Neuropalliative Care

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Editors

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A Guide to Improving the Lives of Patients and Families Affected by Neurologic Disease

Springer

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Preface

When people hear the words "palliative care," they frequently think about hospice and cancer, if they have heard of palliative care at all. This is more than anything a historical accident. The modern palliative care movement began in England with Dame Cicely Saunders' creation of St. Christopher's Hospice in 1967, a model that works particularly well for providing compassionate end-of-life care for cancer patients. From the outset, however, the intent of palliative care was to improve the quality of life of all patients and families facing serious illness by treating them as whole people with needs going beyond the direct management of their disease such as physical symptoms, difficult emotions, social isolation, and spiritual distress. If you have picked up this book, then you likely either work with patients affected by neurologic illness or have experience as a family member or patient, and you don't need to be reminded of the substantial challenges facing this population that are not well met under current models of care. This includes such diverse issues as planning for the future; supporting the caregiver; making difficult treatment decisions in the face of uncertainty; managing grief, guilt, and anger; and treating intractable pain.

Fortunately, over the past few decades, the palliative care movement has continued to expand and evolve and is now recognized to offer support for patients and families from the time of diagnosis through the advanced stages of most serious and chronic illnesses, including neurological disorders. In this book we strive to present the latest research and most relevant skills to clinicians, hoping to meet these challenges and improve the lives of their patients in meaningful ways. This book is intended for all clinicians caring for patients with neurological illness and their families; while it may be of greatest interest to neurologists and palliative care specialists, we believe that other physicians, nurses, chaplains, and social workers – as well as trainees in these disciplines – may find great value in this book. The goal is to define palliative care needs specific to various neurological illness, to develop standards around recognizing and meeting these needs, and to help clinicians incorporate a palliative care approach for patients with serious neurological illness.

When we speak on this topic to neurology patient groups, they quickly turn from asking what palliative care is to why isn't everyone already doing this. The main barriers are educational and institutional – we need to educate clinicians and provide evidence to insurers and policy-makers of the effectiveness and necessity of this approach.

As a new field, we have all found our path to palliative care somewhat by accident, a combination of being touched by the struggles and suffering of our patients and their families and through the good fortune of connecting with outstanding mentors in the field of palliative care. We were also driven by our own personal dissatisfaction with the care we were providing and the meaning of our work, by questions such as "How can I help my patients make better decisions?", "How can I ease some of the grief and hopelessness of my patients and their families?", and "How can I stay open with persons who are declining, suffering, and dying?". Palliative care has provided us with means to answer these questions and tools to better address these issues. As the field of neurology is facing a crisis of physician burnout, we think that a palliative care approach may provide greater connection with patients, deeper meaning in this work, and greater emotional satisfaction, all of which can help build resilience. Just as we look to treat our patients as whole people, we must also care for ourselves as whole people and recognize the unique gifts we all have to offer. We hope this book is a beginning for your own journey into the world of palliative care and that this approach helps you and your patients as much as it has helped us.

Seattle, WA, USA — Claire J. Creutzfeldt
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My gratitude goes to Randy Curtis, Bob Holloway, and Will Longstreth for their inspiration, encouragement, invaluable conversations, and gentle nudges that helped me turn my passion into a career; the visionary Cambia Health Foundation and the wonderful community of Sojourns scholars; and of course my husband Armin, my son Jakob, and my daughter Helena, who keep my mind clear and remind me of what is most important in life.

Claire J. Creutzfeldt

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Benzi M. Kluger

I would like to thank all of my patients, mentors, trainees, and colleagues, including my coeditors, who have provided the inspiration, guidance, and support to help harmonize the field of neurology and palliative care to make neurological health ever better. I would be nowhere without the foundation my parents provided, the joy my children Julie and Melissa bring, and the never-ending love of my wife, Rose, who frequently reminds me “Don’t ever stop practicing palliative care; it’s too important.”

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Neuropalliative Care: An Introduction

1

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Through the history of neurological illnesses, the clinical focus and expectation has rarely been on cure. Rather, clinicians caring for patients with neurologic diseases accompany them on a journey that can sometimes last years and even decades, with often-increasing symptom burden and disability, changing social roles, loss of personhood and prognostic uncertainty. One billion people in this world suffer from a neurological illness and more than one in ten deaths worldwide are related to neurologic disease [1, 2]. The goal of this book therefore, is to provide guidance for clinicians caring for patients with serious neurological illness so they can provide meaningful support to patients and their families throughout their illness. We review the most important palliative care needs of common neurological illnesses; provide in depth instruction in communication skills and the conduct of important conversations; describe frameworks for providing goal-oriented care that is patient and family-centered. We intend this book to be a useful reference to help educate neurology providers about palliative care, and palliative care providers about neurology.

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What Is Palliative Care?

> *Palliative Care is specialized medical care that aims to recognize, prevent, and alleviate physical, social, psychological and spiritual suffering and improve communication about end of life and quality of life for patients with serious illness and their families.*

The past two decades have seen a remarkable development of palliative care worldwide. Originating in the world of cancer, palliative care has now matured into a wide-reaching concept for high quality care for all patients with serious illness. Palliative care can be provided at any time, including at the time of diagnosis, is not limited to those with poor prognoses, and may be provided alongside curative treatment. The most robust evidence supporting palliative care is still found in the oncology literature, where several studies have shown that early palliative care for patients with cancer led to

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reduced symptoms of depression and anxiety, improved quality of life, and even a survival benefit [3–5]. Key components of palliative care include (1) Building a relationship, rapport and trust with the patient and (2) with the patient's family; (3) Identifying and managing distressing symptoms such as pain or other symptoms, as well as spiritual suffering and social struggles; (4) Eliciting patient values to deliver care that respects the individual patient as a person; (5) Helping patients and families cope with life-altering circumstances, loss of independence, social roles and the loss of a loved one, along with preventing or managing grief; (6) Interpreting and communicating medical information and ensuring that patients and family understand their diagnosis, prognosis and treatment options; (7) Identifying and resolving conflicts between or among family members or medical team members; and (8) Planning for death and decline [6, 7]. To do this well, we need to acquire novel communication skills and a fresh understanding of patient- and family-centered care.

