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Tipping Point: Pathogenic Stress and the Biopolitics of Euthanasia

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Abstract

Hopelessness and demoralization following a terminal diagnosis can affect the capacity for self-governance. Such dispositions can increase the allostatic load—the cumulative burden of stress and anxiety—resulting in a neurophysiologic decline that can impair autonomy and influence the desire to end one's life deliberately. An allostatic overload is characterized by the inability to autoregulate stress and is associated with pathological changes to the hypothalamic–pituitary–adrenal axis and hippocampus. These changes raise concerns about the reliability of concepts of autonomy *in extremis*, potentially undermining arguments that are used to justify voluntary euthanasia and medically assisted death. Studies have associated depression and hopelessness with suicidal ideation in the general population. However, fewer studies have examined how patients without a history of depression or suicidal ideation may suddenly contemplate the act when facing a terminal prognosis. This paper will argue that an allostatic overload can help explain how the spectrum of physical and psychological comorbidities associated with the onset of a terminal illness can influence a decision to hasten death. Data show that patients with a terminal disease wishing to hasten death typically exhibit lower rates of clinical depression, higher rates of demoralization, and a greater likelihood of rational suicide. These differences indicate that suicidal ideation in the terminal disease patient population is different. Changes in autonomous decision-making secondary to pathological alterations in the brain may offer an explanation. Such changes have been shown to dysregulate executive control functions, specifically intentionality and voluntariness. Clinical evidence also indicates that spirituality and hopefulness can help manage the allostatic load during the palliative stages of a disease so that patients can better process end-of-life decisions. Based on these data, this paper will further argue that jurisdictions offering euthanasia are morally compelled to make mental and spiritual counseling available to patients seeking this course of action.

Keywords

Allostasis, allostatic overload, autonomy, biopsychosocial health, demoralization, Euthanasia, hope, moral psychology, pastoral counseling, physician assisted suicide

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Introduction

Debates about the moral and ethical implications of legalized euthanasia and medically assisted death often overlook the central question of why (Doré 2023). Why does someone whose moral code may have excluded suicide in life become reconciled with hastening death in sickness? Rather than answer this difficult question, arguments that underpin the legalization of medically assisted dying and euthanasia are justified on the false assumption that dignity in death is simply a respect for autonomy (Sulmasy 2008). However, clinical evidence suggests that the onset of a devastating illness can change the capacity for self-governance, indicating that greater dignity may be found in treating the biopsychosocial dimensions of end-stage disease that threaten to tempt nature.

Facing a terminal disease or debilitating illness, patients may turn to the option of ending their lives before natural death. The reasons are multifaceted. Many choose to hasten death in the belief that they are exercising control over the situation and wish to confront death on their terms (Weir 2017). Loss of dignity and autonomy are other frequently cited concerns (Blanke et al. 2017), as are apprehensions about the burden placed on loved ones (Wiebe et al. 2018). Fear of the unknown and the wish to avoid prolonged pain and suffering that patients believe will be part of the course of their disease can also contribute to a desire for an early exit (Wiebe et al. 2018).

Many terms and phrases exist to describe the act of suicide as an end-of-life measure for patients facing an intractable illness. Distinctions between euthanasia and medically assisted/aided death are becoming increasingly blurred as legislative initiatives are being expanded and commentators come to grips with an appropriate set of terms (Goligher et al. 2017). How does society reconcile a prescription for a lethal pharmacological cocktail to be taken at home versus the use of an intravenous port delivering a similar set of drugs in a palliative care setting as materially different? As various jurisdictions expand legislative opportunities for euthanasia and assisted suicide, these definitions begin to lack specificity. Switzerland does not allow euthanasia but has few limits on assisted suicide (Hurst and Mauron 2003). Laws in The Netherlands and, more recently, Canada, California, and Oregon are permissive and lack regulatory oversight such that "physician assistance" is a perfunctory approval in most situations (Mroz et al. 2021). Others argue that phrases like "physician-assisted suicide" imply that the patient can seek euthanasia for a legitimate medical reason when, in most cases, no justification is necessary (Cavanaugh 2001). In Flanders where reporting is compulsory, only half of the physician-directed cases of euthanasia are reported to authorities (Smets et al. 2010). Comparing physician-assisted deaths with other practices of medicine becomes risible when juxtaposed with standards of medical practice that are enforced by guidelines, regulations, and evidence-based medicine. Finally, the use of prefixes such as medical- or physician-assisted death implies that euthanasia is a legitimate medical procedure in the presence of strong vocal opposition by professional organizations (American Medical Association 2023), physicians (Sulmasy et al. 2016; Hetzler et al. 2019), and other healthcare providers (MacLeod, Wilson and Malpas 2012). Collectively, this paper proposes the phrase self-selected euthanasia (SSE) to include patient intention or consent, family or designated caregiver intention or consent in the case of an incapacitated patient, and the use or nonuse of a healthcare provider in ending life. Self-selected euthanasia is meant to distinguish suicide committed in the fullness of life that is frequently impulsive and secondary to psychiatric illness. In discussing issues of patient autonomy relative to elective end-of-life, SSE is more consistent with autonomous action and intention, the prevailing consideration underlying the action, regardless of the legislative or healthcare environment. The term connotes an elective decision, an ostensibly rational action, by the patient to

