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A comprehensive review of palliative care in patients with cancer

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Abstract

One of the most challenging roles for the psychiatrist is to help guide terminally ill patients physically, psychologically and spiritually through the dying process. Patients with advanced cancer, and other life-threatening medical illnesses are at increased risk for developing major psychiatric complications and have an enormous burden of both physical as well as psychological symptoms. In fact, surveys suggest that psychological symptoms such as depression, anxiety, and hopelessness are as frequent, if not more so, than pain and other physical symptoms in palliative care settings. Psychiatrists have a unique role and opportunity to offer competent and compassionate palliative care to those with life-threatening illness. In this article we provide a comprehensive review of basic concepts and definitions of palliative care and the experience of dying, and the role of the psychiatrist in palliative care including assessment and management of common psychiatric disorders in the terminally ill, with an emphasis on suicide and desire for hastened death. Psychotherapies developed for use in palliative care settings, and management of grief and bereavement are also reviewed.

Palliative care: historical perspectives and definitions

The term ‘palliation’ is derived from the Latin root word *palliare*, which means ‘to cloak’ or ‘to conceal’. *Pallium* also refers to the cloth that covers or cloaks burial caskets. These root words suggest that the dying patient, although not amenable to cure, can be ‘cloaked’ or ‘embraced’ in the comforting arms of the caregiver. The terms palliative care and palliative medicine are often used interchangeably. Palliative medicine refers to the medical discipline of palliative care, an approach to improve the quality of life of patients and their families facing life-threatening illness. The nature and focus of palliative care has evolved over the past century, expanding beyond just comfort for the dying to include palliative care and symptom control that begins with the onset of a life-threatening illness and proceeds past death to include bereavement interventions for family and others (Sepulveda et al., 2002).

Modern palliative care is an outgrowth of the hospice movement that began in the 1840s with Calvaires in Lyon, France, and progressed through 1900 with the establishment of the St Joseph’s Hospice in London, finally culminating with the

progenitor of all modern hospices, St Christopher’s Hospice established in 1967 by Cicely Saunders. By 1975, a large number of independent hospices had been developed in the UK, Canada, and Australia. The first ‘palliative care’ programme at the Royal Victoria Hospital in Montreal was also established around the same period. This period of evolution from the traditional stand-alone, home-based hospice also saw the development of hospital-based pain and palliative care consultation services such as the pain service established in 1978 by Kathleen Foley at the Memorial Sloan Kettering Cancer Center. Modern palliative care thus evolved from the hospice movement into a mixture of academic and non-academic care delivery systems that had components of home care and hospital-based services (Berger et al., 2006; Stjernsward & Clark, 2004).

As noted above, over the years the definition of palliative care has changed from primarily applying to end of life to becoming applicable at all stages of life-threatening disease and emphasizing the importance of addressing psychological, social, spiritual, and cultural elements equally to the control of pain and physical symptoms. The most recent and comprehensive definition of palliative care as outlined by

the World Health Organization (WHO, 2002, 2009) provides a framework for palliative care in all settings. According to this definition, palliative care:

- provides relief from pain and other distressing symptoms,
- affirms life and regards dying as a normal process,
- intends neither to hasten nor to postpone death,
- integrates psychological and spiritual aspects of patient care,
- offers a support system to help patients live as actively as possible until death,
- offers a support system to help families cope during the patient's illness and in their own bereavement,
- is interdisciplinary and uses a team approach including physicians, nurses, mental health professionals, clergy, and volunteers to address the needs of patients and their families,
- will enhance quality of life and may also positively influence the course of illness,
- is applicable early in the course of illness, in conjunction with other therapies to better understand and manage distressing complications.

Palliative care programmes and models of care delivery

Fully developed, model palliative care programmes ideally include all of the following components: (1) a home care programme (e.g. hospice programme), (2) a hospital-based palliative care consultation service, (3) a day-care programme or ambulatory care clinic, (4) a palliative care inpatient unit (or dedicated palliative care beds in hospital), (5) a bereavement programme, (6) training and research programmes, and (7) Internet-based services. National and international organizations such as the WHO, have worked hard to raise global awareness on the importance of palliative care. As of 2009, there were an estimated 10,000 programmes internationally intended to provide palliative care.

Death and dying: what is a good death?

A meaningful dying process is one throughout which the patient is physically, psychologically, spiritually, and emotionally supported by his or her family, friends, and caregivers. Weisman (1972) described four criteria for what he called an 'appropriate death': (1) internal conflicts, such as fears about loss of control, should be reduced as much as possible, (2) the individual's personal sense of identity should be sustained, (3) critical relationships should be enhanced or at least maintained, and conflicts should

be resolved, if possible, and (4) the person should be encouraged to set and attempt to reach meaningful goals, even though limited, such as attending a graduation, a wedding, or the birth of a child, as a way to provide a sense of continuity into the future. The WHO (2002, 2009) outlined guidelines characterizing a 'good' death as one that is (1) free from avoidable distress and suffering for patient, family, and caregivers, (2) in general accord with the patient's and family's wishes, and (3) reasonably consistent with clinical, cultural, and ethical standards. These guidelines and the aforementioned considerations for achieving a good death can serve as general principles for the psychiatrist in caring for the dying.

What is the role of the psychiatrist?

The traditional role of the psychiatrist is broadened in several ways in the care of the dying patient. The psychiatrist's primary role in the palliative care setting is the diagnosis and treatment of co-morbid psychiatric disorders. Psychiatrists can provide expert care and teaching about the management of depression, suicide, anxiety, delirium, fatigue, and pain in terminally ill patients (Breitbart & Holland, 1993; Chochinov & Breitbart, 2009). The role of the psychiatrist, in the care of the dying, extends beyond the management of psychiatric symptoms and syndromes into the existential issues, family and caregiver support, bereavement, doctor-patient communication, and education and training. Psychiatrists can play an important role in the management of social, psychological, ethical, legal, and spiritual issues that complicate the care of dying patients. The psychiatrist can provide assistance in dealing with existential crises posed by a terminal diagnosis. The psychiatrist can help the patient deal with the prognosis and explore treatment options, including palliative care. Conflicts with the physician and staff are common because the clinicians are also stressed; resolution of these conflicts is a critical intervention for the patient's physical and psychological well-being.