The Palliative Care approach

Like most medical subspecialties, palliative care includes certain skills that all healthcare providers should possess as it relates to the illnesses they care for, as well as more specialized skills that require dedicated training and practice. Primary palliative care, the palliative care that is provided by the patients' primary medical team (for example the Neurology team for a patient with Parkinson's disease), involves timely identification of palliative care needs and basic management of pain and other symptoms (for example hallucinations, fatigue, and depression) as well as discussions around prognosis, code status and goals of care, which includes ensuring illness understanding and exploring with the patient their values and preferences. All clinicians providing primary (basic) palliative care should feel comfortable talking about end of life care and referring patients to hospice or other specialized palliative care services if applicable. Specialist palliative care, the palliative care that is provided by a specialized consulting palliative care team, may include management of more complex physical, psychosocial and spiritual suffering; conflict resolution regarding goals or treatment options; care for patients with advanced disease or nearing the end of life; or assistance in addressing cases of potentially inappropriate treatments [8, 9]. Palliative care specialists may serve as part of inpatient, outpatient, or home palliative care teams or work in hospice.

The term "palliative care approach" describes the care that a patient and their family receive rather than the clinician or team providing this care. This approach is motivated by an intention to deliver care that respects the patient as a person and focuses on relieving suffering and improving communication. Therefore, it encompasses both primary palliative and specialist palliative care. The 'approach' also encompasses a wide range of settings where palliative care is provided including home, outpatient, inpatient and hospice settings.

Within this framework, we define a "*neuro*palliative care approach" as palliative care that focuses on the specific needs of patients with neurological illness and their families. Neuropalliative care thus represents both an emerging subspecialty within neurology and palliative care, as well as a holistic approach to people suffering from neurological illnesses.

Is There a Need for Neuropalliative Care?

The past two decades have seen substantial progress in our abilities to understand, treat and manage neurological disease. Nearly every subspecialty in neurology has seen significant advances: disease modifying therapies in multiple sclerosis control disease in over 80% of patients [10]; deep brain stimulation surgery has improved our ability to treat motor symptoms and complications of levodopa in Parkinson's disease [11]; prevention efforts have reduced stroke risk by nearly 50% [12]; acute stroke interventions more than double patient's chances to regain independence [13]; and novel genetic approaches are revolutionizing the landscape of neuromuscular care [14, 15].

Despite this progress, most neurological diseases remain incurable, shorten a person's life span, reduce time to dependence and quality of life and are associated with pain and other physical, psychological and spiritual symptoms that are often difficult to control. In addition, many non-neurologists, including palliative medicine specialists, feel uncomfortable managing neurological disease [16, 17], emphasizing the need to further educate and engage palliative medicine specialists and other clinicians caring for this population. Finally, progress we have made in the past two decades has also brought with it a proliferation of treatment options that include a vast array of more or less aggressive (and expensive) medical or surgical treatments with varying degrees of risks and benefits, many of which have considerable uncertainty, particularly in advanced disease, and which may complicate end-of-life decision making. As patients, their families and clinicians consider these options, they need to evaluate the patient's individual priorities and values and balance those with potential treatment burden and outcomes. This deliberation requires special expertise in navigating patients and families through the uncertainty specific to the disease, the individual and the choices confronting them.

What Are Unique Features of Palliative Care in Neurological Disease?

As palliative care is rapidly integrating into the care of non-cancer serious illness, it is important to recognize unique needs among patients with neurologic disease and their families. Differences in illness trajectories, symptom profiles, existential and psychological issues, caregiver needs and prognostic uncertainty need to be considered.

Illness trajectories One way to assist providers in communicating, planning and delivering appropriate care, is to categorize serious illnesses by the way the patient's function declines as diseases advance from diagnosis to death (Fig. 1.1)

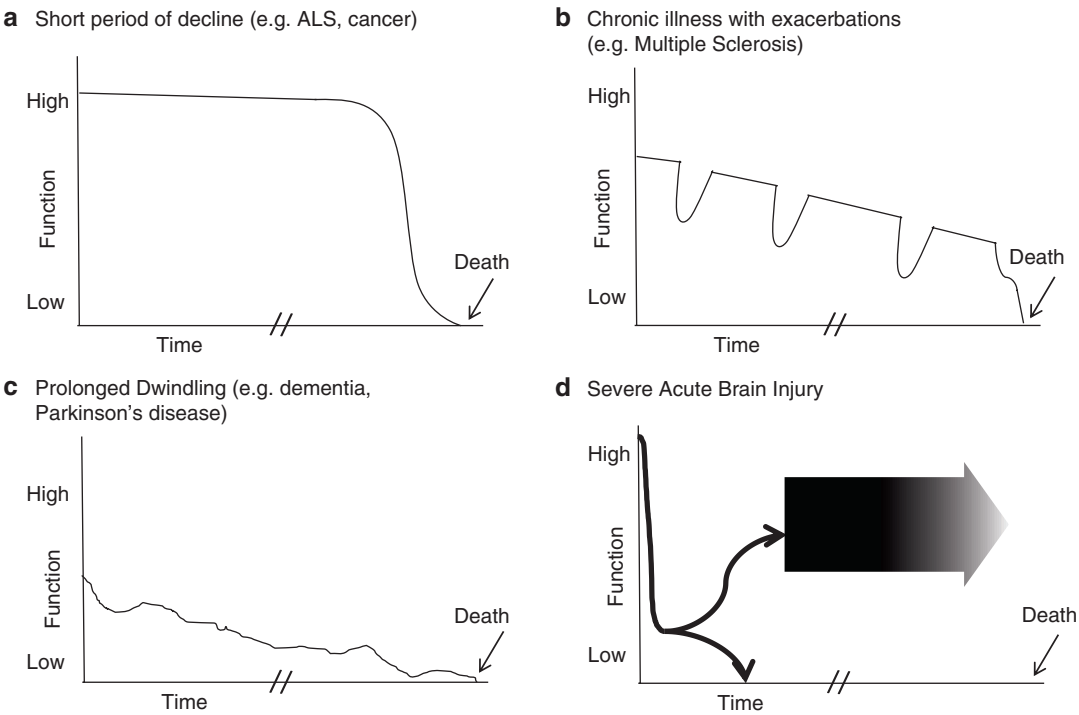

Fig. 1.1 Neurologic illness trajectories. Depicting how function declines to death with certain diseases can help with palliative care. (Adapted by permission from BMJ Publishing Group Limited from Creutzfeldt et al. [18])

