[6] increase the risk for subsequent dementia,[7] worsen cognitive functioning,[8] be an early manifestation of a cognitive disorder,[9] and be precipitated by the onset of dementia.[10]

A relatively controversial issue relates to the nature and frequency of pseudodementia. First coined by Kiloh[11] and later elaborated by Wells[12] and others,[13] the term *depressive pseudodementia* was meant to convey a totally reversible dementia brought on by a major depressive episode.

From the Department of Psychiatry, University of California, San Diego.

Presented at the symposium "Depression in the Elderly: Clinical Considerations and Therapeutic Approaches," which was held April 7, 1999, in Florence, Italy, and supported by an unrestricted educational grant from SmithKline Beecham Pharmaceuticals.

Reprint requests to: Sidney Zisook, M.D., Department of Psychiatry, University of California, 9500 Gilman Dr., La Jolla, CA 92093-0803.

Table 1. Differentiating "Pseudodementia" From Dementia[a]

Clinical Presentation	Diagnosis	
	"Pseudodementia"	Dementia
Cognitive complaints	Embellishes cognitive problems	Conceals cognitive problems
Onset of cognitive problems	Dateable onset	Insidious onset
Mood	Pervasive dysphoria	Labile and reactive affect
Effort	Does not try	Struggles for competence
Pride	Emphasizes personal failures	Emphasizes accomplishments
History		
Past personal	Depression	No depression
Family	Depression	Alzheimer's disease
Examination		
Neurologic	Normal	Aphasia, agnosia, and apraxia, with or without positive glabellar and snout reflexes
Sundowning	No	Yes
Memory	Recent = remote	Recent > remote
Responses	"I don't know" answers	Near misses

[a]Adapted from Wells,[12] with permission.

Table 2. Diagnostic Challenges When Depression and Dementia Coexist

Depression frequently coexists with a variety of dementing, degenerative, and vascular disorders
Depression often subsyndromal or minor
Overlapping symptoms
Alzheimer's disease (dysphoria, decreased interest, poor energy, sleep changes, concentration problems)
Vascular dementia (motor retardation, lack of insight, impairment of executive functions)
Patient may not understand questions or forget answers

Table 3. Clues to Help Diagnose Depression in Patients With Dementia[a]

"Overlapping symptoms" may precede memory complaints
Dysphoria severe, pervasive, persistent
Presence of anhedonia, feelings of worthlessness, suicidal ideation
Social withdrawal, pessimism, helplessness, self-pity, amplification of cognitive deficits, vague somatic complaints and concerns, perseveration on general failures, sad and weepy appearance
Past personal or family history of mood disorder
Observations of family and other care providers

[a]Based on references 21–23.

Table 1 illustrates key differential diagnostic features between "depressive pseudodementia" and dementia as described by Wells.[12] More recent investigators have commented on the relative infrequency of "pseudodementia" and that the very term may be misleading.[14] They emphasize that cognitive disturbances caused by major depression tend to be mild and transient rather than full-blown dementia; further, when the cognitive deficits are severe enough to warrant the diagnosis of dementia, there is nothing "pseudo" about the dementia, even if it is reversible and brought on by depression. In some cases, the depressive disorder may be simply unmasking a heretofore subclinical or evolving dementia that would not otherwise be appreciated until sometime in the future.[15] An empirical study has found that, compared with elderly patients with depression and intact cognitive function, similarly aged patients diagnosed with "depressive pseudodementia" may have higher mortality rates and higher rates of developing unequivocal Alzheimer's disease after only a few years of follow-up.[16] The conclusion of that study is that the apparent "pseudodementia" was actually depression presenting as an early manifestation or prodrome of subclinical, reversible dementia. Thus, *pseudodementia* may be a term that has outlived its usefulness.

Identifying Depression in Patients With Dementia

Perhaps a more pressing problem is identifying depression in the presence of a dementing disorder. Several factors make this a challenging clinical problem (Table 2). For one, depression frequently coexists with a variety of dementing, degenerative, and vascular disorders.[17–19] Secondly, even more prevalent than major depressive episodes, clinically relevant minor and subsyndromal depressions commonly accompany or follow dementing illnesses,[20] and these milder manifestations are often more difficult to demarcate from normal sadness or adjustment disorders. Thirdly, there is considerable overlap between symptoms of major depressive episodes and dementia. In Alzheimer's disease, for example, transient episodes of dysphoria, lack of interest in previously pleasurable activities, poor energy, changes in sleep patterns, and disturbances in concentration are common. Psychomotor retardation also overlaps depression symptomatology in other forms of neurodegenerative disorders, such as Parkinson's disease, and in vascular dementia. Finally, patients with dementia may be unable to give accurate histories, understand questions posed by their clinician, or recall symptoms of depression.

