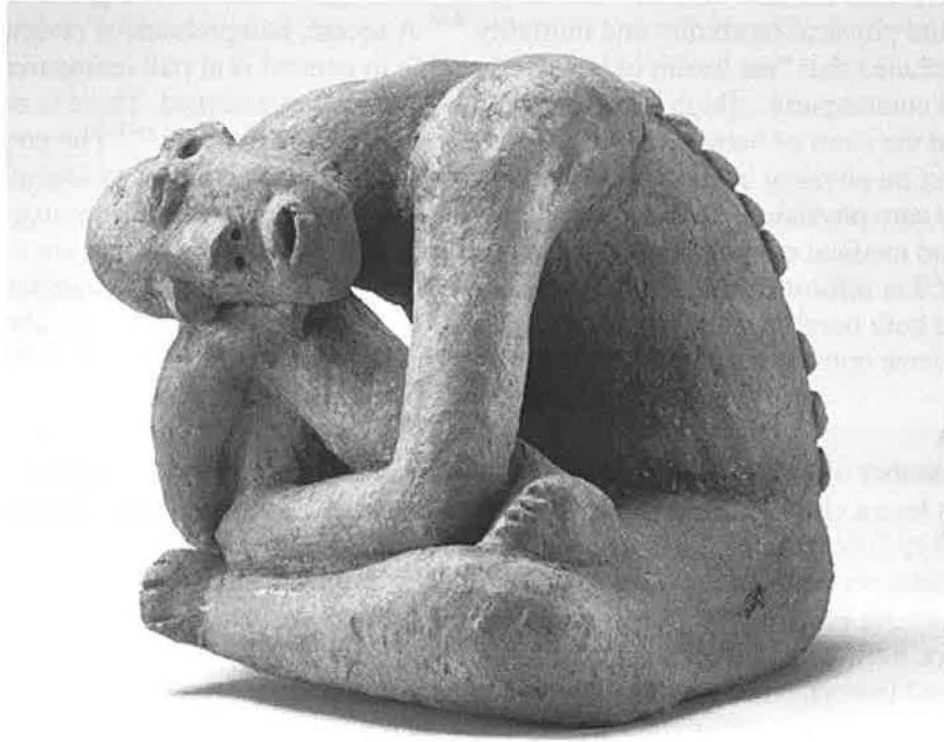


Grief: An Internist's Perspective



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One of the commonly quoted statistics in the field of palliative care is that worldwide the death rate is remaining constant over time at 100%. Losing a loved one is at once a normal part of life, and the most stressful occurrence of a lifetime.^{1,2} As physicians we face this universal phenomenon both personally and professionally. As we age, and as the population ages, our contact with bereavement through both our own losses and those of patients becomes more common. Most people survive bereavement and the feelings of grief that result relatively intact and without the need for intervention,³ but bereavement is associated with heightened risk for both mental and physical morbidity and mortality.⁴⁻²⁴ A recent, comprehensive review of the literature concluded that “the health of bereaved people in general is at risk (compared to their non-bereaved counterparts...[high risk] has by now been well-established. There is no longer any doubt that the costs of bereavement in terms of health can be extreme.”²⁵ The potential for adverse impact on physical health makes bereavement of particular concern to internists and other primary care physicians. This paper will review the normal process of grieving, the psychiatric and medical complications that can occur, and the interventions that are available. Awareness of this information not only gives us insight into this universal phenomenon, helping us understand both ourselves and our patients, but provides an opportunity to recognize patients at risk for adverse outcomes and assist them at a time when they are most vulnerable.

Introduction

The number of people who become bereaved each year is enormous. Between 5 and 9% of Americans lose a close family member each year.² Nearly 2.5 million U.S. citizens died in 2003, and left in their wake multiple millions of survivors to grieve the loss.²⁶ As expected, the burden falls predominantly in the older age groups. The 2003 U.S. Census data reveal that approximately 75% of all deaths occurred in persons aged 65 years and older and that only 3% of all deaths were from unnatural causes (e.g., 1.8% died in motor vehicle collisions and 1.2% from firearms-related injury). Nearly half of all women age 65 and older are widows.²⁷ Given that widowed people visit physicians significantly more than when they were married, even after adjusting for age, sex, and socioeconomic and health status,²⁸ it is likely that bereavement will increasingly be an issue for US physicians.

Normal Grieving

Historically, grief has been regarded as a normal process which, though causing significant impairment, does not warrant intervention. Among the earliest studies of bereavement in the literature is Sigmund Freud's 1917 work, “On Mourning and Melancholia” in which he describes the feelings of grief associated with bereavement, and recognizes grief as a condition distinct from the disorder of depression (“melancholia”). He notes that the act of grieving “involves grave departures from the normal attitude to life...It never occurs to us to regard it as a pathological condition and to refer it to medical treatment” and instead rely on “its being overcome after a certain lapse of time” and view “any interference with it as useless and even harmful.”²⁹ The medical profession and society at large have generally concurred with this position, and for most people grief is overcome by “lapse of time.”³ Society does not consider the bereaved to be sick, nor do bereaved individuals consider themselves ill. Nonetheless, feelings of grief are remarkably consistent in their presentation, and are often severe and disabling.

Initial Response

Eric Lindemann was among the first to make a systematic study of the process of grieving when he interviewed those who had lost loved ones in the Coconut Grove fire in Boston in 1942.³⁰ He observed:

The picture shown by people in acute grief is remarkably uniform. Common to all is the following syndrome: sensations of somatic distress occurring in waves lasting from 20 minutes to an hour at a time, a feeling of tightness in the throat, choking with shortness of breath, need for sighing, an empty feeling in the abdomen, lack of muscular power, and an intensive subjective distress described as tension or pain.