[18]. Illness trajectories are frameworks that can assist providers and healthcare systems anticipate and respond to the needs of patients and families and provide anticipatory guidance to patients and families. Four illness trajectories have been proposed and include (1) a short period of decline typical of cancer or motor neuron disease, (2) an episodic decline with exacerbations typical of congestive heart failure or multiple sclerosis, (3) a prolonged decline as with many neurodegenerative conditions, and (4) a sudden severe decline as with severe acute brain injury (stroke, hypoxic ischemic encephalopathy, and traumatic brain injury) [18]. Neurological diseases add to the complexity of any trajectory because of the often associated cognitive impairment, which can prohibit the patient from expressing their preferences or making decisions about their treatments. The severe acute brain injury trajectory is unique to neurological disease where patients can die an early death, enter a chronic stage of recovery, survive for long periods with significant disability, and potentially shift into any of the other trajectories.

Symptom profiles Symptoms specific to various neurological illnesses are discussed in detail in this book and include among others the cognitive and behavioral deficits that most patients experience. As an example, brain cancer patients differ from other cancers in their common experience of seizures, cognitive decline, headaches and focal neurologic deficits [19]; or the management of delirium and agitation requires a distinct approach for patients with Dementia with Lewy Bodies than is typically taught for other situations of delirium, especially at the end of life.

Existential and psychological suffering Patients with neurological disease and their families struggle with a loss of personhood: for example, family members of patients with neurodegenerative disease have described grieving their loved one even as they are still alive but are slowly slipping away. Severe acute brain injury may rob patients of their personhood more dramatically, and family members wonder whether their loved one is 'still in there' [20]. Patients with motor neuron disease experience more demoralization, hopelessness, and suicidal thoughts than patients with metastatic cancer [21]. In contrast to other diseases such as cancer, which is perceived as extrinsic to the patient and something that can be fought or removed, neurologic illness is often felt as more intrinsic to the person [22], and sometimes even as a personal failure – take, for example, forgetfulness, misbehavior, or clumsiness.

Caregiver needs The burden to caregivers is increased for patients with neurological disease given the profound level of physical and cognitive disabilities experienced, the presence of psychiatric and behavioral issues, and the frequently long duration of caregiving needs. For example, cognitive impairment renders patients unable to make treatment decisions for themselves, leaving their family members to make 'surrogate decisions' based on what they believe their loved one might say. Cognitive deficits can lead to feelings of uselessness to the patient and increased depression in both patients and caregivers. Behavioral problems lead to a high caregiver burden that is made more difficult when there is no respite option for them. Nursing homes are typically ill-equipped or unwilling to care for these patients, especially for young patients such as those with Huntington's disease, multiple sclerosis or traumatic brain injury.

Prognostic uncertainty While not a unique phenomenon, prognostic uncertainty is ubiquitous within neurological illnesses. There are several aspects of neurological illness that compound the potential for uncertainty and the need to properly manage it. Since many neurological diseases are associated with impaired decision-

making capacity, surrogates are often the main decision-makers. Acutely honoring treatment preferences is complicated given the long and progressive course of many neurological diseases and the potential for individuals to incorrectly predict their quality of life and what they would want in a future health state. Recognizing this potential to "miswant" [23] and other biases that enter into managing and communicating information and uncertainty is central to effective decision-making in advanced neurological disease [24].

How Adequate Is Our Current Approach?

Several observations suggest gaps in our current care that may be improved by a systematic neuropalliative care approach. For example, pain and other distressing symptoms are typically under-recognized and undertreated in people with aphasia or other cognitive impairment given their limited capacity of self-report [25, 26], but also because physicians are not asking them [27]. High quality communication about prognosis, goals of care, and palliative care is a cornerstone of high quality care and should start at the time of diagnosis [28, 29]. Studies suggest that clinician-family communication is often inadequate [30, 31] and that poor communication results in worse psychological outcomes for patients and family members [32]. Most clinicians have never received training in such tasks as delivering serious news or discussing goals of care. Shortfalls in advance care planning are one sign of inadequate communication: recent studies suggest that less than 20% of patients with advanced dementia and only 42% of well, able stroke survivors have advance directives [33]. Evidence also suggest that most patients would prefer to die at home, but still almost half of patients with Parkinson's disease, multiple sclerosis and stroke die in the hospital, and hospice is underutilized compared to other illnesses [33, 34].

Finally, observations that care in seriously ill neurological patients varies across hospitals, providers or geographic regions, suggests a lack of a standardized approach to treatments, including goals of care conversations and end of life decisions. Prominent examples of practice variations include the use of gastrostomy tubes in patients with dementia [35] and stroke [36], and regional variations in end-of-life treatment intensity, including the use of early comfort measures only orders after stroke [37, 38]. These variations suggest that different clinicians, driven by local norms, may have different thresholds for deciding when a patient is dying and how and when they introduce advance care planning discussions and limitations of treatment. As a result, approaches that systematize the advance care planning process and triggers for serious conversations may improve the quality of neuropalliative care.

How Should the Palliative Care Approach Be Integrated into Neurological Care?

As we accompany our patients and their families along the trajectory of their illness, palliative care needs may change and opportunities arise for symptom management, information-sharing, family engagement, or a serious illness conversation – to explore patient values, to decide about starting, stopping or continuing a treatment or to engage in end of life or advance care planning. There is a need to make certain aspects of neuropalliative care a routine part of neurologic care to counter the common practice of waiting for "the right time" to address these needs and have difficult conversations. This would include making time to understand patients and families' goals of care, routinely assessing nonmotor symptoms, and ensuring advance directives are complete and up to date.

Certain events that occur during the course of illness may also serve as signposts that a serious illness conversation may be needed.