The psychiatrist helps resolve conflicts among patient, family, and staff by opening lines of communication and helping families to deal with the strong emotions that surround imminent death of a loved one. Psychotherapeutic interventions for patients and families who are experiencing anticipatory grief are also important. During the bereavement period, the family may turn to the psychiatrist who participated in the patient's care and who shares memories of the patient for continuing support.

The psychiatrist also has an ethical role in encouraging discussion of end-of-life decisions regarding treatment, withholding resuscitation, and life support. The capacity of the patient to make rational

judgements and the proxy's ability to make an appropriate decision for the patient may require psychiatric evaluation. The decision to withdraw life support is highly emotional and may require psychiatric consultation (Subcommittee on Psychiatric Aspects of Life-Sustaining Technology, 1996). The psychiatrist's role can include teaching the medical staff about the psychological issues involved in care of dying patients, including how to deliver bad news and discuss do-not-resuscitate (DNR) orders and other treatment preferences, ideally with the patient, or with family when the patient is unable to make such decisions (Levin et al., 2008; Misbin et al., 1993; Weissman, 2004).

Psychiatric disorders in the palliative care setting

Patients with advanced disease, such as advanced cancer are particularly vulnerable to psychiatric disorders (Breitbart et al., 1995; Miovic & Block, 2007). Unfortunately, medical specialists frequently fail to recognize emotional distress and common psychiatric disorders in terminally ill patients (Breitbart & Alici, 2008; Miovic & Block, 2007).

Anxiety disorders

The terminally ill patient presents with a complex mixture of physical and psychological symptoms in the context of a frightening reality, making the identification of anxiety symptoms requiring treatment challenging. Patients with anxiety complain of tension or restlessness, or they exhibit jitteriness, autonomic hyperactivity, vigilance, insomnia, distractibility, shortness of breath, numbness, apprehension, worry or rumination. Often the somatic manifestations of anxiety overshadow the psychological or cognitive ones and are the symptoms that the patient most often presents with (Holland, 1989). The psychiatrist must use these symptoms as a cue to inquire about the patient's psychological state, which is commonly one of fear, worry, or apprehension.

The assumption that a high level of anxiety is inevitably encountered during the terminal phase of illness is neither helpful nor accurate. In deciding whether to treat anxiety during the terminal phase of illness, the clinician should consider the patient's subjective level of distress as the primary impetus for the initiation of treatment. Other considerations include problematic patient behaviour such as non-compliance due to anxiety, family and staff reactions to patient distress, and the balancing of the risks and benefits of treatment (Roth & Massie, 2009).

The prevalence of anxiety in patients receiving palliative care increases with advancing disease and decline in the patient's physical status (Rabkin et al., 1997). In cancer patients, anxiety is commonly associated with depressive symptoms. In a study of patients with advanced melanoma, Brandberg et al. (1995) found that 28% of patients were anxious compared to 15% of control subjects. In the Canadian National Palliative Care Survey younger patients and those with a lower performance status, smaller social networks, and less participation in organized religious services were more likely to have a psychiatric disorder (Wilson et al., 2007). It was also notable that palliative care patients with a DSM-IV anxiety and/or depressive disorder reported more severe distress from several physical symptoms, social concerns and existential issues (Wilson et al., 2007).

Anxiety can occur in terminally ill patients as an adjustment disorder, a disease- or treatment-related condition, or an exacerbation of a pre-existing anxiety disorder (Kerrihard et al., 1999; Massie, 1989). Adjustment disorder with anxiety is related to the existential crisis and the uncertainty of the prognosis and the future (Holland, 1989). When faced with terminal illness, patients with pre-existing anxiety disorders are at risk for reactivation of symptoms. Generalized anxiety disorder and panic disorder are apt to recur, especially in the presence of dyspnoea or pain. Individuals with phobias will have an especially difficult time if the disease or treatment confronts them with their fears (e.g. claustrophobia, fear of needles, fear of isolation). Post-traumatic stress disorder (PTSD) may be activated in patients as they relate their situation to some prior frightening experience, such as the holocaust, a combat experience, or a cardiac arrest. Patients with PTSD may present with high levels of anxiety, insomnia, frequent panic attacks, co-morbid depressive symptoms, and avoidance of medical settings that trigger traumatic memories (Miovic & Block, 2007). Symptoms of anxiety in the terminally ill patient may arise from a medical complication of the illness or treatment (Breitbart et al., 1995; Roth & Massie, 2009). Hypoxia, sepsis, poorly controlled pain, medication side effects such as akathisia, and withdrawal states often present as anxiety (Miovic & Block, 2007). In the dying patient, anxiety can represent impending cardiac or respiratory arrest, pulmonary embolism, sepsis, electrolyte imbalance, or dehydration (Strain et al., 1981). Delirium can present with anxiety and restlessness in palliative care settings. Disturbances in level of consciousness and in level of awareness, impaired concentration, cognitive impairment, altered perception, and fluctuations of symptoms are important diagnostic indicators of delirium as opposed to a

diagnosis of anxiety disorder (Roth & Massie, 2009). During the terminal phase of illness, when patients become less alert, there is a tendency to minimize the use of sedating medications. It is important to consider the need to slowly taper benzodiazepines and opioids, which may have been sustained at high doses for extended relief of anxiety or pain, in order to prevent acute withdrawal states. Withdrawal states in terminally ill patients often manifest first as agitation or anxiety and become clinically evident days later than might be expected in younger, healthier patients due to impairment in metabolism.

Despite the fact that anxiety in terminal illness commonly results from medical complications, it is important to consider psychological factors that may play a role, particularly in patients who are alert and not confused (Holland, 1989; Roth & Massie, 2009). As disease progresses, patients' anxiety may include fears about the disease process, the clinical course, possible treatment outcomes, and death. In addition, anxiety may result from fear of increasing social stigma as the medical illness becomes more evident, as well as fear from the increasing financial consequences of treatment. Patients frequently fear the isolation and separation of death. Claustrophobic patients may fear the idea of being confined and buried in a coffin. These issues can be disconcerting to the psychiatrist, who may find themselves at a loss for words that are consoling to the patient.