The initial response for many is a sense of shock, numbness, and disbelief: “subjectively, survivors may feel like they are wrapped in a cocoon or blanket; to others, they may look as though they are holding up well. Because the reality of death has not yet penetrated awareness, survivors can appear to be quite accepting of the loss.”² Even when a loss is anticipated, they are surprised at how much pain the death brings and may have a hard time believing that it has occurred.³¹⁻³³ Survivors also report insomnia, absentmindedness, problems concentrating, failures of memory, and the tendency to do the same things over and over again. The pain is often described as coming in waves, leaving the bereaved person feeling fine one minute and overwhelmed the next. Joan Didion, in her National Book Award winning memoir, The Year of Magical Thinking, writes, “Grief comes in waves, paroxysms, sudden apprehensions that weaken the knees and blind the eyes and obliterate the dailiness of life.”³⁴ Nowhere is this process more beautifully described than in the diary C.S. Lewis kept after the death of his wife, later published as A Grief Observed:

No one ever told me that grief felt so like fear. I am not afraid, but the sensation is like being afraid. The same fluttering in the stomach, the same restlessness, the yawning. I keep on swallowing. At other times, it feels like being mildly drunk, or concussed. There is a sort of invisible blanket between the world and me. I find it hard to take in what anyone says. Or perhaps, hard to want to take it in. It is so uninteresting. Yet I want the others to be about me. I dread the moments when the house is empty. If only they would talk to one another and not to me. There are moments, most unexpectedly, when something inside me tries to assure me that I don't really mind so much, not so very much, after all... Then comes a sudden jab of red-hot memory and all the 'commonsense' vanishes like an ant in a furnace.³⁵

The strongest and most frequent feelings are those of yearning for the deceased, but also include intense feelings of sadness, anxiety about the future, disorganization, and emptiness. The bereaved may exhibit searching behaviors, experience visual and auditory hallucinations, and often feel like they are going crazy. Over time the intensity of the shock diminishes; and patients may have difficulty adapting to the change, avoid places and people associated with the deceased, feel angry toward the physician, health care system, or even the lost loved one, or feel guilty about what they did or did not do for the before the loss. Depressive symptoms often occur but are usually transient.¹⁰

The Stage Theory of Bereavement

Our understanding of how these feelings resolve with time has changed somewhat over the last decades. Psychiatrist Elisabeth Kubler-Ross's book "On Death and Dying" came out in 1969³⁶ and popularized the idea that patients facing death go through a series of stages on the road to acceptance of death. A similar theory was put forth for adjustment to bereavement,^{37, 38} suggesting that normal grief involves an orderly progression through the following stages: disbelief or shock; separation distress or yearning; angry protest; depressed mood or despair; and ultimate acceptance of or recovery from the loss.³⁹ This stage theory of grief resolution (Figure 1a⁴⁰) has had enormous appeal and acceptance among bereavement experts and laypersons.^{37-39, 41} Recently, data has emerged indicating that grief does not, in fact, resolve in clear-cut stages,⁴² but that instead bereaved subjects experience all of these feelings simultaneously, and that the strength of each feeling abates slowly over time. Figure 1b⁴⁰ shows data from the Yale Bereavement study in which 281 community-based

Fig. 1a

Frequency

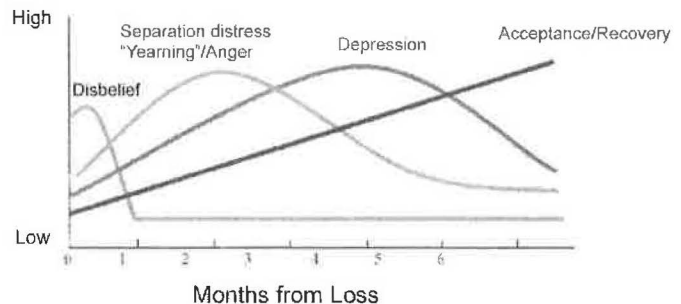
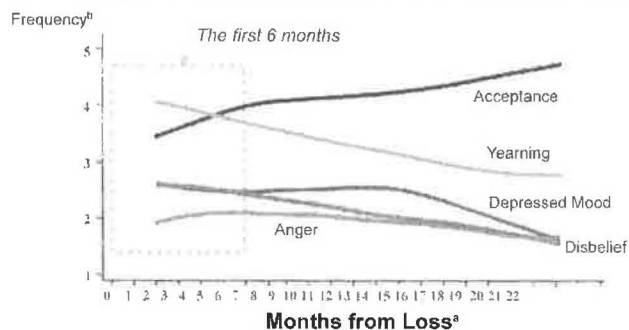


Fig. 1b Unadjusted Mean Grief Resolution Scores Over Time



a: All of the lines start from 2 months after loss and end at 20 months
b: 1=Less than once a month; 2=Monthly; 3=Weekly; 4=Daily; 5=Several times a day except for indicator of "depressed mood"

participants were followed for 22 months starting two months after bereavement. One limitation of the study is that data collection did not begin until month 2, so it may be that the severity of disbelief as response is underestimated, but nonetheless two things are clear. 1.) Yearning is the most frequently endorsed reaction at two months and remains the most common negative symptom throughout the study period, and 2.) Distinct stages of resolution do not exist – the strength of each of the negative

responses diminishes over time as acceptance slowly increases. By six months post-loss most bereaved individuals are at least partially back on their feet with limited signs of impairment.³

Some bereaved individuals do so remarkably well that there is speculation that they either did not have a good relationship with the deceased⁴³⁻⁴⁶ or are denying their feelings^{29, 37, 44, 45, 47} and that intervention ought to be undertaken to get them in touch with their feelings. Recent evidence suggests that this may simply be a more resilient group of individuals who are not denying loss, and are unlikely to benefit from intervention.^{47, 48}

Different Kinds of Losses

Each loss is as individual as the person who is gone, but there are some trends in how people respond to different types of bereavement. The loss of a parent, particularly one who dies after a long life, is heartbreaking but expected, and perhaps consequently, relatively unstudied. Joan Didion writes poignantly about the loss of her parents: "What I felt in each instance was

sadness, loneliness (the loneliness of the abandoned child of whatever age), regret for time gone by, for things unsaid, for my inability to share or even in any real way to acknowledge, at the end, the pain and helplessness and physical humiliation they each endured. I understood the inevitability of each of the deaths. I had been expecting (fearing, dreading, anticipating) those deaths all my life.”³⁴ Most people tolerate the loss relatively well,^{49, 50} though some are at risk of complicated bereavement (details below). In particular, single men who lose their mothers are at increased risk of suicide. There is also “a subtle role change” when an adult loses a parent, “propelling the adult into the next stages of life... This, coupled with the awareness that there are no longer parents to fall back on, may effect a more mature stance in parentally bereaved adults who no longer think of themselves as children.”²

The loss of an older relative after a full life does not have the psychological impact of the death of a spouse or a child. Conjugal bereavement is by far the most studied type of loss in the literature. There are some differences between men and women in response to loss of their spouse. Women are more likely to describe the loss in terms of abandonment, men in terms of dismemberment.⁵¹ Loss of an adult child results in more intense or persistent grief⁵²⁻⁵⁴ than conjugal bereavement or loss of a parent.