Several investigators have offered clinical guidelines for identifying depression in the context of dementia (Table 3).[21–23] One issue to consider is the chronology of symptoms. When several "overlapping" symptoms precede memory complaints, depression is likely. The clinician should also weigh the nature and severity of the symptoms. For example, in dementia uncomplicated by a major depressive episode, dysphoria is generally relatively mild and transient or intermittent, as opposed to severe, pervasive, and persistent. Thus, if dysphoria is intense and persistent, and/or lack of interest constitutes full-blown anhedonia, major depression is likely. Careful consideration should be given to nonoverlapping symptoms, such as feelings of worthlessness or suicidal ideation, that always suggest depression. Finally, when in doubt, the clinician should seek to identify behaviors and symptoms that, while not part of the DSM-IV criteria for depression, are frequently observed in elderly patients with depression. These include social withdrawal, pessimism, helplessness, self-pity, am-

plification of cognitive difficulties, vague somatic complaints and concerns, perseveration over personal failures, and a consistently sad appearance.

As dementia progresses, the diagnosis of comorbid depression becomes even more difficult, posing vexing challenges to even the most experienced clinicians. Sometimes, a sad appearance and vague complaints of somatic distress may be all the clinician has to deal with. A past personal history or family history of mood disturbances (provided by other resources) aid in diagnosis, but such information is not always present or reliable. Although patients with a mild, or even moderate, dementing disorder may be able to give a reasonable reliable report on their current mood state,[24] as the dementia progresses it is increasingly important to utilize observations of family or other caregivers to make the diagnosis of depression.

When in doubt, it makes sense to err on the side of overdiagnosing depression, because untreated depression may have dire consequences. Several studies have found that depressive symptoms, even in the absence of a full major depressive syndrome or dysthymic disorder, can increase disability, caregiver burden, and the risk of nursing home placement in patients with dementia.[25,26]

Treatment of Depression in Patients With Dementia

Several controlled studies suggest that the treatment of depressive symptoms in elderly patients with dementia, whether by pharmacologic,[27–31] behavioral,[32] or other modalities, not only lessens the depression, but may also improve cognitive function.

The efficacy of tricyclic antidepressants (TCAs) has been demonstrated in patients with depression and dementia. In an early large-scale study,[29] clomipramine showed favorable efficacy compared with placebo in patients with depression and Alzheimer's disease. In a smaller trial of Alzheimer's disease patients with and without depression, Reifler et al.[27] did not find a significant advantage for imipramine over placebo. However, only half of those randomly assigned to treatment had a clinical diagnosis of depression. Compared with placebo, imipramine was associated with increased adverse events, including cognitive problems. The selective serotonin reuptake inhibitor (SSRI) citalopram improved symptoms of depression in patients with Alzheimer's disease in a placebo-controlled trial.[28] More recently, comparative studies of SSRIs and TCAs have shown that they share similar efficacy, but that SSRIs benefit from a benign tolerability profile. A recent study[30] found that fluoxetine was equally effective to and better tolerated than amitriptyline. Similarly, in a larger study,[31] both paroxetine and imipramine markedly improved symptoms of depression, but paroxetine was associated with fewer anticholinergic and serious side effects. In each of the latter 2 studies of SSRIs, moderate improvement in cognitive function accompanied the improvement in depressive symptoms.

Thus, the weight of the evidence related to the risk of untreated depression in patients with dementia, the risk of side effects from medications used to treat depression, and the benefits of effectively treating depression point toward active intervention. Although more comparative data would be helpful, it makes sense to use medications that are tolerable and safe, are most likely to be associated with treatment adherence, and lack strong anticholinergic effects. Thus, the SSRIs and some of the other newer classes of medications should be used ahead of the TCAs. In addition, an integrative approach that incorporates patient and family education and appropriate psychotherapy with the medications is ideal.