Treating anxiety in terminally ill patients is most effective when it is multimodal and combines use of psychotherapy and pharmacotherapy. The pharmacological management of anxiety in the terminally ill does not differ much from the approach to treatment in the medically ill. Both would involve the judicious use of benzodiazepines, typical and atypical antipsychotics, antihistamines, antidepressants and opioid analgesics. Some considerations should be kept in mind, for example, when using benzodiazepines, special attention should be paid to respiratory status, hepatic function, and increased risk of mental status changes when used in excess. Patients with impaired respiratory function or delirium may benefit from use of antipsychotics as opposed to benzodiazepines, for management of anxiety symptoms (Breitbart et al., 1996), though there has been no systematic study of use of antipsychotics for treatment of anxiety among patients in palliative care settings (Jackson & Lipman, 2004; Levin & Alici, 2010).

Sedating antidepressants such as trazodone or mirtazapine may help patients with persistent anxiety, insomnia, and anorexia. The utility of antidepressants and buspirone for anxiety disorders is often limited in the dying patient because they require weeks to achieve therapeutic effect.

Opioid drugs are primarily indicated for control of pain but are also effective in the relief of dyspnoea and associated anxiety (Elia & Thomas, 2008). Continuous intravenous infusions of morphine or other narcotic analgesics allow for careful titration and control of respiratory distress, anxiety, pain, and agitation (Portenoy & Foley, 1989). Occasionally one must maintain the patient in a state of unresponsiveness in order to maximize comfort. When respiratory distress is not a major problem, it is preferable to use the opioid drugs solely for analgesia and to add more specific anxiolytics to control concomitant anxiety.

Non-pharmacological interventions for anxiety and distress include supportive psychotherapy, behavioural interventions, and cognitive-behavioural therapy that are used alone or in combination. Brief supportive psychotherapy is often useful in dealing with both crises and existential issues confronted by the terminally ill (Roth & Massie, 2009). Supportive-expressive group therapy has been shown to reduce distress and subsyndromal symptoms of PTSD in women with advanced breast cancer (Classen et al., 2001). Inclusion of the family in psychotherapeutic interventions should be considered, particularly as the patient with advanced illness becomes increasingly debilitated and less able to interact.

Relaxation, guided imagery, and hypnosis may help reduce anxiety and thereby increase the patient's sense of control. Many patients with advanced illness are still appropriate candidates for the use of behavioural techniques despite physical debilitation. A feasibility study of a brief cognitive-behavioural intervention has been shown to reduce anxiety and depression symptoms in a small population of hospice patients (Anderson et al., 2008). A typical behavioural intervention for anxiety in a terminally ill patient would include a relaxation exercise combined with some distraction or imagery technique. The patient is first taught to relax using passive breathing accompanied by either passive or active muscle relaxation. When in a relaxed state, the patient is taught a pleasant, distracting imagery exercise. In terminally ill patients who are highly anxious, relaxation techniques can be used concurrently with anxiolytic medications.

Depression

Depression is prevalent, but under-recognized, under-diagnosed, and under-treated in palliative care settings. Approximately 5–20% of patients with advanced cancer meet criteria for major depression even when the most stringent criteria are used (Wilson et al., 2007). An additional 15–20% of palliative care patients present with depressive disorders

that are less severe, but may still be a major source of suffering and despair to patients (Wilson et al., 2009). Depressed mood and sadness can be appropriate responses as the terminally ill patient faces death. These emotions may be manifestations of anticipatory grief over the impending loss of one's life, health, loved ones, and autonomy.

Depression in the terminally ill has been associated with poor treatment compliance, reduced quality of life, poor survival, desire for hastened death, and completed suicide (Breitbart et al., 2000; Chochinov et al., 1995; Lloyd-Williams et al., 2009; van der Lee et al., 2005). Many have also found a correlation between depression, pain, and functional status (Breitbart, 1989; Potash & Breitbart, 2002; Wilson et al., 2007).

Family history of depression and history of previous depressive episodes further increase the patient's risk of developing a depressive episode (Miovic & Block, 2007). Loss of meaning and low scores on measures of spiritual well-being have also been associated with higher levels of depressive symptoms (Nelson et al., 2002).

When assessing for depression in the terminally ill, feelings of hopelessness, worthlessness or suicidal ideation must be explored in detail. While many dying patients lose hope of a cure, they are able to maintain hope for better symptom control. For many patients hope is contingent on the ability to find continued meaning in their day-to-day existence. Hopelessness that is pervasive and accompanied by a sense of despair or despondency is more likely to represent a symptom of a depressive disorder. Similarly, patients often state that they are burdening their families, causing them great pain and inconvenience. Those beliefs are less likely to represent a symptom of depression than if the patient feels that their life has never had any worth, or that they are being punished for evil things they have done.

Depressed mood and loss of pleasure or interest are also important in assessment of depression in patients with advanced cancer (Spoletini et al., 2008; Weinberger et al., 2009). Almost all patients with advanced illness experience a certain degree of disengagement from areas of interest. However, a pervasive anhedonia that extends to a loss of interest and pleasure in almost all activities merits considerable attention as an important indicator of depression in palliative care settings (Wilson et al., 2009).

Self-report measures and brief screening instruments may be helpful ways of evaluating this particularly vulnerable population. They can serve as relatively simple tools for identifying those likely to have depression.

Depression in cancer patients with advanced disease is optimally managed using a combination of psychotherapy and antidepressant medication

(Wilson et al., 2009). The management of depression should also include treatment of pain and other distressing physical symptoms. Antidepressant medications are the mainstay of treatment of cancer patients with severe depressive symptoms who meet criteria for a major depressive episode. A depressed patient with several months of life expectancy can wait the 2–4 weeks that it may take to respond to a serotonin selective reuptake inhibitor or a tricyclic antidepressant. Conversely, the depressed dying patient with less than three weeks to live may do best with a rapid acting psycho-stimulant (Block, 2000; Homsí et al., 2001). Those who are within hours to days of death and in distress are likely to benefit most from the use of sedatives or narcotic analgesic infusions for distress relief.

Psychotherapeutic techniques including individual or group counselling, have been shown to effectively reduce psychological distress and depressive symptoms in advanced stage cancer patients (Wilson et al., 2009). Cognitive behavioural interventions such as relaxation and distraction with pleasant imagery also have been shown to decrease depressive symptoms in patients with mild to moderate levels of depression (Holland et al., 1987). Supportive psychotherapy for the dying patient consists of active listening with supportive verbal interventions and the occasional interpretation. Despite the seriousness of the patient's plight, it is not necessary for the psychiatrist or psychologist to appear overly solemn or emotionally restrained. Often the psychotherapist is the only person among all of the patient's caregivers who is comfortable enough to allow the patient to talk about his or her life experiences rather than focus solely on impending death. The dying patient who wishes to talk or ask questions about death should be encouraged to do so freely, with the therapist maintaining an interested, interactive stance. Several novel psychotherapies including meaning-centred psychotherapy and dignity-conserving therapy have been developed and are being tested in the treatment of depression, hopelessness, loss of meaning, and demoralization, with promising results.