Miscarriage and death of a newborn may be not recognized as major losses but can precipitate prolonged grief. Bereavement due to suicide or other socially disapproved deaths may lead to more isolation and an increased vulnerability to suicide among some survivors.⁵⁵

Most deaths are not sudden. It has long been taught that patients and families can begin to process a loss in advance of the actual loss if there is warning of its impending arrival. However, this does not seem to initiate separation between the patient and family member, and often results in an increase in closeness. Evidence suggests that the grieving process is not really mitigated by “anticipatory grief” but that when deaths are sudden, the risk of prolonged grief is greater.^{51, 56}

Mental Health Complications of Bereavement

Bereavement can result in significant mental health problems for vulnerable segments of the population. For example, when Parkes studied patients admitted to a psychiatric hospital in the early 1960’s, the number of patients whose illness followed the loss of a spouse was significantly greater than anticipated for people of that age and social group.⁵⁷ There are three major psychiatric disorders that can emerge as a consequence of the loss of a loved one: bereavement-related Major Depressive Disorder (MDD), Posttraumatic Stress Disorder (PTSD), and Complicated Grief. Zisook and Shuchter⁵⁸ reported that 24% of their widowed sample met criteria for depressive episodes and 10% met criteria for Posttraumatic Stress Disorder at two months post-loss. Barry et al.⁵⁹ found that at four months post-loss the rate of Major Depressive Disorder in the first 122 participants enrolled Yale Bereavement Study was 9%, the rate of Posttraumatic Stress Disorder was 5.7%, and the rate of Complicated Grief was 10.7%. Complicated Grief is a distinct syndrome^{5-9, 13} and overlap with MDD and PTSD is modest.⁵⁹ Most of those bereaved subjects diagnosed with either Major Depressive, Posttraumatic or Panic Disorder did not meet criteria for Complicated Grief [10/16 (62.5%)] (although it should be noted that a diagnosis of Complicated Grief does confer increased risk of depressive symptoms and major depressive episodes).^{7-10, 12, 15, 40} Recent analysis of the Yale Bereavement Study sample revealed that of 16/135 (12%) of subjects who met criteria for Complicated Grief, only 6/16 (37.5%) also met criteria for either Major Depressive, Posttraumatic or Panic Disorder. Traumatic losses of very close relatives or friends prove exceptional circumstances in which both symptoms of Complicated Grief and Posttraumatic Stress Disorder may co-occur. A detailed discussion of PTSD and MDD is beyond the scope of this review, but Complicated Grief will be discussed because of the wealth of new data available, and the possibility that it will, for the first

time, be included in the DSM. Internists should be able to recognize this syndrome because it helps identify patients at increased risk for ongoing psychiatric difficulties and an increased risk of suicide.

Complicated Grief

The syndrome of complicated, or prolonged grief (which has also been referred to in the literature as pathological grief, abnormal grief, atypical grief, and pathological mourning) has characteristic symptoms, risk factors, predictable course, and outcomes.^{31, 60} Even Lindemann observed that a small segment of the population he studied exhibited “morbid grief reactions” and needed help getting through the grieving process.³⁰ The bereaved with Complicated Grief have deep mental anguish stemming from their psychological protest against the reality of the loss and a general reluctance to make adaptations to life in the absence of the loved one. The syndrome is characterized by intense longing and yearning for the person who died, and recurrent, intrusive and distressing thoughts about the absence of the deceased make it difficult for survivors to concentrate and to move beyond an acute state of mourning and live in the present. For many, there is a sense that a part of themselves died along with their loved one and that the rest of their life is destined to be empty, dissatisfying and spent missing the deceased. In contrast with bereaved survivors with uncomplicated grief, those with Complicated Grief are essentially frozen or stuck in a state of chronic mourning.³

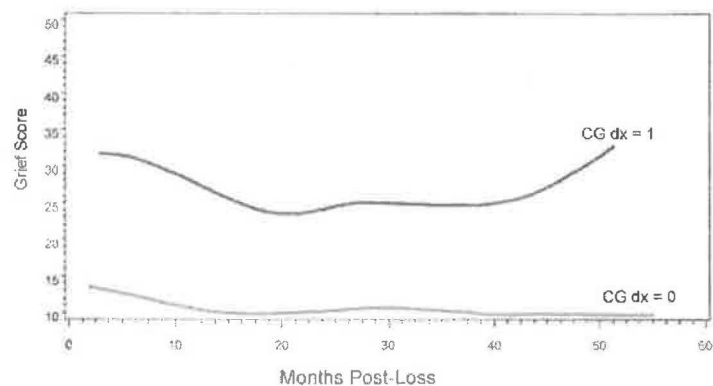
Complicated grief is defined as the persistence, for at least six months, of a constellation of disruptive emotional reactions including yearning^{3, 7, 10, 11} and four of the following eight symptoms: difficulty moving on, numbness/detachment, bitterness, feelings that life is empty without the deceased, trouble accepting the death, a sense that the future holds no meaning without the deceased, being on edge or agitated, difficulty trusting others since the loss. Other indicators include social withdrawal and difficulty re-engaging with life.