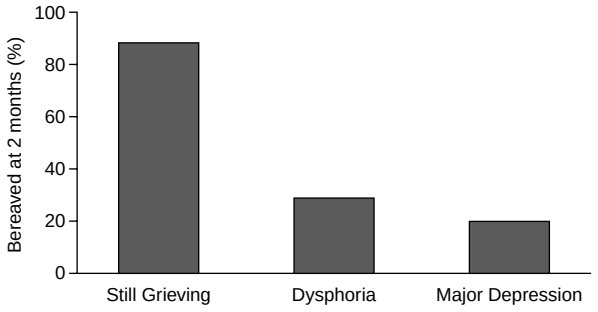
RELATIONSHIP BETWEEN DEPRESSION AND BEREAVEMENT

The underrecognition and misdiagnosis of depression in later life is a well-recognized clinical phenomenon.[33] Clinicians seem reluctant to diagnose major depression in the face of highly disruptive life events that might make anyone demoralized, unhappy, or overwhelmed, such as the development of a disabling general medical problem, the progressive crescendo of cognitive decline, or psychosocial stress. In the context of such stresses, individuals, their families, and even their physicians may substitute "understanding" the dysphoria for making a diagnosis and initiating treatment.

A case in point is bereavement, an extremely common event in later life. The elderly are vulnerable to a myriad of losses—jobs, homes, health, siblings, adult children, friends, etc.—but one of the most prevalent and by far the most studied is the death of a spouse. In the United States, there are over 800,000 new widows and widowers each year. The approximately 11 million widows and widowers make up more than 7% of the population of the United States. Most of these men and women are elderly; the mean age of widowhood is 69 years for men and 66 years for women. Among people aged 65 years or older, more than 50% of women and 13% of men have been widowed at least once. That most of these men and women ultimately were able to grieve for their losses, reengage, and function adequately in their lives is testimony to the adaptive capacities of elderly persons. A significant minority, however, do not come out of their grief unscathed: this minority is at risk for a number of possible complications, including the exacerbation, onset, or persistence of a depressive disorder.[34–36]

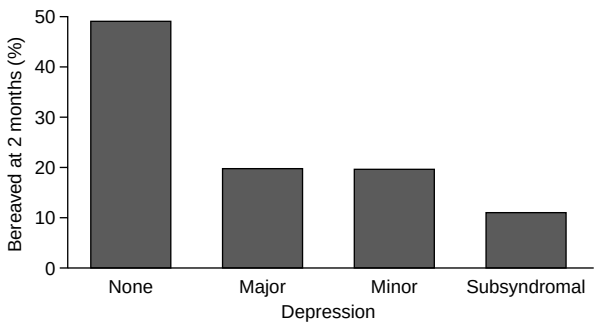
An association between depression and widowhood has long been recognized. In his classic paper on mourning and melancholia, Freud[37] differentiated grief from depression largely by the loss of self-esteem associated with the latter. He, and other key analytic figures after him,[38] recognized the importance of the loss of a loved one in the initiation of a depressive disorder. However, it was not until years later

Figure 1. Incidence of Grief, Dysphoria, and Major Depression 2 Months After Bereavement[a]



[a]Data from Zisook et al.[35] and Zisook and Shuchter.[46]

Figure 2. Incidence of Major, Minor, and Subsyndromal Depression 2 Months After Bereavement[a]



[a]Data from Zisook et al.[36]

that Clayton initiated her landmark series of studies[39–42] on spousal bereavement that empirically validated what others had heretofore only theorized. She and her colleagues found that 35% of widows and widowers met symptomatic criteria for major depression 1 month after their spouses' deaths, 25% at 4 months, and 17% after the first year. Of those depressed at 1 month, 27% remained depressed 1 year later. Although a large number of widows and widowers met symptomatic criteria for major depression, Clayton emphasized differences between grief and depression. She noted that most widows and widowers do not consider themselves clinically depressed, do not seek help for their depression, and rarely experience such classic depressive symptoms as psychomotor retardation, sustained feelings of worthlessness, and suicidal ideation.[39–42]

Largely on the basis of Clayton's work, the DSM-III and DSM-III-R coined the term *uncomplicated bereavement* to denote a syndrome meeting criteria for major depression that begins within months of the death of a close relative. However, as newer data began supporting similarities between major depressive syndromes occurring in the context of bereavement and other major depressive episodes in terms of the nature and number of symptoms, their persistence and consequences,[43] and even their psychological underpinning,[44] the DSM-IV renamed and further refined its concept of "normal grief reactions." According to the DSM-IV,[45] *bereavement* refers to depressive symptoms otherwise meeting criteria for a major depressive episode except that (1) they begin and end within 2 months of the death of a close relative; (2) they are not characterized by guilt feelings, thoughts of death or suicide, morbid preoccupations with worthlessness, marked psychomotor retardation, or hallucinatory experiences; and (3) they are not accompanied by prolonged and marked functional impairment.