end his or her life on the terms they have chosen and differs from suicide in the general population because the decision is precipitated by a devastating change in health.[1]

The decision to pursue SSE is not a medical one but an exercise of autonomous authority (Braun 2023). This authority is frequently employed as the justification for SSE. A purely autonomous view leaves the decision solely to the patient or a designated legal representative. Other views hold that autonomy alone is not sufficient and that an act of SSE must also be morally justified by its beneficence. The "joint view" argues that an option for euthanasia is firstly controlled by the patient and must be judged to be in the patient's best interest. (De Haan 2002). The prevailing public opinion—and the view that largely dominates public discourse and various legislative initiatives—appeals to consequentialism that is grounded in the concept that the opportunity to alleviate suffering is the greater social good (Schmidt 2002). In this regard, most legislative action defaults to a broad concept of autonomy as the primary justification for SSE.

Beauchamp and Childress offer that at a minimum, autonomy is the ability for self-governance free from outside influence (Beauchamp and Childress 2019, 101). Gillon argues that it is precisely because of the *prima facie* nature of autonomy that it is the truest of the four principles proposed by Beauchamp and Childress, the others — nonmaleficence, beneficence, and justice — given to one degree or another to interpretation of scope (Gillon 1994). In a survey conducted among patients seeking assisted deaths in Canada, over half (52%), cited loss of autonomy as the primary reason. Loss of autonomy was the most important concern in 16% of patients with malignancies, 36% with neurological disease, and 24% with end-organ failure (Wiebe et al. 2018). In a report by the Oregon Public Health Division, 91% of the people who requested SSE cited loss of autonomy as the primary reason (Oregon Health Authority 2023).

A more thorough examination of the philosophical arguments that underlie autonomous decision-making is beyond the scope of this paper. This essay pertains largely to concerns of SSE within the legislative domains of Western medicine which predominantly rely on generalized concepts of patient autonomy. The prevailing right of self-determined health is an unassailable pillar in most legislation.[2] Therefore, autonomy used in this context is primarily aligned with the capacity for self-control and the exercise of one's moral agency (Engelhardt 1996). It is in this light that a critical examination will be undertaken regarding the potential for pathogenic stress to alter current concepts of autonomy on which these laws are based.

A Case for Impaired Autonomy

Choosing to end one's life is considered to be the ultimate demonstration of autonomy grounded in a presumptive right to act as one's moral arbiter (Yuill 2015). A sense of control comes from the certainty of things we can achieve mastery of versus things that present as fate. Under normal conditions, we might understand this dynamic as avoiding stepping in front of a moving bus versus knowing the time and method of our death. As death becomes more certain, the decision to hasten the end is generally viewed as a final act of control (Monforte-Royo et al. 2012). However, if one's sense of control can be altered by biochemical changes secondary to the stress and anxiety associated with the confrontation with death, then, according to Beauchamp and Childress, autonomy is no longer free from outside influence. The capacity to freely choose is restricted by a growing inability to resist feelings of hopelessness and despair as death draws closer (Schmidt 2002). When the ability to make the same autonomous decisions that would otherwise occur in an environment of independence and rational freedom becomes compromised in a state of mortal defeat[3] (Cohen 1985) the legitimacy of the decision to pursue SSE must be questioned.

Suicidality in the general population is most closely associated with clinical depression

(Stone 2018). Approximately 90% of suicides are associated with major clinical depression, substance abuse, or both. The lifetime prevalence of passive suicidal ideation in the general population is 10.6% (Liu, Bettis and Burke 2020). Higher rates of ideation are significantly correlated with patients with one or more serious illnesses (Druss and Pincus 2000), and more than twice as high in patients diagnosed with terminal cancer (Fox et al. 1982; Misono et al. 2008). The number of people who commit what has been termed as a "rational suicide"—absent of somatic or psychiatric pathology—is approximately 1–2% (Rabins 2007). Most SSE is characterized as active requests and rational actions (Wittwer 2013), whereas conventional suicide is largely viewed as impulsive secondary to psychiatric illness (Stacy and Schulkin 2022). These differences highlight that the decision-making process leading to suicide and what may be considered rational action is different in the two populations.