Table 1 **Criteria for Complicated Grief Proposed for DSM-V⁴⁰**

Criteria	Description
Criterion A	<p>Yearning, pining, longing for the deceased.</p> <p>Yearning must be experienced at least daily over the past month or to a distressing or disruptive degree.</p>
Criteria B	<p>In the past month, the person must experience four of the following eight symptoms as marked, overwhelming or extreme.</p> <ol style="list-style-type: none"> 1. Trouble accepting the death 2. Inability trusting others since the death 3. Excessive bitterness or anger about the death 4. Feeling uneasy about moving on with one's life (e.g., difficulty forming new relationships) 5. Feeling emotionally numb or detached from others since the death 6. Feeling life is empty or meaningless without the deceased 7. Feeling the future holds no meaning or prospect for fulfilment without the deceased 8. Feeling agitated, jumpy or on edge since the death
Criterion C	<p>The above symptom disturbance causes marked dysfunction in social, occupational, or other important domains.</p>
Criterion D	<p>The above symptom disturbance must last at least 6 months.</p>

Factors that put an individual at higher risk for Complicated Grief include childhood abuse and serious neglect,⁶¹ childhood separation anxiety,⁶² kinship relationship to the deceased (parents, spouses and offspring the most adversely affected),^{52, 63} insecure attachment styles, intense marital closeness and dependence,⁶⁰ lack of preparation for the death⁵⁹ and, in parental bereavement, few or no remaining children.⁶⁴ Taken together, these results suggest that bereaved patients with attachment difficulties, and those who feel unprepared before the death and unsupported after it, are at heightened risk of Complicated Grief. Symptoms of Complicated Grief at six months post-loss are highly predictive of impairment and complications at 13 and 24 months post-loss.^{5, 6} The criteria require that the symptoms be of six months duration in order to make the diagnosis, but these patients have levels of grief that as early as two months post-loss are significantly higher than those who later turn out not to be experiencing this syndrome. Figure 2⁴⁰ displays the mean grief resolution scores (a summation of the nine symptoms presented in Table 1) over time from loss for those with and without Complicated Grief diagnosed at six months post-loss. In contrast with Figure 1, which illustrates a significant average decline in grief symptoms and associated distress by six months post-loss, the mean grief score remains stably high from 2-50 months post-loss for the group diagnosed with Complicated Grief.⁴⁰ In the absence of intervention, the symptoms are remarkably persistent.^{65, 66}

Fig. 2 Mean Grief Score Over Time, Stratified by Complicated Grief Diagnosis



Given the severity of distress experienced by bereaved persons with Complicated Grief, it is not surprising that, even when the influence of Major Depressive Disorder is taken into account, sufferers of Complicated Grief are at heightened risk for suicidal thoughts and behaviors.^{4, 6, 63, 67} Complicated Grief among the bereaved is also associated with heightened risk of other physical and mental impairments. Complicated Grief has been associated with an increased risk of cancer, hypertension, and adverse cardiac events,^{5-10, 38, 39} as well as disability, functional impairments (social, family, and occupational dysfunction), adverse health behaviors such as alcohol and cigarette consumption, hospitalization, and reduced quality of life.¹²⁻¹⁵ For example, in one study, bereaved individuals with Complicated Grief at six months were 1.11 times more likely to develop hypertension at 13 months, 2.72 times more likely to develop depression at 13 months, 16.7 times more likely to experience a change in their smoking habits, and 7.02 times more likely to report change in their eating habits 13 months post-loss. It was also found that bereaved persons experiencing Complicated Grief at six months were more likely to have heart trouble (relative risk = 1.15), and alcohol consumption problems at 25 months post-loss (relative risk = 1.25).⁷

Awareness of the risk factors for complications of bereavement may help providers identify those at highest risk for adverse outcomes in advance. Family members who are identified as having poor coping strategies and inability to accept the inevitability of loss might be referred for mental health interventions before the death occurs. A physician caring for a dying person might be able to prepare survivors for the impending death, encourage them to say their "goodbyes" and to address unresolved issues. The literature suggests that the most acutely

grief-stricken tend to be less likely to seek services from health care professionals than those without bereavement-related complications,⁶⁸ which makes it challenging to connect them with the kind of help they need post-loss. Clinicians should be proactive in identifying and following bereaved persons with risk factors that predispose them to Complicated Grief to help minimize the adverse consequences of poor bereavement adjustment.

There is no definitive evidence for pharmacologic intervention for Complicated Grief. Open trials of selective serotonin reuptake inhibitors have been conducted and suggest the promise of these and similar agents for the reduction of Complicated Grief symptom severity (use of Paroxetine resulted in a 53% reduction in symptoms of complicated grief⁶⁹), but randomized placebo-controlled trials are needed before more definitive conclusions can be drawn. Psychotherapeutic interventions, though still under investigation, appear promising.⁷⁰⁻⁷³ Shear et al.⁷⁴ recently described a psychotherapy developed specifically for Complicated Grief -- Complicated Grief Treatment. When compared with Interpersonal Psychotherapy, both treatments significantly reduced Complicated Grief symptoms, but the response rate was greater for Complicated Grief Treatment (51%) than for Interpersonal Psychotherapy (28%; $P = .02$) and the time to response was shorter for Complicated Grief Treatment ($P = .02$). To date, this is the first randomized, controlled trial of a psychotherapy drug for Complicated Grief and as such provides a solid evidence-base for guiding clinical intervention with bereaved persons with this newly defined disorder. Other studies have shown responses to crisis intervention, brief dynamic psychotherapy, and support groups.¹⁰

Bereavement Associated Depression

Bereavement is associated with a significant risk of depression. Rates of depression during the first year after the loss of a spouse (15-35%) are between four to nine times higher than in general population.⁵⁸ Suicide rates after loss of a spouse are elevated, particularly in older men and in the first year of bereavement.² The diagnosis of depression in the setting of grief can be challenging, because patients who are not depressed may experience a variety of vegetative symptoms, including disturbances of appetite and sleepless. According to Freud, the major difference between depression (“melancholia”) and grief or mourning, is that the latter does not involve a disturbance of “self-regard” and therefore is not pathologic.²⁹ Patients who, after two months, continue to experience hopelessness, helplessness, worthlessness, and guilt along with persistence of the initial and severe symptoms of early grief should be evaluated for depression. The only major difference in diagnostic criteria is that MDD cannot, per the *DSM-IV* guidelines, be diagnosed within two months of major bereavement. There is no data regarding the efficacy of initiating treatment prior to the two month cut-off. In differentiating depression from Complicated Grief, it should be remembered that symptoms of apathy, psychomotor retardation, and anhedonia are all depressive symptoms whereas symptoms of yearning for the deceased, disbelief about the death, feeling emotionally numb and detached from significant others since the death, and feeling bitter and agitated about the death are all specific indicators of Complicated Grief.^{7,9}