These events often represent a change in health status and signal advancing disease with prognostic implications. In this book, we highlight such ***Serious illness conversation triggers*** in the various neurological diseases that should nudge the primary neurological care team to pause with their patient and the family and to consider a new or repeated conversation with them about current treatment, the 'status quo' and to (re-)explore their goals, their hopes and their fears looking ahead. This pause also includes considering a referral to specialty palliative care depending on the specific needs of the patient and family, the skillset of the primary team, and the local resources available. When opportunities for serious illness conversations are missed, discussions have to be held in a crisis situation, when the patient is unable to make decisions for themselves or when a trusted clinician is not available [39–41]. Timely, honest and iterative conversations about advance care planning with seriously ill patients improve patient and family quality of life [3, 42, 43]. Table 1.1 presents a summary of these serious illness conversation triggers.

This book is intended for all clinicians caring for patients with neurological illness and their families. The goal is to define palliative care needs specific to various neurological illnesses, develop standards around recognizing and meeting these needs and to help clinicians provide optimal palliative care to patients with serious neurological illness. Some needs will be addressed by Neurologists and Neurology providers, some by Palliative Care providers and some by a multidisciplinary neuropalliative care approach. In Part I, we review some of the most important palliative care issues in major classes of neurologic illnesses. In Part II, we go into specific communication skills essential to the palliative care approach. In Part III, we cover other issues that are relevant across palliative care settings and neurologic illnesses. We conclude this book with a high level overview of the field and suggestions for future educational efforts and research to ensure a neuropalliative care approach for patients and families.

Table 1.1 Serious illness conversation triggers

General
"Surprise Question": would you be surprised if the patient died within the next year?
Patient or family raise concerns regarding:
Prognosis
Patient's quality of life
Appropriateness of care
Family's own quality of life
Patient or family makes request for hastened death
Diagnosis of a serious neurological illness
At time of diagnosis (after comprehensive diagnostic assessment)
Diagnosis of additional comorbidities
Change in diagnosis (e.g. from essential tremor to Parkinson's disease; from stroke to vascular dementia)
Medical-event
Any hospitalization in a patient with neurological illness
Would you be surprised if the patient died during this hospitalization?
In the ICU >3 days
Hospitalized >7 days
Prolonged mechanical ventilation or need for artificial nutrition
2nd (or more) hospitalization within 1 year due to complications of a neurologic illness (e.g. falls, urinary tract infection, aspiration pneumonia)
Actual or anticipated change in living situation (increased assistance at home, move to assisted living or SNF)
Disease progression
Increased dependence as indicated by
Loss of ability to work
Loss of ability to drive (or concerns with driving)
Change in mobility (falls, need for assistive device)
Need for assistance with activities of daily living (dressing, meals, toileting, bathing)
Weight loss with or without change in appetite
Dysphagia
New behavioral symptom, such as anger, social withdrawal, hallucinations, wandering
Sleeping more than 16 h/day
Time-limited trial[a]
At the beginning and end of a time-limited trial in serious illness
Consider whether the predefined goals were met
Caregiver distress/burnout
Signs of caregiver struggling or strained relationship
Consider talking to family member separately

[a]A time-limited trial is a trial of a certain treatment or intervention over a defined period of time to observe if the patient improves or deteriorates according to agreed-upon clinical outcomes, for example imaging signs of tumor reduction in cancer; pain relief or improvement of motor/non-motor symptoms in parkinson's disease; following commands in SABI. Key is to anticipate and agree on the content and timing of the conversation at the start of the trial.

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Part I

Disease and Symptom-Specific Considerations

Severe Acute Brain Injury

2

Margaret Isaac and Claire J. Creutzfeldt

Case

Ms. B was a 55-year-old very active right-handed woman with untreated hypertension who woke up with left hemiplegia, severe dysarthria and increasing somnolence. Imaging revealed a large ischemic stroke in the territory of the right middle cerebral artery. She arrived in the Emergency Department alone, though her husband was immediately available by phone and agreed that everything should be done to keep her alive. She was intubated for airway protection, and admitted to the neurological intensive care unit.

Severe acute brain injury (SABI) is defined as an acute neurologic catastrophe, caused by one or more distinct disease processes. Examples include ischemic stroke, intracerebral and subarachnoid hemorrhages, traumatic or inflammatory brain injury, and postanoxic encephalopathy following cardiac arrest. These varied disease processes collectively account for over 14 million deaths annually and represent one of the leading causes of disability worldwide [1].

Regardless of the underlying cause, severe acute brain injury (SABI) results in a common clinical scenario with common unique challenges facing patients, their families and clinicians. These include a sudden, unexpected, and devastating neurologic insult, for which treatment decisions must be made quickly, typically with impaired consciousness and communication such that conversations about goals of care have to occur between clinicians and surrogate decision-makers, rather than with the patient themselves. Patients with SABI follow a distinct illness trajectory that we have proposed as the "fourth trajectory" (See Chap. 1 "Neuropalliative Care : Introduction", Fig. 1.1), in which patients either die acutely, typically after withdrawal or withholding of life-sustaining interventions, or survive with a wide range of disability. Thus, specific approaches and considerations particular to the palliative care of patients and their families in this setting are required. These include early identification and management of pain and distressing symptoms, provision of psychosocial support for patients and their families, accurate prognostication, and sensitive conversations, typically with patient's family, about prognosis, goals of care and treatment decisions.

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Symptom Management I: The Acute Setting

Ms. B appeared agitated during her first day of hospitalization. The nurses and physicians caring for her became concerned that she might be in pain due to facial grimacing and ventilator noncompliance, so treated her with small boluses of fentanyl.

The inability of patients to communicate their needs may lead to undertreatment of symptoms. Studies have shown that patients with stroke and aphasia receive fewer pain medications than those without, suggesting that pain and other distressing symptoms are underrecognized [2]. Clinicians must be aware of the prevalence of symptoms, especially pain and anxiety, and particularly attentive to their presence. Table 2.1 lists common symptoms after SABI and their suggested management. Treating any *potential* symptoms and sources of discomfort is important and is often more challenging in this setting given the need to rely on measures other than direct symptom reports from patients. Empiric trials based on clinical suspicion of symptoms can be a reasonable approach in this setting. If opioids or benzodiazepines are used in the acute setting, short-acting forms are preferred to avoid oversedation and clouding of the neurologic exam.