Suicide, desire for hastened death and request for assisted suicide

Suicide, suicidal ideation, and desire for hastened death are all important and serious consequences of unrecognized and inadequately treated clinical depression. Although clinical depression has been demonstrated to be a critically important factor in desire for hastened death, understanding more fully why some patients with a terminal illness wish to seek to hasten their death remains an important element in the practice of palliative care.

Suicidal ideation is defined as thoughts of taking one's own life. For most patients this may only occur as a fleeting consideration they have during particularly distressing moments in their illness. These thoughts may serve as a 'steam valve' for ideations often expressed by patients as 'no matter how bad things become, I always have a way out.' For others it may occur with more frequency and result in a concrete plan of measures one will take to end their own life. When the latter occurs it is a psychiatric emergency that can require involuntary hospitalization to protect the individual from self-injury. Because terminally ill patients frequently experience these thoughts, it is important for providers to feel comfortable assessing suicidal ideation in their patients.

Terminally ill patients are at elevated risk of suicide when compared to the general population. A study done examining data from the Cancer registry of Norway revealed standardized mortality ratios (SMRs) of 1.55 for men and 1.35 for women (Hem et al., 2004). Patients with advanced illness are at highest risk, perhaps because they are most likely to have such complications as pain, depression, delirium, and physical disability. Delirium and other cognitive disorders place terminally ill patients at risk for suicidality by impairing impulse control and judgement. With advancing disease, the incidence of significant cancer pain increases. Uncontrolled pain in cancer patients is an important risk factor for suicide. The vast majority of cancer suicides in several studies showed that these patients had severe pain, which was often inadequately controlled and poorly tolerated (Bolund, 1985; Farberow et al., 1963, 1971; Fox et al., 1982; Louhivuori & Hakama, 1979). The presence of depressed mood increased the risk of suicidality in the palliative care setting. Depression also appears to be important in terms of patient preferences for life-sustaining medical therapy. It has been found that among older depressed patients, an increase in desire for life-sustaining medical therapies followed treatment of depression in those subjects who had been initially more severely depressed, more hopeless, and more likely to overestimate the risks and to underestimate the benefits of treatment (Ganzini et al., 1994). Whereas patients with mild to moderate depression are unlikely to alter their decisions regarding life-sustaining medical treatment in spite of treatment for their depression, severely depressed patients – particularly those who are hopeless – should be encouraged to defer advance treatment directives. In these patients, decisions about life-sustaining therapy should be discouraged until after treatment of their depression (Ganzini et al., 1994).

Hopelessness is the key variable that links depression and suicide in the general population. Further,

hopelessness is a significantly better predictor of completed suicide than is depression alone (Beck et al., 1975). Studies have correlated hopelessness more highly with suicidal ideation in terminally ill patients compared to the level of depression (Chochinov et al., 1998). With the typical cancer suicide being characterized by advanced illness and poor prognosis, hopelessness is commonly experienced. In Scandinavia the highest incidence of suicide was found in cancer patients who were offered no further treatment, and no further contact with the healthcare system (Bolund, 1985; Louhivuori & Hakama, 1979). Being left to face illness alone creates a sense of isolation and abandonment that is critical to the development of hopelessness.

Loss of control and a sense of helplessness in the face of one's illness are important factors in suicide vulnerability. Control refers to both the helplessness induced by symptoms or deficits due to the illness or its treatments, as well as the excessive need on the part of some patients to be in control of all aspects of living or dying. Patients who were accepting and adaptable are much less likely to commit suicide than patients who exhibited a need to be in control of even the most minute details of their care (Farberow et al., 1963). This need to control may be prominent in some patients and cause distress with little provocation. However, it is not uncommon for illness-related events to induce a great sense of helplessness even in those who are not typically controlling individuals. Impairments or deficits induced by the patient's illness or its treatments often include loss of mobility, paraplegia, loss of bowel and bladder function, amputation, aphonia, sensory loss, and inability to eat or swallow. Most distressing to patients is the sense that they are losing control of their minds, especially when they are confused or sedated by medications. The risk of suicide is increased in patients with such physical impairments, especially when accompanied by psychological distress and disturbed interpersonal relationships due to these deficit factors.

Fatigue, in the form of emotional, spiritual, financial, familial, communal, and other resource exhaustion increases risk of suicide in the seriously physically ill patient (Breitbart, 1987). Due to advancements in treatment, illnesses such as cancer now often follow more of a chronic course. Increased survival is accompanied by increased number of hospitalizations, complications, and expenses. Symptom control thus becomes a prolonged process with frequent advances and setbacks. The dying process also can become extremely long and arduous for all concerned. It is not uncommon for both family members and healthcare providers to withdraw prematurely from the patient under these circumstances. A suicidal patient can thus feel even more

isolated and abandoned. The presence of a strong support system for the patient that may act as an external control of suicidal behaviour reduces the risk of suicide significantly.