There appears little novel to recommend for depressed bereaved patients beyond referring to standard practice guidelines for the treatment of Major Depressive Disorder,⁷⁵ which include the prescription of selective serotonin reuptake inhibitors or tricyclic antidepressants. There are pre-loss interventions that can help decrease the risk of depression in survivors. One example is hospice enrollment. Early hospice enrollment may reduce the risk of Major Depressive Disorder during the first 6-8 months of bereavement.⁷⁶ This may be a function of hospice preparing the survivors for the death, or may reflect a tendency of those who are better able to accept change

and the coming death to prefer hospice. Barry et al.⁵⁹ found that the perception of the death as more violent was associated with Major Depressive Disorder at four months post-loss. Steps to minimize the perceived violence of the death may help minimize post-loss complications.

Similarly, a study conducted in the Netherlands⁷⁷ indicated that the bereaved family and friends of cancer patients who died by euthanasia had less severe grief symptoms and posttraumatic stress reactions than the bereaved of comparable cancer patients who died a natural death. Because family members of patients who opted for euthanasia would be expected to be more accepting of and prepared for the death than those who did not, this may reduce the risk of developing complications and make the grieving process less painful for the survivors.

A 29-year-old woman comes to the physician for a consultation one month after her 7-year-old daughter was killed in a motor vehicle collision. The patient is upset and restless and wrings her hands frequently. She cannot sleep at night, has lost her appetite, and cries easily and frequently. She is preoccupied with thoughts of her daughter and sometimes thinks she momentarily sees her daughter sitting in the living room. She says she wishes that she had been hit by the car, too. She denies any thoughts of killing herself. Which of the following is the best explanation for these findings?

- (A) Dysthymic disorder
- (B) Major depressive disorder
- (C) Normal grief reaction
- (D) Obsessive-compulsive disorder
- (E) Schizoaffective disorder

Health Effects of Grieving

Bereavement is a very stressful event, and historically, the feelings experienced as grief have been associated with the heart. A widower who quickly follows his spouse to the grave is said to have died of a broken heart, and we do not, as a culture, find it strange when this happens. This cultural acceptance of potential adverse health effects of grief and bereavement is validated by the literature on bereavement. Even people with uncomplicated bereavement suffer adverse health consequences during a period of time after the loss. There is controversy about the magnitude of the effect, but it is very clear that older men are at increased risk for adverse physical outcomes. It is also well established that there are increases in alcohol consumption and smoking and greater use of tranquilizers or hypnotic medication (or both) among the bereaved. This is usually among people who are already using the substances, but there are some new users as well. Additionally, sleep deprivation and lack of exercise may exacerbate pre-existing health conditions.

The literature regarding excess mortality associated with bereavement ranges over many decades. Parkes et al first described in the 1950's the excess mortality associated with the period of bereavement. Generally, subsequent studies have confirmed that conjugal bereavement is associated with an increased risk of mortality in the surviving spouse compared with married persons of the same age,^{24, 78-91} although agreement is not universal.⁹²⁻⁹⁴ In their study of conjugal bereavement, Helsing and Szklo⁸¹ studied 4032 white persons aged 18 and over who became bereaved and matched them with married controls for race, sex, year of birth and geography of residence. In 12 years of follow-up, there was no excess mortality for women, but among widowed males the excess mortality was statistically significant in age groups 55-64 and 65-74 years. They suspected it was even higher in younger men, but the sample size was too

small to demonstrate it. In contrast to most other studies, the excess mortality did not start until the second year. Schaefer et al.²³ in a prospective study of 12,522 spouse pairs, found that among the 1453 men and 3294 women who became bereaved during the study period, there was excess mortality in both men and women (RR 1.9, CI 1.35-2.71), and excess mortality was again higher in the younger age groups. Although there are questions about whether there is excess mortality in women after conjugal bereavement, mortality is probably increased among both men and women after the death of a child. Li et al.⁷⁸ based on study of the Danish national registers, observed an overall mortality rate in mothers whose child had died (hazards ration of 1.43, 95% CI 1.24-1.64; $p<0.0001$). Excess mortality from natural causes was not observed for women until 10-18 years after the loss, but excess mortality from unnatural causes was higher both for men (RR 1.57, CI 1.06-2.32; $p=0.04$) and for women (RR=3.84, CI 2.48-5.88; $p<0.0001$) in the first three years after the loss. In a study of parents whose adults sons had been killed at war, there was increased mortality only among widowed or divorced mothers.⁹⁵

Mediators of Excess Mortality in the Period of Bereavement

The etiology of the increase in mortality above and beyond deaths by suicide and accidents has not been definitively explained. There are some who argue that mental stress in and of itself is deleterious to health, and that the excess mortality associated with bereavement is a response to extreme stress. Others argue that the increase in mortality is a function of changes in behavior, specifically in regard to poor sleep and increased use of alcohol and tobacco, in those who because of their age are already at increased risk for adverse outcomes. Finally, there are others who attribute the excess mortality to loss of social support (loss of the spouse or social network maintained primarily by the deceased spouse) or material support (loss of income, support in everyday tasks such as cleaning, preparing food, taking medication).⁸⁷ Those who adhere to the stress hypothesis suggest that the state of constant stress associated with bereavement takes a toll on the survivor, specifically in regard to cardiovascular health. Most theories are based on the idea that a prolonged state of adrenergic stress is the driving force, and there is evidence to suggest that bereavement is associated with endocrinologic changes.⁹⁶ This can cause not only adverse cardiac outcomes, but is hypothesized to result in immunosuppression that may then result in an increase in infectious disease and neoplasia.⁹⁷ For example, Irwin et al (1987)⁹⁸ studied NK activity and T cell subpopulations in women whose husbands were undergoing medical treatment for diagnosed metastatic lung cancer ($n=16$), women whose husbands had died of lung cancer in the prior 1 to 6 months ($n=10$), and women whose husbands were in good health ($n=11$). The women whose husbands were healthy had significantly higher levels of NK activity than both those whose husbands were being treated for cancer and those whose husbands had died.