Patients electing SSE often attribute suffering to a physical decline and have fewer psychiatric comorbidities (Gramaglia, Calati, and Zeppegno 2019). In both situations, the conditions under which autonomous decision-making is thought to be operational are compromised (Petersen and Dige 2023). For suicide to be rational, it must be an action taken in the wholeness of life characterized by an ability to exercise control without undue outside influence. Gramaglia and colleagues suggest that a rational suicide is possible. However, the presumption of competency in these patients may be premature in some instances, suggesting that silent or indirect symptomatology must be further explored.

The rather clear association between clinical depression and suicide becomes opaque with the onset of terminal disease and the confrontation with death. In this case, hopelessness appears to be more positively correlated than depression alone in suicidal ideation (Chochinov et al. 1998; Breitbart et al. 2000; Abbey et al. 2006). Some studies have suggested that patients who opt for SSE have relatively low rates of clinical depression, leading to a higher proportion of rational suicides (Pearlman et al. 2005; Cheung, Douwes and Sundram 2017). However, the authors are careful to point out that when depression is present, feelings of hopelessness can heighten cognitive distortions. Numerous studies suggest multiple reasons why a patient may elect SSE, including loss of autonomy, independence, and control, along with fear of the unknown and pain (Wiebe et al. 2018). While these reasons singularly or in combination may lead one to consider hastening death, the underlying question of why terminal patients without a history of suicidal ideation or clinical depression may become receptive to euthanasia remains unanswered (Breitbart et al. 2000).

A potential explanation for this difference is a pathological change in brain function secondary to an allostatic overload (AO) that affects one's autonomy. McEwen and Stellar introduced the concept of allostasis and allostatic loading as "the cost of chronic exposure to fluctuating or heightened neural or neuroendocrine response resulting from repeated or chronic environmental challenge that an individual reacts to as being particularly stressful" (McEwen and Stellar 1993). The concept describes how cumulative exposure to endogenous and exogenous stressors can alter the physiological response to stress. The body's primary response to stress comes from regulating the metabolism of cortisol, an essential hormone that controls many important physiological processes. In normal circumstances, the body works to carefully regulate the amount of cortisol seeking homeostasis. During periods of stress, the body will increase levels of cortisol to help manage the response. However, repeated exposure to anxiety and stress can interfere with cortisol metabolism and disrupt homeostasis, leading to negative changes in health (Yaribeygi et al. 2017). High ALs are negatively correlated with survival and quality of life in serious and end-stage illnesses including cancer (Mathew et al. 2021, Fava et al. 2023), cardiovascular (Parker et al. 2022), and neurological disease (Carbone 2021). Increases in AL are also

associated with a greater risk for all-cause mortality (Parker et al. 2022) and with suicidal ideation (O'Connor, Gartland, and O'Connor 2020).

When the stress overwhelms the body's ability to cope, the patient enters a state of AO (Fava et al. 2019). An AO is a somatic decoupling indicative of a disruption of the parasympathetic and immunometabolic systems that manage cognition and other mental health faculties (Carbone 2021). Allostatic overload is associated with the dysregulation of executive control functions in the brain including the capacity for autonomy, specifically intentionality, understanding, and voluntariness (Workman et al. 2000) and is positively correlated with suicide (Stacy and Schulkin 2022).

A probable mechanism for the neurophysiologic decline and loss of autonomy is an adverse change to the hippocampus due to the sustained production of cortisol consistent with an AO. The hippocampus regulates important emotional components of the brain including memory recall and executive function (Frodl et al. 2006). Under normal circumstances, the hypothalamic–pituitary–adrenal (HPA) axis responds to stress by regulating cortisol and signaling the hippocampus (Dunlavey 2018). Symptoms of sustained HPA suppression include depression, anxiety, fatigue, and loss of autonomy. Animal and human studies have demonstrated that abnormally high ALs and sustained AO with a corresponding overproduction of cortisol lead to pathological changes in the hippocampus, including dendritic remodeling and atrophy of the neurons, resulting in debilitating depression and anhedonia (McEwen 2006; Ullmann et al. 2019).

Stacy and colleagues have highlighted the correlation between AO and the desire to find solace in death. However, the dynamics that influence suicide in the general population compared to terminal patients seeking a hastened death suggest that the effects of AO act differently in each group. The mechanisms contributing to the AL in both patient populations are complex and closely associated with declines in mental and physical health (Mathew et al. 2021). The relationship between AL and depression is an ongoing area of interest, though Beck and colleagues have associated a robust biological response to stress indicative of AO leading to pathological changes in the HPA axis as a potential contributor to the cognitive triad of depression, namely alterations to expectations of the future (hopeful vs. hopeless) (Beck and Bredemeier 2016).