Assessment and management of the suicidal terminally ill patient

Assessment of suicide risk and appropriate intervention are critical. Early and comprehensive psychiatric involvement with high-risk individuals can often avert suicide in the cancer setting. A careful evaluation includes a search for the meaning of suicidal thoughts, as well as an exploration of the seriousness of the risk. The clinician's ability to establish rapport and elicit a patient's thoughts is essential as he or she assesses history, degree of intent, and quality of internal and external controls. The clinician should listen sympathetically, not appearing critical or stating that such thoughts are inappropriate. Allowing the patient to have discussions about suicidal ideation often decreases the risk of suicide. The myth that asking about suicidal thoughts 'puts the idea in their head' should be dispelled (Rosenfeld et al., 2000). Patients often reconsider and reject the idea of suicide when the physician acknowledges the legitimacy of their option and the need to retain a sense of control over aspects of their death. Once the setting has been made secure, assessment of the relevant mental status and adequacy of pain control can begin. Analgesics, antipsychotics, or antidepressant drugs should be used when appropriate to treat agitation, psychosis, major depression, or pain. Underlying causes of delirium or pain should be addressed specifically when possible and initiation of a crisis-intervention-oriented psychotherapeutic approach, mobilizing as much of the patient's support system as possible is important. A close family member or friend should be involved in order to support the patient, provide information, and assist in treatment planning. Psychiatric hospitalization can sometimes be helpful but is usually not desirable in the terminally ill patient. Thus, the medical hospital or home is the setting in which management most often takes place. Whereas it is appropriate to intervene when medical or psychiatric factors are clearly the driving force in a cancer suicide, there are circumstances when usurping control from the patient and family with overly aggressive intervention may be less helpful. This is most evident in those with advanced illness where comfort and symptom control are the primary concerns. Ultimately, the psychiatrist may not be able to prevent all suicides in the terminally ill patients that he or she cares for. The emphasis of intervention should be to aggressively attempt to prevent suicide that is driven by the desperation of uncontrolled physical and psychological

symptoms such as uncontrolled pain, unrecognized delirium, and unrecognized and untreated depression. Prolonged suffering caused by poorly controlled symptoms may lead to such desperation, and it is the appropriate role of the palliative care team and the psychiatrist to provide effective management of physical and psychological symptoms as an alternative to desire for hastened death, suicides, or requests for assisted suicide by their patient.

Desire for hastened death

The desire for hastened death is an issue that may be commonly encountered by the palliative care physician. It may present as a passive wish for death, the decision to forego aggressive therapy that could alter survival outcomes, the decision to discontinue life-prolonging treatment, suicidal ideation or a request for physician-assisted suicide (Breitbart et al., 2000). In the hospice setting patients may indicate a desire for hastened death. This most commonly occurs as a fleeting wish, but in a smaller percentage of patients it may be more persistent (Chochinov et al., 1995).

Because of its frequency, being able to identify underlying factors contributing to a patient's desire for hastened death is key for care providers. In a recent study examining terminally ill cancer patients, depression and hopelessness were the strongest predictors of desire for hastened death among terminally ill cancer patients (Breitbart et al., 2000). They were also found to have significantly more pain and less social support when compared to patients without desire for hastened death. Existential concerns such as loss of meaning and purpose, loss of dignity, regret, awareness of incomplete life tasks and anxiety around what happens after death have been associated with a desire for hastened death. Terminally ill cancer patients with a lowered sense of dignity are more likely to report a loss of will to live (Chochinov et al., 2005). Terminally ill cancer patients who had low spiritual well-being can be also more likely to endorse a desire for hastened death, hopelessness and suicidal ideation (McClain et al., 2003).

In summary, common risk factors associated with desire for hastened death include depression or history of psychiatric illness, hopelessness, physical distress (including pain and other symptom burden), poor social support, fear of being a burden to others as well as existential concerns such as loss of meaning and loss of dignity.

Request for assisted suicide

As mentioned in the section above, a desire for hastened death may present as a request for physician-assisted suicide. This has become a highly

controversial topic in palliative medicine. Several states across the USA (Oregon, Montana and Washington) as well as Switzerland and the Netherlands have legalized physician-assisted suicide for terminally ill patients. Those opposed to physician-assisted suicide argue that its legalization will alter the fundamental role of the doctor as healer and may place certain more vulnerable communities at risk of abuse, error and coercion. Advocates argue that allowing patients a legal and socially accepted way of controlling their own death would avoid people having to plan in secrecy and endure the difficult process alone. They also feel that safeguards, such as a thorough informed consent process and the requirement of an independent second opinion would protect against most risks (Bondreau et al., 2013).

What is generally agreed upon is that clinicians should allow patients to discuss their wishes for hastened death and physician-assisted suicide in an open, frank manner. Being empathic and non-judgemental are essential to facilitating these often difficult to discuss issues. Through such conversations one may be able to identify underlying reasons for such wishes, for example hopelessness or depression, and offer appropriate interventions. Breitbart et al. (2010) examined depression and desire for hastened death in patients with advanced AIDS. Patients who were diagnosed with major depressive disorder were placed on antidepressant treatment and assessed weekly for symptoms of depression and desire for hastened death. The results indicated that a patient's desire for hastened death decreased dramatically in patients who responded positively to antidepressant treatment. A prospective Dutch study of 138 terminally ill cancer patients examined the association between depression and requests for euthanasia. They found that of the 22% of patients who requested euthanasia, 23% were depressed at baseline, and 44% of those depressed requested euthanasia compared to 15% of the non-depressed. The rate of request was 4.1 times greater than that of patients without depression (van der Lee et al., 2005).

Regardless of what one's personal beliefs are on physician-assisted suicide, being able to address treatable symptoms and reduce suffering is at the core of palliative medicine. Clinicians should pay particular attention to underlying depression, hopelessness and physical distress when such requests are made. When a terminally ill patient requests assistance in dying, the first step to take is to make sure the person is getting the best possible palliative care and when applied with skill and expertise, good palliative care can address most, but not always all, end-of-life suffering (Quill, 2012). The focus of palliative care has been to eliminate suffering, which can generally be ameliorated by excellent physical,

psychological, existential and spiritual interventions (Breitbart, 2010).

Interventions for despair at the end of life

In the past two decades clinicians working with terminally ill patients have developed psychotherapy techniques targeting factors that contribute to suffering at the end of life. In this section we will describe interventions that address some of these common factors including spiritual suffering, demoralization, loss of dignity, and loss of meaning.

Spiritual suffering

For some patients spiritual well-being is felt to be a crucial aspect for coping with terminal illness. Often when faced with dying, patients struggle with questions about their own mortality, the meaning of life and the existence of a higher power. Some may turn to religion for such answers, while others rely on different spiritual beliefs. When spiritual well-being was examined in a population of terminally ill hospice patients, it was found that those with a sense of spiritual well-being had some protection against end-of-life despair (McClain et al., 2003). This finding points to the importance of addressing spiritual concerns in the terminally ill. By asking about their spiritual beliefs, assessing the importance of spirituality in patients' lives, exploring whether they belong to a spiritual community and offering chaplaincy referrals, one may be able to address some of these concerns.