Parkes et al⁸⁰ were among the first to document the increase in cardiac morbidity and mortality that occurs after bereavement. They found a 40% increase in the mortality rate among widowers in the first 6 months following bereavement, more than half of which was attributed to cardiovascular causes. Parkes & Weiss⁹⁹ showed that bereaved men with CHF and HTN are at particular risk for disease exacerbation in response to real or threatened loss of a relationship. Although some studies have confirmed this association^{83, 100}, other studies have not.^{86, 87, 101, 102} Kaprio et al.²⁴ reviewed data from over 95,000 persons widowed between 1972-1976, and found that the excess mortality from natural causes was greatest in the first week of bereavement for both men and women and in all age groups, and deaths from ischemic heart disease during that period were increased above the population baseline by 2.3 fold for men, and 3.5 fold for women.

Cardiovascular Effects of Bereavement

There is ample evidence that exposure to severe, acute stress results in an increase in cardiac mortality, both from myocardial infarction and from arrhythmias. For example, mortality rates from myocardial infarction increase in response to earthquakes,^{103, 104} blizzards¹⁰⁵, missile attacks.¹⁰⁶ There was a dramatic increase in the firing of ICD's both in New York and in remote areas around the time of 9/11.^{107, 108} There is also evidence of increased cardiac morbidity in response to psychosocial stressors, including bereavement, job loss and divorce.¹⁰⁹ One of the largest studies to examine the effects of psychosocial risk factors with myocardial infarction is the INTERHEART study, which matched 11,000 patients with first MI with over 13,000 matched controls from 52 countries on six continents.¹¹⁰ Stressful life events, including marital separation or divorce, loss of job or retirement, loss of crop or business failure, violence, major intrafamily conflict, major personal injury or illness, death or major illness of a close family member, death of a spouse, or other major stress had occurred more frequently within the prior year among patients than among controls (16.1 v 13.0 percents; odd ration 1.48; 95% CI 1.33 to 1.64).

How exactly myocardial infarction occurs in response to emotional stress has not been definitely explained, but a variety of factors are believed to play a role. Increased sympathetic activity enhances cardiac vulnerability in both the normal and ischemic heart. Increase in heart rate and blood pressure lead to an imbalance in oxygen supply and demand due to increased cardiac metabolic activity and coronary vasoconstriction, particularly in vessels with injured endothelium, increasing the risk of plaque rupture¹¹¹ and subsequent myocardial infarction.^{112, 113} Adrenergic stress also appears to increase the risk of arrhythmias, causing potentiation of Purkinje fiber automaticity, early depolarizations, and prolongation of the QT interval which may lead to a reduced threshold for ventricular fibrillation.^{114, 115} Eighteen patients with ICD's underwent electrophysiologic testing at baseline and under mental stress; during the stress phase, the VT was faster, more difficult to terminate, and correlated with an increase in norepinephrine levels >50% above baseline.¹¹⁶

Takotsubo Syndrome

The most extreme manifestation of stress of the myocardium is stress-induced cardiomyopathy, which also goes by the names transient left ventricular (LV) apical ballooning, takotsubo cardiomyopathy, and broken heart syndrome. This phenomenon, with its characteristic echocardiographic changes in systole in the absence of significant coronary artery disease, has been well-described in the literature as a response to extreme emotional stress, most commonly the sudden death of a loved one.^{117, 118} The name of the syndrome comes from the changes seen in the heart on echocardiography. At end-systole, the left ventricle balloons out, creating a shape reminiscent of the pots used by Japanese fisherman to catch octopus. It is far more common in women than in men, and post-menopausal women account for 82 to 100% of cases, with mean age 62 to 75 years. While the clinical presentation mimics acute myocardial infarction, and is usually accompanied by ST elevation on ECG, but patients are found not to have significant coronary artery disease when angiography is performed. Generally cardiac enzymes are lower than would be expected for a large myocardial infarction.¹¹⁸ This phenomenon is believed to be related to catecholamine-induced microvascular spasm or dysfunction, resulting in myocardial stunning. Wittsein et al.¹¹⁸ compared catecholamine levels in patients with stress induced cardiomyopathy with those in patients with Killip class III myocardial infarction, and found that both epinephrine and norepinephrine levels were dramatically increased in the stress induced cardiomyopathy group epinephrine (1264 v 376 pg/ml) and norepinephrine (2284 v 1100 pg/mL). Complications can include tachyarrhythmias (including ventricular tachycardia and

fibrillation), bradyarrhythmias, pulmonary edema, and cardiogenic shock, and 13-18% have left ventricular outflow tract obstruction and need to be treated accordingly. By definition, the disorder is a transient wall motion abnormality in the distribution of more than a single epicardial vessel associated with new ST segment elevation or T wave inversions on ECG in the absence of coronary artery disease by angiography, or history of recent significant head trauma, intracranial bleeding, pheochromocytoma, myocarditis, or hypertrophic cardiomyopathy. Patients who survive the acute episode typically recover normal ventricular function within 1 – 4 weeks. Optimal long-term therapy has not been defined.