Objective assessment tools have been validated in critically ill, mechanically ventilated patients but are not specific to neurologically critically ill patients and may be helpful in evaluating the symptom burden in patients with communication barriers and altered sensorium. Examples of such tools include the Behavioral Pain Scale (**BPS**, Table 2.2) [11] and the Critical Care Pain Observation Tool (CPOT) [12]. However, the utility of these tools can be compromised in patients with SABI who may have limitations in these behaviors due to their underlying injury and tend to exhibit a broader range of behavioral responses to pain than other patient populations [13].

Table 2.1 Common symptoms and management recommendations after severe acute brain injury

Symptom	Management recommendations
Early	
Pain	*Headache:* APAP, gabapentin, pregabalin
	Spasticity: Physical therapy and motion exercises, baclofen
	Opioids: short-acting opioids are acceptable only in the acute setting; prefer non-opioid pain medications
Depression	SSRIs such as fluoxetine [3]
Delirium	Non-pharmacologic interventions – e.g. early mobilization, reorientation, day-night routine with lights and noise [4]
Storming	Beta-blockers [5], morphine [6]
Status myoclonus	Clonazepam, valproic acid [7]
Chronic	
Pain	Pharmacologic – tricyclic antidepressants (amitryptiline) or SSRIs (venlafaxine, citalopram)
	Nonpharmacologic – e.g. massage; physical therapy; motor cortex stimulation, deep brain stimulation [8]
Fatigue	Non-pharmacologic: sleep hygiene, diagnose and treat sleep disorders such as obstructive sleep apnea
	Pharmacologic: consider modafinil [9]
Depression/ anxiety	Psychotherapy and SSRIs [10]

Table 2.2 Behavioral Pain Scale (BPS) [11]

Item	Description	Score
Facial expression	Relaxed	1
	Partially tightened (e.g. brow lowering)	2
	Fully tightened (e.g. eyelid closing)	3
	Grimacing	4
Upper limbs	No movement	1
	Partially bent	2
	Fully bent with finger flexion	3
	Permanently retracted	4
Compliance with ventilation	Tolerating movement	1
	Coughing but tolerating ventilation for most of the time	2
	Fighting ventilator	3
	Unable to control ventilation	4

From Payen et al. [11], Table 1 with permission of Wolters Kluwer Health, Inc.

For pain, physiologic markers such as tachycardia and hypertension can be used as indicators in comatose and/or sedated patients, though these signs are nonspecific and can be affected by many other factors. Depression is common and similarly hard to recognize. Clinicians should screen patients regularly for depression and consider SSRIs, especially early in the course of stroke [3].

Myoclonus after hypoxic ischemic brain injury is characterized by abrupt, irregular contractions of muscles. It can occur early (acute) or late (chronic). Post-hypoxic myoclonic status epilepticus may portend a poor prognosis. The treatment of choice is benzodiazepines, though non-sedating anticonvulsants such as valproic acid or levetiracetam can also be used.

'Storming' or paroxysmal sympathetic hyperactivity is seen after various types of severe acute brain injury and characterized by episodes with various combinations of hyperthermia, hypertension, tachycardia, tachypnea, increased muscle tone, diaphoresis and other symptoms of sympathetic hyperactivity. Once causes such as seizures, infection, pain and/or metabolic derangements have been ruled out, first-line treatment consists of opioids, intravenous anesthetics such as propofol and beta-blockers (especially propranolol). Benzodiazepines and gabapentin may also be used [14] (See also Chap. 3 'Prolonged disorders of consciousness').

Caregiver Support

Case continued

Ms. B.'s husband did not leave her bedside, and anxiously reported every movement he saw. His sons made sure he was eating, and the neuro-ICU staff provided him with pillows and a blanket. The physician team sat down with the family about 24 h after she presented to discuss the current situation and provide support.

Seeing a loved one experience any serious illness is incredibly challenging, and acting as a surrogate decision-maker for patients with critical illness has been associated with longer term psychiatric symptoms and syndromes such as post-traumatic stress symptoms [15], post-traumatic stress disorder [16], anxiety, and depression [17–19]. Early in the course of SABI, the clinical course can be rapidly changing and the ICU setting, in particular, can be unfamiliar and overwhelming to caregivers. Small gestures by ICU staff can go a long way in promoting comfort with family members – these include open visiting hours [20], comfortable waiting areas, refreshments, and facilities for showers and personal care [21].

Families describe a loss of personhood through brain injury, and identify the need for clinicians to maintain this personhood by talking to the patient, even when unresponsive, and by asking the family about the patient as a person, prior to this injury [21]. Clinicians can further support this awareness of patient personhood by defining surrogates' responsibility for decision-making within a substituted judgment framework. In other words, clinicians can ask surrogates to communicate the voice of their loved one rather than making decisions in the best interest of their loved one. Some phrases that can be helpful in clarifying this for surrogates include:

- "What we're asking you to do is to bring Rita's voice into the room. If she could be here right now talking with us about what's happened, what do you think she would say?"
- "We are not asking that you make decisions for Rita based on your own values – that's an impossibly difficult position for you to be in. What's most important is to get a sense of what Rita would want in this situation. Has she ever spoken about issues like this before?"

When discussing the patient's condition, family members have expressed a need for hope when presented with uncertainty [21]. One helpful way to maintain hope with the family in a time of immense loss is by reframing the focus of hope. Clinicians can ask what families are hoping for and help them shift their hope, if not on survival, perhaps on re-uniting with a family member; if not on recovery to independence, perhaps on being able to participate in an important future

event. (See Chaps. 18 "Spiritual Care" and 20 "Caregiver Assessment and Support").

Given the "fourth trajectory" described above [22] and shown in (Fig. 2.1), the prolonged period of convalescence following hospitalization with significant debility and functional dependence also confers a large psychological, financial, and physical burden on caregivers. Many patients are discharged to skilled nursing facilities or adult family homes, and one in five patients with stroke require institutional care at 3 months after the acute event [23]. After patients are discharged from the acute care setting, outpatient follow-up is paramount for symptom identification and management, psychosocial support and ongoing conversations addressing goals of care as the patient's condition evolves.