Rousseau (2000) outlines an approach for the treatment of spiritual suffering composed of the following steps:

1. controlling physical symptoms,
2. providing a supportive presence,
3. encouraging life review to assist in recognizing purpose, value, and meaning,
4. exploring guilt, remorse, forgiveness, reconciliation,
5. facilitating religious expression,
6. reframing goals,
7. encouraging meditative practices, focusing on healing rather than cure.

Rousseau has presented an approach to spiritual suffering which is an interesting blend of basic psychotherapeutic principles. Psychotherapeutic techniques that are particularly adaptive to psychotherapy with the dying such as life narrative and life review are also included. There is an emphasis on facilitating religious expression and confession that in fact may be extremely useful to many patients, but is not applicable to all patients and not necessarily an intervention that many clinicians feel comfortable

providing. What Rousseau's work suggests is that novel psychotherapeutic interventions aimed at improving spiritual well-being, sense of meaning and diminishing hopelessness, demoralization, and distress, are critically important for provision of best palliative care to the terminally ill.

Demoralization

Kissane and colleagues (2001) have described a syndrome of demoralization in the terminally ill patient which consists of a triad of hopelessness, loss of meaning and existential distress expressed as a desire for death. They argue that this syndrome is distinct from depression because, unlike depression, it is not usually associated with anhedonia. Demoralization is often seen in patients with life-threatening illness, disability, bodily disfigurement, fear, loss of dignity, social isolation and feelings of being a burden. Kissane and his group describe a treatment approach for demoralization syndrome that is both multidisciplinary and multimodal. It consists of:

- ensuring continuity of care and active symptom management,
- ensuring dignity in the dying process,
- utilizing various types of psychotherapy to help sustain a sense of meaning, to limit cognitive distortions and maintain family relationships (i.e. meaning-based, cognitive-behavioural, interpersonal, and family psychotherapy interventions),
- using life review and narrative,
- paying attention to spiritual issues,
- using pharmacotherapy for co-morbid anxiety, depression and delirium.

The goal of this approach is to restore hope by valuing and affirming the story of their lives, their roles, accomplishments and sources of fulfilment (Kissane et al., 2009).

Loss of dignity

Dignity is defined as the quality or state of being worthy, honoured, or esteemed. Dignity therapy, developed by Harvey Chochinov and colleagues (2002), is a therapeutic approach designed to decrease suffering, enhance quality of life and bolster a sense of dignity for the patient's approaching death. They examined how dying patients understand and define the term 'dignity', in order to develop a model of dignity in the terminally ill. A semi-structured interview was designed to explore how patients cope with their advanced cancer and to detail their perceptions of dignity. Three major categories emerged from a detailed qualitative analysis, including illness-related concerns (concerns that

derive from or are related to the illness itself, and threaten to or actually do impinge on the patient's sense of dignity), dignity-conserving repertoire (internally held qualities, personal approaches or techniques that patients use to bolster or maintain their sense of dignity), and social dignity inventory (social concerns or relationship dynamics that enhance or detract from a patient's sense of dignity). These broad categories and their carefully defined themes and sub-themes form the foundation for an emerging model of dignity amongst the dying. The concepts of dignity and dignity-conserving care offer a way of understanding how patients face advancing terminal illness, and present an approach that clinicians can use to explicitly target the maintenance of dignity as a therapeutic objective and principle of bedside care for patients nearing death. In the therapy patients are invited to discuss issues that matter most or that they would most want remembered. Sessions are transcribed and edited, with a final version that they can bequeath to a loved one. In 2005 Chochinov and colleagues (2005) studied 100 terminally ill patients who received dignity therapy: 91% reported feeling satisfied or highly satisfied with the intervention, 86% found it helpful or very helpful, 76% found that it heightened their sense of dignity, 68% indicated that it increased their sense of purpose, 67% reported that it improved sense of meaning and 47% indicated that dignity therapy increased their will to live (Chochinov et al., 2005).

Chochinov et al. (2011) reported their findings of the effect of dignity therapy on distress and end-of-life experience in terminally ill patients from a randomized controlled trial. No significant differences were noted in the distress levels before and after completion of the study in the three groups, namely dignity therapy, client-centred care, or standard palliative care. For the secondary outcomes, patients reported that dignity therapy was significantly more likely than the other two interventions to have been helpful, improve quality of life, increase sense of dignity, change how their family saw and appreciated them, and be helpful to their family. Dignity therapy was significantly better than client-centred care in improving spiritual well-being, and was significantly better than standard palliative care in terms of lessening sadness or depression. Although the ability of dignity therapy to mitigate outright distress, such as depression, desire for death or suicidality, has yet to be proven, its benefits in terms of self-reported end-of-life experiences support its clinical application for patients nearing death.

Loss of meaning

Interventions for hopelessness and loss of meaning and purpose in the terminally ill are of particular

importance when addressing the issues of desire for death and despair at the end of life. Breitbart and colleagues (2004) have developed an intervention termed 'meaning-centred' psychotherapy for advanced cancer patients, an intervention based on the concepts and principles of Viktor Frankl's writings and logotherapy. Viktor Frankl, a holocaust survivor and psychiatrist, described that the will to meaning is an inherent drive to connect with something greater than one's own needs, and through this one finds meaning and self-transcendence particularly at times of intense psychological and physical suffering (Frankl, 1959). Meaning-centred psychotherapy has aimed at restoring a sense of meaning, peace and purpose in patients with advanced cancer (Breitbart et al., 2004). Meaning-centred psychotherapy is a manualized intervention that consists of eight 90-minute weekly sessions. Each session includes didactics, discussion and experiential exercises focused around particular themes related to meaning and advanced cancer. The session themes include:

- Session 1: Concepts and sources of meaning
 - Introductions to interventions and meaning
- Session 2: Cancer and meaning
 - Identity, before and after cancer diagnosis
- Session 3: Meaning and historical context of life
 - Life as a living legacy (past)
- Session 4: Storytelling, life project
 - Life as a living legacy (present, future)
- Session 5: Limitations and finiteness of life
 - Encountering life's limitations
- Session 6: Responsibility, creativity, deeds
 - Actively engaging in life (via creativity and responsibility)
- Session 7: Experience, nature, art, humour
 - Connecting with life (via love, beauty and humour)
- Session 8: Termination, goodbyes, hopes for the future
 - Reflections and hopes for the future

In a recent study, Breitbart and colleagues (2010) found that when compared to supportive group psychotherapy, patients involved in meaning-centred group psychotherapy had significant benefits in areas of spiritual well-being and enhancing a sense of meaning (Breitbart et al., 2010). A later study examining individual meaning-centred psychotherapy found that patients with advanced cancer had clear short-term benefits for spiritual suffering and quality of life when compared to therapeutic massage (Breitbart et al., 2012).