Depression and Cardiac Morbidity

Depression is also associated with an increase in cardiac morbidity and mortality, perhaps because of its association with changes in autonomic tone which may put patients at increased risk by influencing heart rate variability¹¹⁹ and increasing likelihood of arrhythmia.¹²⁰ As early as 1937, it was observed that mortality among 1900 patients hospitalized for depression was found to be six fold greater than that of an age-matched population.¹²¹ More recently, the Women's Health Initiative Observational Study of 93,000 post-menopausal women found that, after four years of observation, those with a history of depression (12%) and current depression (16%) had significantly higher rates of cardiovascular death (0.79 vs. 0.52%) and all-cause mortality (2.87 v 2.18%).¹²² In the INTERHEART study, depression was significantly more common among patients with a first MI than among controls (24.0 vs. 17.6%).¹¹⁰ Whether this is causal or an association is not clear. Severity of depression does seem to correlate with the increase in risk for adverse cardiac outcomes.^{123, 124} Even more intriguing are the findings of the Systolic Hypertension in the Elderly Program (SHEP), in which 4736 subjects 60 or older with isolated systolic hypertension were followed for an average of 4.5 years, and depressive symptoms assessed every six months. Though baseline depressive symptoms did not predict future CV events, but there was an increase in depression score before MI, CVA, or death.¹²⁵ Pennix et al.¹²⁶ found similar results: men, but not women, over 70 years with recent onset of depression (not chronic) associated with increased risk of CV mortality (relative risk of 1.75), CV and CHD events (RR 2.07 and 2.03 respectively) and all cause mortality (relative risk 1.4).

Based on the data presented above, an argument could be made that both the stress of bereavement and higher incidence of depression in the bereaved explain the apparent excess mortality in this group. However, other authors have suggested the mortality difference can largely be explained on the basis of bereavement-related changes in lifestyle in an already vulnerable population. Regardless of the etiology, there are distinct subgroups of bereaved people who are clearly at risk regardless of the etiology. Men, in particular, seem to be vulnerable to cardiac problems following bereavement. For example, Young et al.⁸⁹ followed 4,486 recent widowers in the UK for five years and found significantly higher death rates for widowers in the first six months following bereavement than for married. Two hundred and thirteen of 4486 widowers 55 years old and older died within the first six months of the loss of the spouse, an increase of about 40 percent above that expected for married men of the same age.

The Role of the Internist in Management of Grief

Based on the available literature, the following general recommendations can be made:

- 1.) Patients at increased risk for Complicated Grief should be identified early and followed closely. If possible, those with poor coping skills should be referred for psychological support prior to the death. If symptoms persist at six months post-loss or for a period of six

consecutive months any time after the loss, the patient should be referred for treatment as symptoms are unlikely to remit without intervention.

2.) Depressive symptoms are very common in the first months of bereavement. Between 10 and 20 percent of men and women who lose a spouse are still depressed a year later. Patients who meet criteria for depression two months post-loss should be treated as one would treat Major Depressive Disorder in the absence of bereavement.

3.) The following groups are at increased risk for adverse health outcomes:

a.) Men under the age of 75 have an increase in all-cause mortality when faced with conjugal bereavement, particularly in the first year but for up to six years post-loss in those who do not remarry.

b.) Among widowers, there is an increase in the relative risk of death from accidents, cardiovascular disease, and some infectious disease. In widows, the relative risk of death from cirrhosis rises.

c.) There is an increase in suicide in the first year of bereavement, particularly by older widowers and by single men who lose their mothers. There may be a slight increase in suicide by widows. The USPSTF recommends that clinicians be alert for suicidal ideation in people who have had a recent bereavement.¹²⁷

4.) All studies document increases in alcohol consumption and smoking and greater use of tranquilizers or hypnotic medication (or both) among the bereaved. For the most part, these increases occur in people who already are using these substances; however, some of the increase is attributable to new users.

5.) Perceived adequacy of social support and remarriage protect the bereaved from adverse outcomes, and support groups can help facilitate resolution of grief.¹²⁸

Additionally, there are a variety of low-burden, low-cost interventions that can be undertaken both pre- and post-loss to help minimize adverse impact on survivors. Physicians caring for terminally ill patients can help the family members who will be left behind by giving them the information they need to understand the prognosis and anticipate the loss. Attention to the quality of the death should also include leaving the survivors with as little guilt as possible that they, and the professional caregivers, have done “the right thing” for the patient, especially if the family has had to make decisions about treatment withdrawal or limitation. Hospice referrals should be made as early as possible, when appropriate, because hospice use by patients is associated with decreases in both bereavement-related depression⁷⁶ and mortality among surviving spouses.¹²⁹

Post-loss interventions can be undertaken either by a patient’s primary care physician, or by a physician who was caring for the deceased, or, ideally, by both. Immediately after the death, the physician caring for the deceased should contact family members not present, offer condolences, answer questions, and offer family members the option to view the body. Afterwards, a letter of condolence is very much appreciated by the family, as would be a phone call or note acknowledging the loss, particularly at anniversary or holiday times. The patient’s primary care physician, if aware of the loss, may want to reach out through a personal phone call or offer of an appointment to “check in” since the bereaved often find it difficult to initiate actions.¹⁰ Patients at increased risk for adverse mental or physical health outcomes as outlined above should be monitored closely and treated as outlined. Additionally, sleep disruption is a common problem, and though short term sleep aids or anxiolytics may be helpful, long-term they are not recommended.

Conclusions

All of us experience bereavement, both personally and professionally. Grieving is painful work, and the stress leaves patients at increased risk of adverse physical and mental health outcomes. Awareness of the problem among primary care providers may promote interventions that help defray some of the damage. One remaining question is why, given the evidence presented above, physicians do not take a more active role in assisting with bereavement. First, there is debate in the literature about whether or not it is appropriate to consider grief a pathologic process. Many feel that it is a natural emotional reaction that should not be “medicalized” or “pathologized.” Others, however, feel that the potential adverse effects are such that it should be considered a medical state. In an editorial in the *New England Journal of Medicine*, Rogers & Reich¹³⁰ assert that “The physician owes it to the patients to point out the strengths of the human response rather than the susceptibilities that are often belabored in the media...to emphasize human resilience and the power of life.” Regardless of one’s philosophical approach to this question, it must be acknowledged that the process is very painful and distressing, is associated with adverse outcomes, and therefore should be of interest to the medical community. Pragmatically, if the bereaved is the patient, there may be concerns that office visits for bereavement care and telephone calls to family members are time-consuming and not well-reimbursed. However, if a system for condolence letters is put into place, the cost should be no more than that of a card and stamp and the time it takes to sign your name. Another question is that of responsibility. Physicians may assume that care of a patient does not extend to care for the patient’s family. Once our patient has died, we may feel that our obligations have been fulfilled. The patient’s family, however, may feel otherwise. Prigerson & Jacobs (2001)¹⁰ quote a woman’s whose husband had died two years earlier:

“My husband’s doctor...as soon as [my husband] died, that was the end of him. That’s one of the things I object to: all the doctors just suddenly go...there’s no support. If I felt like [my husband’s] physicians had enough respect and affection for me and would call me occasionally, that would be nice...my husband’s doctor should have been there [for me].”