Prior conversations about serious illness and health care directives can help guide surrogates and clinicians. However, the language in advance directives (ADs) is often vague and the applicability can be difficult to determine, failing to capture the uncertainty inherent in clinical medicine generally, and in the case of SABI, specifically. Physicians vary in the degree to which they capture uncertainty in their prognostic conversations with patients and their families. The uncertainty in outcomes present in the majority of patients with SABI makes interpretation of ADs challenging, though they may amplify a family's understanding of their loved one's wishes. Family members find ADs more useful than do physicians [24] – which may speak to physicians' understanding of the nuance and complexity of a clinical situation and discomfort with the applicability of ADs. Moreover, treatment preferences are not always stable over time [25] which can also limit the applicability of ADs. Addressing goals of care more generally can open the door to a broader conversation about a patient's values and priorities and help frame specific decisions about medical interventions in the context of a patient's life.

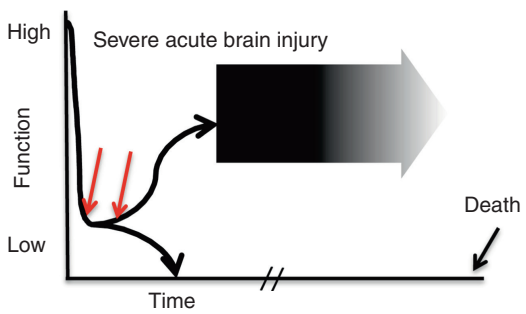

Fig. 2.1 Severe Acute Brain Injury trajectory. The two red errors symbolize the two periods of treatment decisions described in the text (very early and early). (Adapted by permission from BMJ Publishing Group Limited from Creutzfeldt et al. [22])

Case continued

On hospital day 2, a meeting was conducted between Ms. B.'s family and the medical team. They continued to assert that she would want every possible intervention to improve her chances of meaningful recovery and consented to a decompressive hemicraniectomy, which she underwent that same day.

Estimating and Communicating Prognosis

Accurate prognostication in the setting of SABI is critically important to help surrogates with decision making. While the focus is often on the likelihood of survival, families want to know the likelihood and extent of functional recovery and quality of life after SABI. Centering the conversation on "How long?" and "How well?" can help focus discussions on both longevity and function/quality of life – which is particularly salient in the setting of SABI [26]. Threading the needle between optimism and pessimism, between hope and truth-telling, is one of the greatest challenges in communicating with families of patients with SABI. The presence of many different clinicians with discordant prognostic estimates can complicate communication and decision-making.

Although many individual signs and symptoms correlate with survival, the strength of these correlations is rarely strong enough to rely upon when prognosticating. To construct a more accurate short- and long-term prognosis, an enormous number of diagnostic tests, clinical severity grading scales and prognostic models have been

described that are reviewed in detail elsewhere [27–29]. These scales use various clinical and radiological signs of illness severity to predict longer term mortality, and sometimes functional status. While such scales may allow for the use of multiple variables that add up to an approximate prognosis, these models are fairly limited in their ability to accurately prognosticate for individual patients, and are fraught with uncertainty and biases [30]. There are rare instances in SABI when prognostic markers have a high accuracy of a poor outcome prediction. These occur in patients who present with severe hypoxic ischemic encephalopathy (HIE) after cardiac arrest. In these patients, the absence of pupillary light or corneal reflexes on day 3 or absent cortical (N20) responses on somatosensory evoked potentials by day 1–3 uniformly predicts a poor prognosis defined as death or severe disability [31].

It usually takes at least 6 months after cardiac arrest or stroke [32] and 1–2 years after severe traumatic brain injury [33] until the stage of chronic recovery is reached. These time frames are typically marked by institutionalized care with extended use of life-sustaining treatment such as artificial hydration and nutrition or respiratory support, and complications and comorbidities leading to recurring hospitalizations. As clinicians discuss prognosis and treatment decisions with individual families in the acute stages, the range of possible outcomes needs to include the potential burden of continued acute and chronic treatment and considered alongside the patients' previously stated or presumed values and goals. In the fast-paced, often chaotic environment of the Intensive Care Unit, it is important to address the potential for recovery and adaptation over a longer time horizon. (See Chap. 11, "Communicating Effectively", Chap. 12 and "Prognostication", and 13, "Improving Medical Decisions").

Serious Illness Conversation Triggers

Discussions with surrogate decision-makers about prognosis, treatment decisions and goals of care are best thought of as a series of conversations, beginning early in hospitalization and occurring at regular intervals throughout the acute hospitalization. Certain clinical events and treatment decisions that occur in the course of SABI can function as watershed events or "serious illness conversation triggers" (Table 2.3), prompting the team and family to readdress prognosis and goals. During the initial hospitalization for SABI, there are typically two periods of treatment decisions: very early and early (Fig. 2.1).

Table 2.3 Triggers for serious conversations

General
Age >80 years and hospitalized
Metastatic cancer, advanced dementia or other serious comorbidity
Patient or family asks to discuss these issues
Would you be surprised if patient died during this hospitalization?
Would you be surprised if patient died in the next year?
Emergent ('Very Early' – hours to 1 day)[a]
Intubation and mechanical ventilation
Nasogastric tube if needed for urgent medication[b]
Emergent brain surgery (for example external ventricular drain placement, decompressive craniotomy, clot evacuation)
Early (days to weeks)
>3 days of intubation
Starting artificial nutrition[b]
Considering transition from nasogastric feeding to percutaneous gastrostomy
Considering transition from endotracheal tube to tracheostomy
Any unexpected change or decline (for example new infection, need to re-intubate, reinsert feeing tube or readmit to ICU)
Late (months and years)
Scheduled: every patient who was discharged to a nursing or long-term care facility, or who was discharged with artificial support (feeding or breathing tube), should have a scheduled appointment for a serious illness conversation 3–6 months after admission
Event-driven: any unexpected change or decline (for example new infection, need to re-intubate, reinsert feeing tube or readmission to the hospital)

[a]Serious illness conversations should not be confused with conversations around consent for procedures. Emergent procedures should be followed up by a more extensive, deliberate conversation about what to expect and to address patients and families hopes and fears.
[b]While the optimal timing to start artificial nutrition is not known, it is acceptable to wait 3–7 days, [34, 35] allowing for a conversation to establish patient goals and values [29]