Delirium

In the palliative care literature, delirium occurring at the end of life is referred to as 'terminal delirium', 'terminal restlessness', or 'terminal agitation'. Despite being the most common neuropsychiatric complication of advanced illness, delirium is often under-diagnosed and untreated in palliative care settings. Delirium is a harbinger of impending death among terminally ill patients, and also a significant source of distress for patients, families and staff. It can interfere dramatically with the recognition and control of other physical and psychological symptoms such as pain in later stages of illness. Palliative care clinicians should thus be familiar with the assessment and management of delirium, as well as the controversies regarding the goals of management in the terminally ill (Breitbart & Alici, 2008; Breitbart et al., 2002; Coyle et al., 1994).

The experience of delirium for patients, families and staff

Delirium causes significant distress in patients, families, and staff (Breitbart et al., 2002; Buss et al., 2007; Morita et al., 2004). In a study of terminally ill cancer patients, Breitbart et al. (2002) found that 54% of patients recalled their delirium experience after recovery from delirium. Factors predicting delirium recall included the degree of short-term memory impairment, delirium severity, and the presence of perceptual disturbances (the more severe, the less likely recall). Patients, spouses or other caregivers, and nurses each rated distress related to the episode of delirium. The most significant factor predicting distress for patients was the presence of delusions. Patients with hypoactive delirium were just as distressed as patients with hyperactive delirium.

Assessment and management of delirium in the terminally ill

In the palliative care setting several instruments have been validated for diagnosing and monitoring severity of delirium, such as the Memorial Delirium Assessment Scale (MDAS) and the Confusion Assessment Method (Breitbart et al., 1997; Lawlor et al., 2000; Ryan et al., 2009). The MDAS is a 10-item tool useful both for diagnostic screening and assessing delirium severity among patients with advanced disease (Breitbart et al., 1997). The Confusion Assessment Method is a 9-item delirium diagnostic scale based on the DSM-III-R criteria for delirium (Inouye et al., 1990; Ryan et al., 2009). The standard approach to managing delirium remains relevant in the terminally ill, including a search for

underlying causes, correction of those factors, and management of the symptoms of delirium (Breitbart, 2001; Breitbart & Alici, 2008; Breitbart et al., 2000). The ideal and often achievable outcome is a patient who is awake, alert, calm, cognitively intact, not psychotic, and communicating coherently with family and staff. In the terminally ill patient who develops delirium in the last days of life (terminal delirium), the management differs, presenting a number of dilemmas, and the desired clinical outcome may be significantly altered by the dying process.

Delirium can have multiple potential aetiologies. In patients with advanced cancer, for instance, delirium can be due to the direct effect of cancer on the central nervous system (CNS), indirect CNS effects of the disease or treatments (e.g. medications, electrolyte imbalance, failure of a vital organ, infections, vascular complications), and/or pre-existing CNS disease (e.g. dementia) (Bruera et al., 1992; Lawlor et al., 2000). Given the large numbers of drugs terminally ill patients require and the fragile state of their physiological functioning, even routinely ordered hypnotic agents may be enough to tip patients over into delirium. Narcotic analgesics, especially meperidine, are common causes of confusional states, particularly in the elderly and terminally ill.

In confronting delirium in the terminally ill or dying patient, a differential diagnosis should always be formulated as to the appropriate extent of diagnostic evaluation that should be pursued in a dying patient with a terminal delirium (Breitbart, 2001). Most palliative care physicians would undertake diagnostic studies only when a clinically suspected aetiology can be identified easily, with minimal use of invasive procedures, and treated effectively with simple interventions that carry minimal burden or risk of causing further distress. Most often, the aetiology of terminal delirium is multifactorial or may not be reported. When a distinct cause is found for delirium in the terminally ill, it may be irreversible or difficult to treat. Studies in patients with earlier stages of advanced cancer have demonstrated the potential utility of a thorough diagnostic assessment (Bruera et al., 1992; Coyle et al., 1994). When such diagnostic information is available, specific therapy may be able to reverse delirium.

A diagnostic work up, in terminal delirium, should include basic assessment of potentially reversible causes of delirium while minimizing any investigation that would be burdensome for the patient. A full physical exam should be conducted to assess for evidence of sepsis, faecal impaction, dehydration, or major organ failure. Medications that could contribute to delirium should be reviewed. Oximetry can rule out hypoxia; one set of blood draws can assess for metabolic disturbances and

haematological abnormalities. Imaging studies of the brain and assessment of the cerebrospinal fluid may be appropriate in some instances if they have the potential to identify lesions amenable to palliative treatment.

Delirium: pharmacological interventions

Antipsychotics or sedatives are often required to control the symptoms of delirium in palliative care settings. Low doses of neuroleptic medication are usually sufficient in treating delirium in the terminally ill, but high doses have sometimes been required (Breitbart & Alici, 2008). Haloperidol remains the drug of first choice and may be given orally or parenterally (Breitbart & Alici, 2008). Many palliative care clinicians use low dose atypical antipsychotics in the management of delirium in the terminally ill (Boettger & Breitbart, 2005; Breitbart, 2001; Breitbart & Alici, 2008). A Cochrane review comparing the efficacy and the adverse effects of haloperidol and atypical anti-psychotics concluded that haloperidol, risperidone, and olanzapine were all effective in managing delirium, and that extrapyramidal adverse effects did not differ significantly between atypical antipsychotics and haloperidol (Lonergan et al., 2007). Psychostimulants have also been suggested for the treatment of hypoactive delirium, with the aim of improving cognitive functioning and psychomotor activities. The evidence for the use of psychostimulants in delirium is still limited.