Another issue may be that physicians feel guilty about the death, even if it was expected, especially if they are concerned that the quality of the death was not optimal or that the family might be angry. The literature suggests that bereavement outcomes are improved if there is better communication with the family, and that rather than inviting anger, outreach to the family after the death helps minimize it.^{131, 132} Physicians may feel uncomfortable dealing with the intense emotion that almost invariably surfaces in the setting of acute bereavement, or just do not know what to say. A table of strategies for communication with and caring for bereaved patients is included as an appendix.

Ultimately, physicians are among the very few who are privileged to participate in the most powerful and formative events that occur over a lifetime. It is the expectation of our patients that we will be able to walk with them on the hardest journeys they have to take, and that we will provide them with guidance and support along the way. It is therefore incumbent upon us not to fail our patients or their families during what is likely to be among the most terrible times they will endure. By doing so, we help not only those we care for, but also ourselves. Sharing the pain of loss increases our emotional intimacy with patients and families and gives us the gratification of knowing that we have honored our professional obligations.

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Table 2. Strategies for Communication With and Caring for Bereaved Patients

Things to say . .	Because . . .
I'm sorry, or I'm sorry she/he's gone.	Acknowledges the loss and lets the bereaved person know you feel for them. Not saying this much is often perceived as a lack of respect or concern.
I can't imagine what you're going through.	Bereaved patients are often frustrated by people who minimize or assume they know how they are feeling. No one can fully understand another's loss and admitting this is appreciated.
What are you remembering about [the deceased] today?	Bereaved patients are always remembering the deceased. Don't worry about bringing up sad memories—they are there. Help them to express their thoughts and they will feel like you care. They will appreciate your interest.
Say [deceased's] name.	Bereaved patients will never forget the deceased. Let them know you won't forget him/her either by mentioning his/her name.
Talk about the deceased. Depending on your relationship to the deceased, you may want to say it was an honor to know him/her and that you will miss him/her.	Bereaved patients worry that others, and even they, will forget the uniqueness of the deceased. Talking about the deceased helps keep everyone remembering. If you did not know the deceased person, acknowledge that and express regret.
Do you have any questions about the final illness and treatment?	Most bereaved people are extremely interested to know about the events leading up to the death and many have unanswered questions that have bothered them. Providing a response may help to provide closure.
How are you feeling since [the deceased's death]? How has [the deceased's death] affected you?	Bereaved patients will appreciate the concern and this may save time by getting to the reason or need for the visit.
Things Not to Say	Because . . .
Call me.	Passive effort puts the burden on the bereaved person. A sincere effort is to make a personal call to the bereaved patient.
How are you? (casually)	Only if you have time to listen. If not, don't ask.
I know how you feel.	It seems presumptuous for anyone to claim to know how another person feels.
It was probably for the best.	A bereaved person does not view it this way.
[She/He's] happy now.	You have no way of knowing this and the patient may resent your presuming to know.
It is God's will.	Those who are in mourning typically protest. Saying God wanted it this way may confuse the religious and offend the nonreligious.
It was his (or her) time to go.	Bereaved patients have trouble seeing it this way. Those in mourning protest their loved one's departure and almost never think the time was "right." However, if you see that they are tormented by what they did or did not do to prevent the loss, it may be in order to say that there are things that are not within anyone's control.
I'm sorry I brought it up.	Don't be sorry; bring it up. Bereaved patients want you to know about their loss.
Let's change the subject.	Don't change the subject. Bereaved patients want to talk with you about their loss.
You should work toward getting over this by now.	Bereaved people never "get over" their loss, but learn to live with it. Putting pressure on them to "move on" is, in a sense, blaming them for their continued grief, may instill guilt, and add to their concerns. If grief is prolonged, it may be time for a referral for expert help.
I had another patient who had the same illness [as the deceased] and he suffered for a long time. You should be glad [the deceased] passed away quickly.	Though some may find comfort in this comparison, others will not because they feel that it doesn't matter how long a loved one suffered, it matters that she/he did. Safer to avoid these sorts of comparisons.
You're strong enough to deal with it.	Mourning is about the loss and not about the mourner's strength. A more appropriate response might be to say to the bereaved, "I hope you find the strength to bear your loss."
Practices to Implement	How . . .
Death notification	Try to establish a system whereby you are notified of patient deaths, recent losses, and deaths within patient's families. Encourage patients, colleagues, and funeral directors to notify you if there has been a death in the family, and/or have patients complete a brief form while in the waiting room that asks about recent losses.
Outreach—express sorrow, invite discussion, schedule visit, and monitor symptoms	Once notified of a death, have staff contact bereaved patients to acknowledge loss, see how they are doing, and encourage a scheduled visit.
Have useful information available	Provide a list of resources for bereaved patients. Make available information on literature and Web sites, support groups, clergy, mental health professionals, lawyers, and financial planners.
Practices to Avoid	Because . . .
Passivity	Try not to be passive, vague, or insincere. Refrain from asking bereaved patients to take the initiative, thereby putting the burden on them.
Avoidance	Bereaved patients want you to know that they recently lost a significant person in their life. They typically want you to know how this upsets them and want to talk about it with you. To avoid their grief denies them an opportunity to express and address their concerns, and may obscure the real reason for their visit.
Making comparisons with other losses	Try not to compare one person's loss with other patient deaths or deaths in your family. If handled well, empathy may provide some solace and acknowledging that it could be worse may minimize regrets, but comparisons run the risk of minimizing the significance of an individual's loss.
Pressure and inappropriate positivity	Avoid encouraging them to put the past behind them. Try not to imply that they should be making larger strides towards moving forward with their life. Do not try to locate them on a linear grief trajectory, place them in a stage of grief, or suggest their outlook be more positive.