Even this conservative definition of bereavement may result in nonrecognition or misdiagnoses of major depressive episodes. It should be noted that no other psychiatric or general medical condition is negated by the experience of bereavement and that no other life stressor negates the diagnosis of major depression when 5 or more symptoms are present for an adequate duration. Thus, it may be more pragmatic to make the diagnosis of major depressive episode on Axis I if warranted by symptoms and to code bereavement on Axis IV to note the recognition of bereavement as a precipitating factor that may be important when formulating treatment decisions. The following paragraphs summarize some of the data supporting this view.

1. Grief ≠ depression

Although symptoms of sadness, irritability, and anger are important aspects of the emotional and cognitive responses to loss, the majority of bereaved individuals do not meet full criteria for a major depressive episode for 2 weeks or longer. By 2 months, 88% of widows and widowers feel they are still grieving,[46] but only 29% feel dysphoric for most of the time and only 20% meet full criteria for major depression[35] (Figure 1).

2. Depression ≠ major depression

As with other patients with mood disorders, the full burden of depression in bereaved individuals is not accounted for by major depressive episodes alone. Thus, at 2 months after a spouse's death, 20% of widows and widowers meet criteria for major depression, another 20% for minor depression, and 11% for subsyndromal depression (Figure 2).[36] Furthermore, both minor and subsyndromal depressions place patients at risk for future major depressive episodes and adversely affect psychosocial functioning as well as adjustment to widowhood.[35,36] In the context of bereavement, depressive reactions vary in intensity over time, and major, minor, and subsyndromal depressions may be pleomorphic manifestations of a homogeneous unipolar depressive episode. Recent epidemiologic data concerning depressive syndromes in

the community suggest the same is true in non–bereavement-related depression.[47]

3. Major depressive episodes in the wake of bereavement are chronic and recurrent

Clayton[41] found that 27% of widows and widowers meeting criteria for major depression remained depressed for at least 1 year. Similarly, we found that 28% of widows and widowers meeting criteria for major depression at 2 months continued to meet criteria at 13 months.[43] Thus, the chronicity of the depressions of widowhood is comparable to reports in the literature that 20% to 30% of patients with major depressive episodes can expect their depression to last for at least 1 year.[48] Furthermore, individuals who meet criteria for major depression at 2 months spend over 76% of their time over the next 2 years in a depressive category (major, minor, or subsyndromal depression) and only 24% of their time in an asymptomatic state,[36] similar to results found in nonbereaved patients with depression.[47] Thus, depressive syndromes seen immediately after bereavement tend to be as chronic and/or recurrent as other depressive disorders seen in nonbereaved samples.

4. Major depressive episodes associated with bereavement interfere with functioning

Compared with those who are not depressed, widows and widowers who meet criteria for major depression are more likely to feel ill, visit general medical physicians, have poor work performance, and have problems in interpersonal relationships with friends and relatives over the next 2 years.[36,43] They are less likely to remarry or get involved in new relationships during this time. Thus, the biopsychosocial casualties of depression associated with bereavement closely resemble those seen in other forms of depression.

5. Risk factors for major depressive episodes after bereavement

Since the risk for developing a major depressive episode after bereavement is substantial and the morbidity of untreated depression is great, it is important to identify risk factors. Other than gender, the risk factors for major depression after bereavement mimic those for depression in general: past history,[36] family history, substance use/abuse, and poor general medical health[34] are the most frequently cited risk factors.

6. Diagnostic conclusions

Depression following the death of a loved one can be differentiated from grief; symptoms find expression in various forms and intensities over time, are as chronic as other major depressive episodes, and interfere with functioning. Furthermore, risk factors for depression after bereavement are similar to those for other depressions. We therefore urge clinicians to diagnose major depressive episodes as major depression even within weeks or months of the loss of a loved one. Indeed, loss of a loved one is a risk factor for depression and should not be written off or rationalized. Just because grief is painful and disruptive and includes symptoms that overlap with symptoms of depression, it does not follow that a diagnosis of depression cannot be made in a bereaved individual. To deny diagnosis and treatment may be putting a large number of primarily older persons at risk for prolonged and unnecessary suffering.