Although neuroleptic drugs are generally very beneficial in reducing agitation, anxiety, and confusion in delirium, this is not always possible in terminal delirium. A significant group (at least 10–20%) of terminally ill patients experience delirium that can only be controlled by sedation to the point of a significantly decreased level of consciousness (Fainsinger et al., 2000; Lo & Rubenfeld, 2005; Rietjens et al., 2008). The goal of treatment in those cases is quiet sedation only. Before taking on such an intervention, the clinician should discuss with the family (and with the patient if he or she has lucid moments), the concerns and wishes for the type of care that can best honour the patient's and family's values. Family members should be informed that the goal of sedation is to provide comfort and symptom control and not to hasten death. Terminal sedation intended to maximize the patient's comfort is not euthanasia.

Several aspects of the use of neuroleptics and other pharmacological agents in the management of delirium in the dying patient remain controversial in some circles. Some view delirium as a natural part of the dying process that should not be altered and argue that pharmacological interventions are

inappropriate in the dying patient. Another concern often raised is that these patients are so close to death that aggressive treatment is unnecessary. Parenteral neuroleptics or sedatives may be mistakenly avoided because of exaggerated fears that they might hasten death through hypotension or respiratory depression. Many clinicians are unnecessarily pessimistic about the possible results of neuroleptic treatment for delirium. They argue that since the underlying pathophysiological process often continues unabated, no improvement can be expected in the patient's mental status. Clinical experience in managing delirium in dying patients suggests that the use of neuroleptics in the management of agitation, paranoia, and hallucinations is safe, effective, and often quite appropriate (Breitbart, 2001; Breitbart & Alici, 2008). Management of delirium on a case-by-case basis seems wisest.

Delirium: non-pharmacological interventions

In addition to seeking out and potentially correcting underlying causes for delirium, environmental and supportive interventions are important. In fact, in the dying patient these may be the only steps taken. The presence of family, frequent reorientation, correction of hearing and visual impairment, reversal of dehydration, and a quiet well-lit room with familiar objects are all helpful in reducing the severity and impact of delirium in seriously ill patients. However, these interventions are less applicable in the last days of life, and there is little likelihood that they would prevent terminal delirium.

Bereavement

Bereavement care is an integral dimension of palliative care, particularly for the 20% of bereaved individuals who develop complicated grief, for which effective therapies are available. Normal grief is an inevitable dimension of humanity, an adaptive adjustment process, and one that, with support, can be approached with courage. As the patient and family journey through palliative care, the clinical phases of grief progress from anticipatory grief through to the immediate news of the death, to the stages of acute grief, and potentially for some, complications of bereavement.

Anticipatory grief generally draws the supportive family closer. In contrast, for some families difficulties emerge as they express their anticipatory grief. Impaired coping is exhibited through protective avoidance, denial of the seriousness of the threat, anger, or withdrawal from involvement. Most commonly, sub-threshold or mild depressive or anxiety disorders develop gradually as individuals struggle to adapt to unwelcome changes. During this phase of

anticipatory grief, families that are capable of effective communication should be encouraged to openly share their feelings as they go about the care of their dying family member or friend. Saying goodbye needs to be recognized as a process that evolves over time, with opportunities for reminiscence, celebration of life and contribution of the dying person, expressions of gratitude, and completion of any unfinished business (Meares, 1981). These tasks have the potential to generate creative and positive emotional aspects of what is otherwise a sad time for all.

Sometimes staff will have concerns about the emotional response of the bereaved. If there is uncertainty about its cultural appropriateness, consultation with an informed cultural intermediary may prove helpful.

Complicated grief has been conceptualized as a stress response syndrome that results from failure to integrate the loss, making it difficult to function in a world without the deceased, with avoidance a central feature (Shear et al., 2007). According to DSM-V, a diagnosis of persistent complex bereavement disorder could be made if, since the death of someone with whom a person had a close relationship, they have experienced persistent yearning/longing for the deceased, or intense sorrow and emotional pain in response to the death, or preoccupation with the deceased, or preoccupation with the circumstances of the death. Any one of the symptoms should be experienced on more days than not and to a clinically significant degree, as well as having persisted for at least 12 months after the death.

A common form of complicated grief, chronic grief is particularly associated with overly dependent relationships in which a sense of abandonment is avoided by perpetuation of the relationship through memorialization of the deceased and maintenance of continuing bonds. Social withdrawal and depression are common. A fantasy of reunion with the deceased can cause suicide to be an increasingly attractive option. Active treatment using antidepressants and cognitive behavioural therapy to reality test the loss and promote socialization is often appropriate for chronic grief.

When the death has been unexpected or its nature is in some way shocking – traumatic, violent, stigmatized, or perceived as undignified – its integration and acceptance may be interfered with by the arousal and increased distress that memories can trigger. Intensive recollections including flashbacks, nightmares, and recurrent intrusive memories cause hyperarousal, disbelief, insomnia, irritability, and disturbed concentration that distort normal grieving (Prigerson & Jacobs, 2001). The shock of the death can precipitate mistrust, anger, detachment, and an unwillingness to accept its reality. These reactions at a sub-threshold level are on a continuum with the

full features of acute and post-traumatic stress disorders, but sub-threshold states have been observed to persist for years and contribute substantial morbidity. Palliative care deaths involving profound breakdown of bodily surfaces, gross disfigurement due to head and neck cancers, or other changes eliciting fear, disgust, or mortification may generate traumatic memories in the bereaved. Schut et al. (1997) found that PTSD was often correlated with the perceived inadequacy of goodbye and suggested that rituals to complete this be integrated into grief therapies.

Grief therapies

The most basic model is a supportive-expressive intervention in which the person is invited to share his or her feelings about the loss to a health professional who will listen and seek to understand the other's distress in a comforting manner. The key therapeutic aspects of this encounter are the sharing of distress and, through the relational understanding that is acknowledged, some shift in cognitive appraisal of the reality that has been forever altered. For most, although bereavement is painful, personal resilience will ensure normal adaptation. Early intervention should be considered for those at risk of maladaptive outcomes, and those who later develop complicated bereavement need active treatments. The spectrum of interventions spans individual, group, and family oriented therapies and encompasses all schools of psychotherapy as well as appropriately indicated pharmacotherapy. A typical intervention entails six to eight sessions over a several-month period.

Conclusion

The psychiatrist can play an important role in the care of patients with advanced cancer. Palliative care for terminally ill patients must include not only control of pain and physical symptoms but also assessment and management of psychiatric and psychosocial complications. In the palliative care setting the psychiatrist is commonly consulted to assess and manage anxiety, depression and delirium, but also must be adept in dealing with issues of existential despair, spiritual suffering and issues of bereavement.

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