– *Very early treatment decisions (hours to days).*

Very early treatment decisions occur during the first hours to days of admission and include immediately life-saving procedures such as tPA and/or mechanical thrombectomy for ischemic CVA, temperature management for HIE, decompressive hemicraniectomy, ventricular drain placement or clot evacuation to manage of increased intracranial pressure. The acute need for intervention leaves little time for deliberation and these are often the first major decisions that families must make about whether to proceed with aggressive interventions. Deciding for such a life-saving intervention means deciding for survival with a wide range of disabilities. For example, after a large ('malignant') ischemic stroke (as described in our case), there is good evidence that decompressive hemicraniectomy (DHC) within 48 h decreases mortality from 70% to 20% in younger patients (<60 years), and to 35% in older patients; among the young ones who survive, one in two undergoing DHC will gain independence, among the older ones this proportion drops to one in ten [36, 37]. There is a well-described discrepancy between the interventions that healthy patients think they would want when presented with theoretical clinical scenarios, and the actual satisfaction of those who have received those interventions – particularly in the case of surgical decompression. Affective forecasting describes the process of predicting for oneself how one may feel in a future state. Patients often fail to predict how they will adapt to a new baseline, focusing more on what will change than what will stay the same, and underestimating their own ability to cope [38]. Most healthy people say that they would not want to undergo DHC in the setting of a malignant cerebral infarct if the outcome were moderate or severe impairment [39]. However, most patients who have undergone this procedure and their caregivers reported feeling satisfied with this decision, despite significant disability and say they would make the same decision again [40, 41]. When communicating with surrogate decision-makers, it can be helpful to educate them about this "disability paradox" or to help them "imagine the unimaginable" [42]: to help them imagine what life might be like, and to share the experiences of others as they try to imagine a life for their loved one that may feel unfamiliar and frightening.

– *Early treatment decisions (weeks)*

Once patients have moved into the more subacute phase of their illness, the need for decision-making around tracheostomy and percutaneous enteral gastrostomy (PEG) tube placement can serve as another watershed moment for family conferences (Fig. 2.1, **blue arrow**). At least one in 20 patients with stroke are discharged from the acute care hospital with a feeding tube [23] - this number varies widely across hospitals [43]. Among patients with severe traumatic brain injury who underwent PEG tube placement, one in three were independent at 1 year; in that same small study, the persistence of a PEG tube at 3 months was associated with much greater disability, as only 5% of patients achieved independence [44]. In stroke patients who undergo PEG placement, 2-year mortality may be as high as 66% [45]. Among survivors, about one in ten regain independence, while all others will have a varying range of long-term disability, the risk for which increases with age [45].

The indication for tracheostomy placement in critically ill patients is to facilitate weaning from mechanical ventilation, for long-term airway protection, or a combination of the two. Approximately one in ten of all (medical and surgical) patients who receive mechanical ventilation will go on to receive a tracheostomy; the majority of patients with tracheostomies are discharged to long-term care facilities [46], and 1 year survival may be as low as 10%, although these numbers are not specific to patients with SABI [47].

The decision for placement of a PEG or tracheostomy after SABI, ideally, would be guided by evidence- and preference-based prognostication, i.e. by predicting the degree of future recovery and dependence as well as the patient's ability and willingness to adapt to such a life. However, uncertainties and biases in prognostication are common after SABI [48], especially early in the course of the illness, when surrogates

and clinicians are faced with the decision to either shift to comfort measures only or continue a potentially burdensome treatment for a time that some may perceive as too long [49, 50]. To accommodate this tension, a third strategy is recommended as an alternative to all-or-nothing approaches, often referred to as a *time-limited trial*: clinicians and surrogate decision makers agree to use certain medical therapies – such as trial of nasogastric feeding before PEG placement – "over a defined period of time to observe if the patient improves or deteriorates according to agreed-upon clinical outcomes." [49] Engaging in such a trial requires clinicians to educate the families about what to look out for and to provide a clear follow up plan to re-evaluate the clinical situation (See Chap. 13, "Improving Medical Decisions"). Transitioning to comfort measures only can be more challenging in the later subacute and chronic setting if there is no acute event to prompt that transition. Outpatient follow-up with neurologists, primary care providers, and palliative medicine specialists can help frame and guide decision-making for patients and families in the longer term.

Establishing Goals of Care

Developing trust takes time. Additionally, surrogate decision-makers need time to fully grasp the nature of what is occurring and the implications of medical decision-making. Thus – addressing goals of care and patient values in the setting of SABI is best viewed not as a single event but as a series of conversations over time that frames medical decisions within the greater context of a patient's values and priorities. If consistent with a patient's goals of care, aggressive measures with thorough and careful attention to medical details and family communication early on in the disease course can demonstrate to surrogates that the care team is deeply invested in the best clinical outcome for their loved one. If and when a poor prognosis becomes clear, or the patient decompensates further, families are more likely to trust negative prognostic data provided by that same team. Furthermore, setting the stage for the future can help families "hope for the best and prepare for the worst" [51]. (See Chap. 11, "Communicating Effectively") Sample language early in the hospital course might include:

- "I hear you telling me that Gary would want 'everything done'. Right now, we are doing everything we can to keep him alive – we're making sure he's getting enough oxygen by putting in a breathing tube and connecting him to a breathing machine. We're keeping a careful eye on his blood pressure and may need to think about surgery to reduce the pressure around his brain. I'm hopeful that he will improve, and I also want to let you know that I'm worried things could get worse. I'll be talking to you a lot over the next few days, and I'm going to be honest with you about what's going on."
- "We're going to do everything we can to try to make Gary better. If we get to the point where I think that's not possible, I'm going to let you know that too. I also want you to let me know if we get to a point when you feel that he would no longer want the aggressive treatment we're providing."

Best Case, Worst Case, and Most Likely Case

Because prognosis is often uncertain in the setting of SABI, presenting best, worst, and most likely outcomes can be one strategy to help families manage the uncertainty associated with recovery [42, 52]. Some possible phrases might include:

- "Because we don't have a crystal ball, I can't tell you for certain what the future holds for Tom. I think that the best case scenario is that he recovers enough to be able to talk and interact with the people he cares about – he would likely still need help with his usual daily activities like eating, dressing, and bathing, but, with enough help, might be able to return home eventually. I think the worst case scenario is that he does not wake up and will need life support to keep his body alive for the long-term. I think the most likely scenario is

somewhere in between – awake, able to track your movement around the room, but not able to talk and interact with you and the family. What do you think about all of that?"