Suicide typically follows a prolonged psychological struggle. On average, a completed suicide is preceded by eighteen nonfatal suicide attempts (Hirschfeld and Russell 1997), which are the strongest single predictor of suicide (Haukka et al. 2008). Increases in AL leading to suicide can exacerbate preexisting comorbid psychiatric conditions such as schizophrenia and bipolar disorders (Stacy and Schulkin 2022). Conversely, patients pursuing SSE have lower rates of psychiatric illness and suicidal ideation before the onset of their disease (Ganzini, Goy, and Dobscha 2008).[4] For most, late-onset suicidal ideation in the terminal patient population is secondary to the diagnosis. Stress from the loss of independence, fear, and dissatisfaction with the quality of life are coincident or in some cases slightly precede thoughts of suicide and have been shown to have a greater impact on suicidal ideation than symptomatic decline (Suarez-Almazor et al. 2002). For these reasons, increases in AL leading to AO in the SSE population are thought to be more closely associated with changes resulting from factors that contribute to biopsychosocial stress (Ruckenbauer, Yazdani and Ravaglia 2007).

The stress that comes from the onset of injury or illness can alter the capacity for autonomy and autonomous decision-making (Savulescu 2009). Similarly, various attributes associated with the progression of a terminal illness, including depression (Biegler 2010), loss of dignity (Mendonça 2019), loss of independence, and feelings of powerlessness (Richardson, MacLeod, and Kent 2010), can also act against normal perceptions of

autonomy. Patients who follow through with SSE cite multiple reasons for their decision, suggesting that a cumulative burden from one or more of these concerns can lead to thoughts of suicide (Wiebe et al. 2018). While the literature presents extensive correlation between these various stressors and SSE, the evidence for causation (i.e., which stressors in which combination lead to SSE) remains unclear (Friesen 2020). Changes in autonomous decision-making secondary to an AO may help explain two essential aspects of suicidal ideation in terminally ill patients. First, it offers a clinical explanation for how multiple correlates can act singularly or in combination to produce thoughts of hastening death. Second, an AO leading to an alteration in autonomy may also explain why patients without a history of suicidal ideation or clinical depression become receptive to the idea.

Hopelessness, Demoralization, and Allostasis

The connection between SSE and AO likely starts with the loss of hope. The same erosion of hope that leads to SSE is associated with increases in AL and AO (Mitchell et al. 2020). Destruction of hope in these situations connotes a devastating loss. Sullivan characterizes this kind of hopelessness as the attachment to the irretrievable absence of hope that comes from a declining state of health and the anticipation of suffering. "Hopelessness at the end of life is therefore not simply the absence of hope, but attachment to a form of hope that is lost" (Sullivan 2003). The distinction is important. Transient hopelessness, which might also be considered a deficit of optimism, can often be treated with counseling and other nonmedical interventions and is different from what Sullivan describes as trait hopelessness (Sachs et al. 2013). Trait hopelessness is the devastating loss of hope resulting from overwhelming negative emotions that displace the ability to hope and is a crucial factor in persistent patient desires for a hastened death (Sullivan 2003). For some, the confrontation with a terminal illness can obliterate hope (demoralization) and initiate a rapid downward spiral of one's somatic and cognitive well-being suggesting that the loss of hope in a patient with a terminal disease may be irrecoverable (Ratcliffe 2013). Examples of pathogenic stress leading to a sense of hopelessness include unexpectedly finding oneself in an ICU for a devastating illness. Such an experience can permanently alter the cognitive domain and lead to changes in individual personality or psychological integrity (Leach 2016).

For many, the sudden loss of hope that occurs from the collision with death is connected to a lack of preparation for the event. The SUPPORT study was undertaken to improve end-of-life decision-making processes to reduce the crisis of care that often accompanies end-of-life situations in the hospital (Connors 1995). The study sought to understand how better healthcare provider engagement, including patient–physician communication, at the time of death could mitigate the confrontation with it and lessen the overall tragedy. The investigators concluded that most patients and their caregivers delay the difficult discussions about end-of-life care—nearly half the DNR orders are written within the last two days of life—leading to a transition into palliative care for many patients very late in the process. While the study sought insights into ways to manage end-of-life care better, it also identified that most patients, hospitals, and caregivers are reluctant to give in to death. Consequently, the decision to pursue SSE in a terminal situation may begin with a high baseline of pathogenic stress—a preexisting elevated AL—compounded by the sudden understanding of the imminence of death and the exhaustion of hope.