To make the diagnosis of major depression shortly after the death of a loved one, several considerations should be kept in mind. First, there is substantial overlap in symptoms, since bereaved, nondepressed persons may have sadness, insomnia, poor concentration, and other symptoms found in depression. However, these symptoms tend to occur sporadically, in waves or bursts, in grief as compared with the relatively enduring patterns seen in depression. Second, the waves or "pangs" of grief tend to be precipitated by thoughts or reminders of the deceased, whereas in depression, the dysphoria is more autonomous. Third, certain depressive symptoms, such as psychomotor retardation, feelings of worthlessness, and actual suicidal plans are not generally seen in uncomplicated grief. When in doubt, family and past personal histories of depression may help tip the diagnostic balance. The overriding principle, however, is that if full symptomatic criteria for major depression are met, the diagnosis of depression should be made, regardless of time since death, and bereavement should be rated on Axis IV.

Treatment of Depression in the Bereaved

Fortunately, the unfounded notion that the treatment of depression in the bereaved interferes with grief is no longer held with near the tenacity it once was. Rather, it is believed that depression interferes with grief and that its effective treatment allows the bereaved person to more effectively adjust to the loss; denial of treatment of depression deprives persons of available relief. Although there are no data on the preventive effects of treatment, the consistent finding that past personal history is a risk factor for major depression after bereavement suggests that persons with past major depression—if not already on maintenance medication—should be considered for prophylactic treatment around the time of a significant loss.

Table 4. Management Guidelines for Depression Associated With Bereavement

If spouse at high risk for depression (e.g., past history of depression), consider primary prevention before the loss
Within the first 2 months, treat major depressive episode if:
Past history of major depression episode
Symptoms or impairment marked
Psychomotor retardation, feelings of worthlessness, or suicidal ideation present
Patient requests active treatment
After the first 2 months, treat major depressive episode or minor depression like any non–bereavement-related depression
Always consider an integrative approach including psychoeducation, psychotherapy, and psychopharmacology

At least 2 open studies[49,50] and 1 controlled study[51] suggest efficacy of antidepressant treatment for major depressive episodes several months after bereavement. In the open studies, both Jacobs et al.[49] and Pasternak et al.[50] found that desipramine and nortriptyline, respectively, provided substantial symptomatic relief of depressive symptoms in men and women who had been bereaved for at least 6 months and experienced major depressive episodes. While grief intensity lessened, significant grief issues remained even after successful treatment of the depression. Treatment of depression did not adversely affect grief. In a more recent double-blind, controlled study, Reynolds et al.[51] found nortriptyline to be more effective than placebo in treating major and minor depressive syndromes following bereavement. Interpersonal psychotherapy was not more effective than no psychotherapy, but did improve treatment adherence when combined with nortriptyline. In related open studies and case series, Zisook and Shuchter[52] found an integrative approach involving both antidepressant medications and grief-specific psychotherapy effective; Miller et al.[53] found interpersonal psychotherapy effective for depressions associated with bereavement; and Zygmont et al.[54] found paroxetine effective for what they termed "traumatic bereavement," a syndrome of intense grief with symptoms reminiscent of posttraumatic stress disorder. Although the focus of the latter study was not major depression, over three quarters of the subjects had depressive spectrum disorders. The study is also notable in that both grief intensity and depressive symptoms responded robustly to paroxetine.

None of these studies deals specifically with major depressive syndromes seen within the first 2 months after the death of a loved one. However, preliminary results of one small, open study using bupropion sustained release to treat major depressive episodes seen 6 to 8 weeks after spousal bereavement have been encouraging.[55] Over two thirds of the patients had a good antidepressant response, and scores on grief intensity measures also showed improvement. This preliminary study further supports the advisability of prompt, aggressive treatment of major depression, even when it occurs immediately after the loss of a loved one. Table 4 summarizes treatment guidelines.

CONCLUSION

Dementia and bereavement are 2 of many adverse life experiences that are all too common in later life. These 2 syndromes may precipitate major depressive episodes in vulnerable persons and may delay recognition, diagnosis, and treatment of depressive episodes. In both conditions, symptom overlap with depression makes diagnosis challenging. In addition, the depression seen after either of these situations may have multiple and diverse manifestations over time. Untreated, the depression can have devastating results. Awareness that dementia and bereavement are risk factors for the onset or worsening of major depression should better arm clinicians to initiate prompt and appropriate treatment.

Drug names: amitriptyline (Elavil and others), bupropion (Wellbutrin), citalopram (Celexa), clomipramine (Anafranil and others), desipramine (Norpramin and others), fluoxetine (Prozac), nortriptyline (Pamelor and others), paroxetine (Paxil).

REFERENCES

1. Roberts RE, Kaplan GA, Shema SJ, et al. Does growing old increase the risk of depression? Am J Psychiatry 1997;154:1384–1390
2. Reynolds CF III. Treatment of depression in special populations. J Clin Psychiatry 1992;53(9, suppl):45–53
3. Zisook S, Downs NS. Diagnosis and treatment of depression in late life. J Clin Psychiatry 1998;59(suppl 4):80–91
4. Bolla KI, Lindgren KN, Bonaccorsy C, et al. Memory complaints in older adults: fact or fiction? Arch Neurol 1991;48:61–64
5. Robins CJ, Luten AG. Sociotropy and autonomy: differential patterns of clinical presentation in unipolar depression. J Abnorm Psychol 1991;100: 74–77
6. Cassens G, Wolfe L, Zola M. The neuropsychology of depression. J Neuropsychiatry Clin Neurosci 1990;2:202–212
7. Devanand DP, Sano M, Tang MX, et al. Depressed mood and the incidence of Alzheimer's disease in the elderly living in the community. Arch Gen Psychiatry 1996;53:175–182
8. Yaffe K, Blackwell T, Gore R, et al. Depressive symptoms and cognitive decline in nondemented elderly women: a prospective study. Arch Gen Psychiatry 1999;56:425–430
9. Chen P, Ganguli M, Mulsant BH, et al. The temporal relationship between depressive symptoms and dementia: a community-based prospective study. Arch Gen Psychiatry 1999;56:261–266
10. Forsell Y, Winblad B. Major depression in a population of demented and nondemented older people: prevalence and correlates. J Am Geriatr Soc 1998;46:27–30
11. Kiloh L. Pseudodementia. Acta Pscyhiatr Scand 1961;37:336–351
12. Wells CE. Pseudodementia. Am J Psychiatry 1979;136:895–900
13. Yesavage J. Differential diagnosis between depression and dementia. Am J Med 1993;94:23S–28S
14. Raskind MA. The clinical interface of depression and dementia. J Clin Psychiatry 1998;59(suppl 10):9–12
15. Himmelhoch JM, Auchenbach R, Fuchs CZ. The dilemma of depression in the elderly. J Clin Psychiatry 1982;43(9, sec 2):26–32
16. Alexopoulos GS, Meyers BS, Young RC, et al. The course of geriatric depression with "reversible dementia": a controlled study. Am J Psychiatry 1993;150:1693–1699
17. Reifler BV, Larson E, Poulsen M. Dementia of the Alzheimer's type and depression. J Am Geriatr Soc 1986;34:855–859
18. Cummings JL. Depression and Parkinson's disease: a review. Am J Psychiatry 1992;149:443–454
19. Alexopoulos GS, Meyer BS, Young RC, et al. 'Vascular depression' hypothesis. Arch Gen Psychiatry 1997;54:915–922
20. Koenig HG, Blazer DG. Minor depression in late life. Am J Geriatr Psychiatry 1996;4(suppl):S14–S21