Hopelessness comes from a loss of control. The situation leads to defeat and entrapment and shares similar symptoms with clinical depression (Taylor et al. 2011). Studies have associated hopelessness and ensuing depression with suicidal ideation in older adults (Lynch et al. 2004). Fewer studies have

considered how the erosion of hope secondary to intractable physical or mental illness may contribute to hopelessness and the patient's disposition and desire for early release (Chochinov et al. 1998). While many patients choosing SSE exhibit varying levels of depression; hopelessness; and an overall lower sense of independence, self-reliance, and spirituality, these findings are not consistent and the correlations are not always clear (Breitbart et al. 2000; Abbey et al. 2006). Most patients seeking SSE are not clinically depressed (Ganzini, Goy, and Dobscha 2008). A more relevant description may be "demoralization syndrome" in which the existential distress from the loss of hope leads to a sense of impotence and helplessness that can eventually progress to a desire for death (Kissane 2004).

Demoralization is defined as a persistent inability to cope secondary to feelings of helplessness, hopelessness, meaninglessness, and incompetence (Clarke and Kissane 2002). Whereas depression is differentiated by anhedonia and apathy (Kaneriya et al. 2023), demoralization is more likely to be differentiated by loss of control (Robinson et al. 2017). The two may coexist, but they are frequently considered independent clinical phenomena (Woźniewicz and Cosci 2023). Nearly half of patients diagnosed with major depressive disorder do not exhibit symptoms of demoralization, and more than two-thirds of the patients clinically demoralized do not satisfy clinical criteria for major depressive disorder (Fava and Guidi 2023). Patients with advanced cancer who exhibit symptoms of serious or moderate demoralization frequently exhibit lower rates of depression (Mehnert et al. 2011). These findings further complicate the landscape for SSE. Trait hopelessness leading to demoralization secondary to an AO cannot be ignored. Consequently, Gramaglia and colleagues' suggestion that suicidal ideation and suicide late in life can be rational in the absence of a diagnosable mental disorder indicates that the clinical detection of trait hopelessness can be difficult.

From these observations, an argument can be made that hope and allostasis are inversely related. The argument is made stronger when concepts of hope are more clearly defined. Hope is often used synonymously with a sense of optimism or a positive mental attitude; attributes generally regarded as an important psychological state necessary to cope with the stress associated with a terminal disease (Gallagher and Lopez 2009). The trivialization of hope leads to a degree of cynicism. For example, Friesen has argued that part of the tragedy of suicide is the loss of the hope that was still on the table for the decedent, whereas SSE only shortens the life of someone who has already lost hope (Friesen 2020). These concepts belie the more important constituents of hope that have been shown to positively alter neurohormonal pathways.

The opposite of trait hopelessness is dispositional hope and differs from optimism in the belief that circumstances can change. Like conventional concepts of hope, dispositional hope is also often mistreated in literature. Perhaps because dispositional hope necessarily attaches itself to a metaphysical element, there is some reluctance to explore its other side. According to W. W. Meissner, a physician and Jesuit priest, dispositional hope exists on the boundary that separates our physical and existential awareness (Meissner 1973). That is, our ability to hope only exists if we believe that some agency can deliver on the ask. Christianity and many other faiths tie hopefulness to a knowledge that lies beyond the empirical. God's plans are opaque. Faithful cross into these mysteries through prayer and intercession. Kant, in some contrast to a purely religious point of view—although some have argued that Kant's willingness to accept God is manifested in the concept of hope (Beyleveld and Ziche 2015)—argues that hope is a right. Kant further distinguished between a wish—a desired outcome—and hope—an anticipated goodness (Chignell 2022). A wish cannot become a hope unless some agency can affect the outcome. Our "happiness always remains a wish that cannot become a hope unless some other power is added" (Meissner 1973). Day offers that the opposite of hope is fear (Day 1970). Therefore, another way to consider

the concept of trait hopelessness is a loss of faith in any agency that can change the outcome and fear of the unknown. Its loss is enduring (Wilson et al. 2007).