21. Katz IR. Diagnosis and treatment of depression in patients with Alzheimer's disease and other dementias. J Clin Psychiatry 1998;59(suppl 9):38–44
22. American Psychiatric Association. Practice Guideline for the Treatment of Patients With Alzheimer's Disease and Other Dementias of Late Life. Am J Psychiatry 1997;154(suppl 5):1–39
23. Cummings JL, Ross W, Absher J, et al. Depressive symptoms in Alzheimer disease: assessment and determinants. Alzheimer Dis Assoc Disord 1995;9: 87–93
24. Katz IR. On the inseparability of mental and physical health in aged persons: lessons from depression and medical comorbidity. Am J Geriatr Psychiatry 1996;4:1–16
25. Pearson JL, Teri L, Reifler BV, et al. Functional status and cognitive impairment in Alzheimer's patients with and without depression. J Am Geriatr Soc 1989;37:1117–1121
26. Fitz AG, Teri L. Depression, cognition, and functional ability in patients with Alzheimer's disease. J Am Geriatr Soc 1994;42:186–191
27. Reifler BV, Teri L, Raskind M, et al. Double-blind trial of imipramine in Alzheimer's disease patients with and without depression. Am J Psychiatry 1989;146:45–49
28. Nyth AL, Gottfries CG. The clinical efficacy of citalopram in treatment of emotional disturbances in dementia disorders: a Nordic multicentre study. Br J Psychiatry 1990;157:894–901
29. Petracca G, Teson A, Chemerinski E, et al. A double-blind placebo-controlled study of clomipramine in depressed patients with Alzheimer's disease. J Neuropsychiatry Clin Neurosci 1996;8:270–275
30. Taragano FE, Lyketsos CG, Mangone CA, et al. A double-blind, randomized, fixed-dose trial of fluoxetine vs amitriptyline in the treatment of major depression complicating Alzheimer's disease. Psychosomatics 1997;38: 246–252
31. Katona CL, Hunter BN, Bray J. A double-blind comparison of the efficacy and safety of paroxetine and imipramine in the treatment of depression with dementia. Int J Geriatr Psychiatry 1998;13:100–108
32. Teri L. Behavioral treatment of dementia: an overview. Semin Clin Neuropsychiatry 1997;2:100–101
33. Schneider LS, Reynolds CF, Lebowitz BD, et al. Diagnosis and Treatment of Depression in Later Life: Results of the NIH Consensus Development Conference. Washington, DC: American Psychiatric Press; 1994
34. Zisook S. Major depression associated with widowhood. Am J Geriatr Psychiatry 1993;1:316–317
35. Zisook S, Shuchter SR, Sledge PA, et al. The spectrum of depressive phenomena after spousal bereavement. J Clin Psychiatry 1994;55(4, suppl): 29–36
36. Zisook S, Paulus M, Shuchter SR, et al. The many faces of depression following spousal bereavement. J Affect Disord 1997;45:85–94
37. Freud S. Mourning and melancholia. In: Strachey J, ed. Standard Edition of the Complete Psychological Works of Sigmund Freud. London, England: Hogarth Press; 1975;4:152
38. Abraham K. Notes on the psychoanalytical investigation and treatment of manic-depressive insanity and allied conditions. In: Selected Papers of Karl Abraham. London, England: Hogarth Press; 1948:137
39. Clayton PJ, Halikas JA, Maurice WL. The depression of widowhood. Br J Psychiatry 1972;120:71–77
40. Clayton PJ. The sequelae and nonsequelae of conjugal bereavement. Am J Psychiatry 1979;136:1530–1534
41. Bornstein PE, Clayton PJ, Halikas JA, et al. The depression of widowhood after thirteen months. Br J Psychiatry 1973;122:561–566
42. Clayton PJ. Bereavement and depression. J Clin Psychiatry 1990;51(7, suppl):34–38
43. Zisook S, Shuchter SR. Uncomplicated bereavement. J Clin Psychiatry 1993;54:365–372
44. Zisook S, Shuchter SR, Irwin M, et al. Bereavement, depression, and immune function. Psychiatry Res 1994;52:1–10
45. American Psychiatric Association. Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition. Washington, DC: American Psychiatric Association; 1994
46. Zisook S, Shuchter SR. Depression through the first year after the death of a spouse. Am J Psychiatry 1991;148:1346–1352
47. Judd LL, Akiskal HS, Maser JD, et al. A prospective 12-year study of subsyndromal and syndromal depressive symptoms in unipolar major depressive disorders. Arch Gen Psychiatry 1998;55:694–700
48. Keller MB, Lavori PW, Mueller TI, et al. Time to recovery, chronicity, and levels of psychopathology in major depression: a 5-year prospective follow-up of 431 subjects. Arch Gen Psychiatry 1992;49:809–816
49. Jacobs S, Nelson JD, Zisook S. Treating depressions of bereavement with antidepressants: a pilot study. Psychiatr Clin North Am 1987;10:501–510
50. Pasternak RE, Reynolds CF III, Schlernitzauer M, et al. Acute open-trial nortriptyline therapy of bereavement-related depression in late life. J Clin Psychiatry 1991;52:307–310
51. Reynolds CF III, Miller MD, Pasternak RE, et al. Treatment of bereavement-related major depressive episodes in later life: a controlled study of acute and continuation treatment with nortriptyline and interpersonal psychotherapy. Am J Psychiatry 1999;156:202–208
52. Zisook S, Shuchter SR. Psychotherapy of the depressions in spousal bereavement. In Session Psychother Pract 1996;2:31–45
53. Miller MD, Frank E, Cornes C, et al. Applying interpersonal psychotherapy to bereavement-related depression following loss of a spouse in late life. J Psychother Pract Res 1994;3:149–162
54. Zygmont M, Prigerson HG, Houck PR, et al. A post hoc comparison of paroxetine and nortriptyline for symptoms of traumatic grief. J Clin Psychiatry 1998;59:241–245
55. Zisook S, Shuchter SR, Deaciuc SC, et al. Bupropion sustained release treatment of bereavement. In: New Research Program and Abstracts of the 152nd Annual Meeting of the American Psychiatric Association; May 20, 1999; Washington, DC. Abstract NR667:257