Medicine reveals important psychological and physical dimensions of hope that are associated with positive clinical outcomes (Kubzansky et al. 2023). To be clear, both optimism and dispositional hope can benefit the patient. The largest bodies of research have focused on hope as a coping mechanism that is necessary to effectively manage patients by reducing the debilitating consequences of depression and despair (Cheavens and Whitted 2023) and its comorbid relation to the progression of disease and illness (Everson et al. 1996). It has been established that a positive mental framework grounded in hope leads to quantifiable improvements in quality-adjusted life years[5] and is associated with positive cognitive changes that can reduce anxiety (Wang et al. 2017). The management of end-stage or major life-altering disease benefits from hope when it is incorporated into the treatment plan (Pleeging 2022). In contrast, feelings of hopelessness, fear, and anxiety are comorbid, work against the aims of healthcare, and can accelerate the disease process (Dai et al. 2023).

As an example, hope has been extensively studied in oncology populations and is positively correlated with survival and improvements in quality of life (Xing et al. 2018). Corn and colleagues evaluated subgroups within the ENABLE I and ENABLE II studies—large, randomized trials to assess the role of palliative care in cancer patients—and concluded that dispositional hope, which the authors define as inherent hopefulness, is positively correlated with survival (Corn et al. 2022). While numerous studies associate hopefulness with improvements in the quality of life for terminal cancer patients (Ross et al. 2002), some have suggested that the will to live that comes from authentic hope can lead to increased survival by moderating the immune system (Spiegel and Giese-Davis 2003).

This evolving yet less well-understood aspect of hope and its potential to alter certain physiological processes suggests that dispositional hope may be protective against allostasis (Barnett 2014).[6] In a similar way that AL can upregulate pernicious biomarkers for inflammation, dispositional hope resulting from religiosity is associated with the downregulation of biomarkers for inflammation (Shattuck and Muehlenbein 2020). Similarly, reductions in AL are associated with changes in specific biomarkers of disease (e.g., changes in blood pressure in cardiac disease, and C-reactive protein in inflammatory disease) (Rodriquez et al. 2019). Hope has also been shown to be generally protective against AL, however, important observed ethnic differences require additional investigation (Mitchell et al. 2020). Importantly, Mitchell and colleagues did not discriminate between optimism and dispositional hope. Others have associated the failure to identify and treat AL and AO with higher rates of dysregulation of immune and endocrine pathways, tumor proliferation, inflammation, and poorer survival in terminal cancer patients (Alamoudi et al. 2023). These data indicate that dispositional hope may be "alloprotective" by reducing the demoralization that contributes to an AO while also minimizing the potential disruption to autonomy that follows a somatic decoupling.

This previously unidentified relationship between AO and pathological changes in autonomy leading to SSE indicates that an accurate assessment of the sources of demoralization and hopelessness, both antecedent to and strongly correlated with AL, is important for those working with the terminally ill (Abbey et al. 2006). The failure to recognize the unique nature of suicidal ideation in a terminal patient population secondary to an AO is likely missing a critical component of end-of-life care and suggests important areas of concern.

Implications of an AO

If AO resulting from a loss of hope compromises autonomy and precipitates a desire for SSE, then the clinical obligation to treat the antecedents of AL through the encouragement

and preservation of hope in the palliative stages of disease is necessary.

The confrontation with death is a personal experience. The engenderment of hope begins with the physician but cannot be the physician's sole responsibility. Some have argued that inspiring hope is the physician's most important role in exercising care for the patient (Temple 2018). Unfortunately, many physicians are ill-prepared for these difficult discussions and often leave the explanation of the grim details to other providers including physician's assistants, chaplains, and hospice and palliative care teams (VandeKieft 2001). According to the American College of Surgeons *Residents' Guide to Palliative Care*, a majority of patients expect their physicians to ask about spiritual and religious issues and to make appropriate referrals as part of the treatment plan (Dunn, Martensen and Weissman 2009).

The data presented in this essay and elsewhere reinforce the conviction that the terminally ill patient needs to encounter reasons for hopefulness at the outset and throughout the continuum of care to mitigate increases in AL that can influence the decision for SSE. Stressors that come from feelings of being a burden to loved ones, loss of religiosity, and financial concerns often have a greater effect on suicidal ideation than the physical symptoms of the disease. Moreover, because many signs of depression often manifest somatically, unless the patient is seen by a qualified healthcare provider, identifying occult signs of hopelessness and demoralization in this population is likely to be missed (Dugdale, Lerner, and Callahan 2019). The psychiatric and physical benefits that come from instilling and maintaining hope must be considered at times when hope is at its most vulnerable. The fact that few terminally ill patients seeking SSE are offered psychiatric care and even fewer are offered spiritual care suggests that instilling hope is not a priority.