Discussion

Dementia and Bereavement: Adverse Life Experiences Complicating Depression in Later Life

Dr. Montgomery: What recommendations would you like to make?

Dr. Zisook: One main point is that we do people a disservice by maintaining the term *bereavement* in DSM-IV. (In DSM-III, the term used was *uncomplicated bereavement*.) It's maintained on the basis of outworn notions of "reactive" depression and clinical "wisdom" and because there are overlapping symptoms, which is true of all of the problems we are talking about. One of the most common underlying conditions for major depression in late life is loss of a loved one, and these people are being systematically ignored and untreated not only by primary care physicians but also by psychiatrists. Therefore, I would recommend that we eliminate the term *bereavement* as a V-code. There is no other condition that negates major depression. If you develop major depression in the context of divorce or loss of income, you are depressed. If you develop it in the context of bereavement, which also precipitates depression, you are not considered depressed. Also, there is no other condition that is negated by the life event of bereavement. If you develop panic attacks after a spouse dies and have 5 spontaneous panic attacks in a week, you have panic disorder. Cardiovascular risk in bereavement is substantial, but if you develop chest pain, no cardiologist will dismiss it as bereavement.

Dr. Montgomery: I've never understood why that should be. When we looked at early studies in depression, which included bereaved patients, before it was made an exclusion criterion, they showed a good drug-placebo effect.

Dr. Salzman: But there is one condition that does negate depression, which is the whole point of this conference, and that's aging. I think the elegance of your data serves as a model for everything we are discussing. It is important to consider depression and its impact on individuals, as well as society, as opposed to whether it's understandable. It's the actual presence of depression that's important.

Dr. Zisook: And late-life depression that's not vascular—the first onset of late-life depression—is more likely to occur in the context of loss, and when it occurs it's like any other depression and needs to be treated.

Dr. Beekman: I was impressed by your data and liked the parallels that emerged: bereavement, dementia, physical illness. The question is: Would you suggest throwing out of our classification any mention of whether bereavement is associated with depression? Should we recommend that our diagnostic statement be enlarged with bereavement as a probable etiologic factor?

Dr. Montgomery: Specifically, would you accept, for the purpose of our guidelines, that we say bereavement should not be a bar to diagnosing and treating major depression?

All: Absolutely.

Dr. Sadavoy: Are your data generalizable in terms of the populations?

Dr. Zisook: That is a good question, and I don't know. We studied a predominantly white, middle-class population, most of whom had some college education. It would be good to do a similar study in other populations. The data are generalizable to other stressors, in the sense that this is simply a stressful life event.

Dr. Sadavoy: Are we dealing with a stress model? Rather than focusing only on specific events, such as bereavement or chronic disability, we should talk about the stress factors of old age. Depression or depressive mood associated with stress should not be ignored or attributed to the stress itself.

Dr. Montgomery: In your presentation, you also asked us to consider pseudodementia and whether the term should be abolished.

Dr. Zisook: Currently, the term continues to be used. Even physicians dealing with the elderly continue to diagnose pseudodementia and, in a way, deny that dementia is there.

Dr. Thompson: I agree that we are looking at a formulation in which, if you have depression and dementia together, you make both diagnoses.

Dr. Montgomery: If early dementia and depression occur together, the dementia appears to worsen, which is a good parallel with the model for physical illness and depression.