Deflecting spiritual pain is largely overlooked in palliative care (McGrath 2003). In general, guidelines within jurisdictions that permit SSE lack formal oversight and are often disregarded by healthcare providers (Miller and Kim 2017). Tragically, SSE is more likely to be offered to disadvantaged patients including lower-income (Tran et al. 2022), less educated (Chambaere et al. 2013), and female and lonely individuals (Limb 2014). Importantly, many of these patients are already likely to have higher baseline ALs associated with less favorable socioeconomic statuses (Duru et al. 2012; Schulz et al. 2012; Obeng-Gyasi et al. 2022). Access to SSE does not discriminate and any history of preexisting AL is likely to be overlooked which may explain some of the observed disparities. Approximately 70% of the assisted deaths in Oregon were elderly cancer patients, of whom fewer than 5% had been referred for mental health counseling (Dugdale, Lerner, and Callahan 2019). Of the 10,061 Medical Aid in Dying (MAiD) provisions in Canada in 2021, fewer than 7% were referred to a psychiatrist (Doré 2023). Based on these data, it is safe to conclude that even fewer patients are referred to pastoral care or spiritual counseling (Schuhmann et al. 2021). These findings further reinforce an understanding that psychological and spiritual counseling work against the aims of laws permitting euthanasia. In most jurisdictions, it is far simpler to access the machinery of SSE than it is to seek mental healthcare (Pereira 2011). "We cannot afford to have these conversations conducted within unrealistic time constraints that do not allow for a fair and faithful determination that this is the right procedure for this person at this time" (Pesut et al. 2021).

Canada's MAiD program has been sharply criticized by religious and nonreligious groups for its failure to correctly evaluate and detect symptoms of late-onset depression due to disease progression that contributes to suicidal ideation (Gallagher, Passmore, and Baldwin 2020). Studies assessing suicide rates in cancer patients in Scandinavian countries found that patients who were not offered further treatment or access to the healthcare system experienced a higher rate of suicide further emphasizing the connection between

abandonment and hopelessness (Breitbart 1987).

Within the palliative care setting, there are opportunities to reinforce hope through the encouragement of spirituality. Many studies recognize the importance of spirituality in the hospice setting. However, within these settings, the meaning of spirituality is loosely defined. In general, most programs understand spirituality as a state of mental well-being and connectedness to nature versus the more traditional understanding of spirituality found in organized religions such as Christianity, Judaism, Islam, and others (Walter 2002). There is a trend among hospital chaplains to generally present themselves as spiritual care counselors who provide moral support to religious and nonreligious struggling with existential issues (Schuhmann et al. 2021). Attention to one's spiritual beliefs is an essential component of the palliative care process, and it is incumbent upon these ministers to move beyond reason for transient hope and find cause for dispositional hope.

Evidence connects religiosity and the dispositional hope that follows with clinical improvements. Patients who regularly attend church have lower ALs and associated mortality compared with those without an affiliation (Bruce et al. 2017). Researchers Shattuck and Muehlenbein conducted a random effect meta-analysis to establish the connection between the hope derived from religiosity and spirituality to various biomarkers including blood pressure, C-reactive protein, and cardiovascular health markers, showing that the hope stemming from these engagements is positively correlated with the activation of certain biochemical pathways that can mitigate increases in AL (Shattuck and Muehlenbein 2020). Others have shown a functional relationship to biomarkers associated with religiosity (Kharitonov 2012). Regular religious praxis leads to a psychosocial environment that benefits the patient in multiple ways including self-esteem, coping through personal mastery, emotional control, and the ability to reciprocate love and forgiveness, all important elements of maintaining control and minimizing AL. Breitbart and colleagues conducted a small, randomized control study demonstrating the use of spiritually meaningful group therapy, resulting in a significant improvement in spiritual well-being and quality of life while reducing hopelessness and the desire for a hastened death (Breitbart et al. 2015).

Studies have also shown that the stigma of patients facing a terminal illness that leads to demoralization and hopelessness can be successfully intervened with appropriate psychotherapeutic therapies focused on behavior modification, potentially mitigating the effects of allostasis (Nelson and Hope 2012). Interventions targeted at lowering AL can result in reproducible clinical benefits in a wide range of patients (Rosemberg et al. 2020). Studies have indicated that nonpharmacological activities such as exercise and social interaction are also effective at reducing AL in at-risk patient populations (D'Alessio et al. 2020).

Finally, brain plasticity remains an area of intense medical research. Studies have shown that dispositional hope and reduced AL are positively correlated with gray matter volume in adolescents (Wang et al. 2020). Anecdotal data also suggest that loss of hippocampal volume may be reversible in some situations suggesting that some of the effects of AO can be reversed (Pickering 2003; McEwen and Gianaros 2011). Studies that control for physical health, social ties, and stressors are also associated with overall reductions in stress and anxiety and indicate that changes in the HPA axis can be reversed with appropriate intervention to lower the AL (Ozbay et al. 2007).

Summary and Conclusions

Preventing an AO and restoring hope in terminally ill patients could potentially lessen the desire for SSE. Reasons for wanting to hasten the end of life in the presence of a devastating illness are a complex mix of multivariate factors. Suicidal ideation is highly correlated with hopelessness following

depression. Most suicide is impulsive and committed in the backdrop of a full life. These dynamics change in a patient population facing a terminal disease. In this population, ideation is more strongly associated with trait hopelessness and demoralization. These patients are more likely to view a decision to end life early as a rational act stemming from practical concerns of avoiding pain and suffering, burdening others, and exercising control over death. However, a question remains about whether degenerative changes in autonomous facilities may predispose patients to SSE when the loss of hope becomes profound.

This paper has proposed that a probable tipping point may be the pathological change to the executive functions of the brain that control autonomy occurring from a rapid increase in AL leading to an AO. The cumulative burden that comes from the confrontation with death can overwhelm the body's ability to manage stress, eventually shutting down biological pathways that regulate neurohormonal responses to stress. This paper has also proposed that allostasis and hope are inversely related and a possible therapeutic avenue for patients with end-of-life disease is the management of AL and its antecedents.

If this mechanism proves valid, then the justification of laws that permit SSE that are established using universal concepts of patient autonomy is called into question. Evidence suggesting that pathological alterations in autonomy are associated with untreated stress and AO undermines the central foundation of these regulations. Failure to recognize and treat sources of hopelessness and other stressors that contribute to the AL may predispose patients to SSE who might otherwise make a different choice in full possession of their autonomous decision-making faculties. Indiscriminate access to SSE is indicative that jurisdictions regard the patient's autonomous state as unchanged at the time SSE is sought. If autonomy has been compromised and left untreated, then the presumed autonomous faculties used to promulgate these laws must be questioned.

The evidence is also clear that the management of end-stage or major life-altering disease benefits when psychosocial–spiritual care is incorporated into the treatment plan. In contrast, feelings of hopelessness, fear, and anxiety are comorbid and work against the aims of healthcare in ways that can accelerate physical and mental decline leading to abject despair and isolation. A sudden increase in AL that negatively affects the neurohormonal balance may enhance the putative desideratum offered in SSE. The potential to preserve and possibly even return patients to full control of their autonomous decision-making capacity by reducing AL requires access to mental health counseling and spiritual care and is essential to ensuring that decisions made *in extremis* are not compromised by the lack of care and are consistent with a patient's values before the encounter with death.

Avenues for further investigation include a more careful understanding of how concepts of autonomy may change during times of extreme stress brought on by the recognition of being in a terminal state. Are these changes associated with an individual desire for SSE? Do the putative protections from religiosity and other spiritual activities lower allostatic loads in nonterminal and terminal patients alike? Are pathological changes associated with dysregulation of the HPA axis and hippocampus leading to changes in autonomy reversible through the restoration of hope? Finally, can interventions intended to increase hopefulness reduce the use of SSE as a rational choice in end-of-life situations? The answers to these questions challenge the current narrative about how SSE can be justified based on a single, universal concept of patient autonomy.

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Notes

1. A reasonable interpretation of this statement understands that decisions for SSE or suicide are rarely binary in nature. There are clearly some patients with a history of suicidal ideation or other psychological illness prior to their diagnoses. In these cases, decisions for SSE are more complex that those made in the absence of any preexisting disease. Consequently, patients identified with severe persistent mental illness likely arrive at a decision SSE differently and must be considered as a distinct cohort with separate medical needs (Trachsel and Jox 2022).
2. Within this narrow definition of autonomy, some mention of "precedent autonomy" is necessary. When the legally authorized representative acts in the interests of an incapacitated and incompetent patient to make decisions. In such situations, it is generally recognized that a proxy is obligated to exercise the patient's stated will according to an advanced directive. Precedent authority can be difficult to apply in end-of-life situations because often the conditions in which the directive was promulgated may change once capacity for autonomous decision making is lost (Davis 2002).
3. Cohen argues that the "ultimate defeat" is not death but institutionalization.
4. In patients with a history of psychiatric disorders, up to half have a history of attempted suicide prior to SSE (Kim, De Vries, and Peteet 2016).
5. A quality adjusted life year (QALY) is a unit of measure. One QALY is equivalent to one year of perfect health. QALY's are frequently used in health economics outcome assessment but can also be applied to the relative effectiveness of a therapy to determine its ability to extend life in a meaningful way.
6. It seems almost certain that the kind of hope that can alter physiological process is dispositional. See Krafft et al.

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