- "I'd like to talk to you about what we call an 'acceptable level of better'. How much better do you think Tom would have to be to have a life that is meaningful for him?"
- "If Tom could be a part of this conversation now, talking to us about his wishes, what do you think he would say? If he could tell us about what's most important – longevity or living as long as possible, comfort, and independence – which one do you think he'd value the most?"

Anticipatory guidance is a way to help patients and family prepare for anticipated developments, expect complications and plan for potential decisions that may ensue.

- "I'm worried that, down the road, Nancy's condition might worsen – people with her type of brain injury often get infections, for example, and that could make things worse. I'm worried that aggressive care in the ICU at that point might really make her more uncomfortable. With that in mind, I think it would be reasonable to continue with what we're doing right now, and also plan that, in the future, if she gets worse, that we won't escalate her care, or bring her back to the ICU, because we'd see that as a sign that she probably wasn't going to get well enough to return home. What do you think?"

Shared Decision-Making: Balance Between Paternalism and Autonomy

Decision control can be viewed as existing on a spectrum with patient autonomy on one end in which patients and/or surrogates make decisions independently, and paternalism (parentalism) on the other, in which clinicians make decisions on behalf of patients. (See Chap. 13, "Improving Medical Decisions") In between is shared decision-making, in which patients and clinicians share responsibility and make decisions together in a collaborative fashion. Multiple critical care societies have come to consensus [53, 54] that shared decision-making is a best practice, though in reality, patients and surrogates are variable in the amount of control they prefer to have over complex medical decision making vs. letting the physician decide [55, 56].

SABI presents a clinical scenario in which clinicians may have a great deal of experience, and surrogates usually have very little. Clinicians therefore have an opportunity to share their experience and make recommendations that are in line with a patient's stated values [48]. Directiveness by physicians is more appropriate when prognosis is certain. In the setting of SABI, communicating prognostic uncertainty is one of the greatest communication challenges. Making serious decisions in the face of clinical uncertainty is one of the key struggles that family members face. It can be a temptation to present prognosis in more certain terms in a well-intentioned effort to ease the burden of decision-making, but physicians have a moral obligation to communicate honestly with patients and their surrogates. How physicians discuss prognosis [57] and goals of care has a significant impact on the decisions that patients and families make. In this situation of substantial uncertainty, clinicians have to be humble and sensitive to the power of our words to impact the lives of our patients and of their loved ones.

Case continued

Mrs. B. spent about 2 weeks in the neurointensive care unit and was eventually discharged to a rehabilitation facility with persistent left hemiparesis and neglect, some cognitive deficits and a PEG tube. Over the next several years, she was able to live independently with her husband, but continued to have severe L sided pain which limited her mobility and her ability to participate in hiking and many of the other outdoor activities that had given her joy and connected her to a social community.

Symptom Management II: The Subacute and Chronic Setting

Survivors of SABI can have a high chronic symptom burden, with a high prevalence of fatigue, major depressive disorder, generalized anxiety, and chronic pain (Table 2.1). Even patients with good recovery after stroke can suffer from depression, cognitive impairment and trouble reintegrating into normal living [58]. Fatigue is reported in up to 50% of stroke survivors, and around a third experience depression and/or anxiety [59]. Similar numbers have been reported after traumatic brain injury [60] and cardiac arrest [61]. After evaluating and treating for secondary causes of fatigue, including depression and sleep apnea (estimated in over half of patients with ischemic stroke) [62], management of fatigue should start with behavioral approaches such as sleep hygiene and exercise; medications such as modafinil or methylphenidate may be considered in refractory situations. Post-stroke depression can be treated effectively with SSRIs, ideally in combination with psychotherapy [59], and some suggest that SSRIs may help prevent depression following TBI [63]. One quarter of stroke survivors experience pain [64], so careful attention to the its diagnosis and management with both pharmacologic and non-pharmacologic approaches is important in the long-term setting (**see** Table 2.1).

Case continued

Ms. B, now 65 years old and 10 years after her first stroke, presented to the emergency room with sudden onset confusion, right hemiplegia and left gaze preference. She had no advance directive documented. Her head CT demonstrated a left thalamic intraparenchymal hemorrhage with intraventricular extension. Her family consented to emergent placement of an external ventricular drain (EVD), but on hospital day 3, she suffered a worsening in her neurologic status with increasing somnolence, no spontaneous eye opening or movement; and eyes with downward gaze. With stimulation, she had spontaneous movement of left upper and lower extremities and weak but purposeful withdrawal to noxious stimuli. Repeat imaging demonstrated evidence of a delayed EVD tract-associated hemorrhage.

The neurology team met with the family, who indicated they did not think that Ms. B would want to live with a significant decline in her functional status. They felt that she could "barely tolerate" the pain and functional limitations associated with her prior ischemic stroke. The neurology team met with the patient's sons and husband. After discussing the "best case" and "most likely" scenarios, the decision was made to transition to comfort measures only. She died peacefully one day later, surrounded by family.

EOL Care Including Hospice

End of life care for patients with SABI includes both the care patients receive in the hospital and the care they may receive in other settings, including skilled nursing facilities, inpatient hospices, and home. In the hospital setting, palliative care services are a resource to assist with complex medical decision-making, direct efforts at symptom management, and navigate challenging family dynamics.

Hospice can add an additional layer of support for patients in the terminal stage of their disease, either at home or in an institutional setting. Patients with stroke or coma are considered to be eligible for hospice if they meet the following Medicare Guidelines (See Chap. 16). These guidelines are meant to standardize criteria for this disease category but clinicians should assess specific needs and prognostic estimates individually for each patient when setting a treatment plan.

- An inability to maintain hydration and caloric intake with one of the following:
  - Poor functional status with Palliative Performance Scale [65] score <40%.
  - Weight loss >10% during the past 6 months or >7.5% in past 3 months;
  - Serum albumin <2.5 g/dL;
  - Current history of pulmonary aspiration without response to interventions;
  - Sequential calorie counts documenting inadequate caloric/fluid intake;
  - Dysphagia severe enough to prevent the patient from receiving food and fluids necessary to sustain life, and patient does not receive artificial nutrition and hydration.

Brain Death Some patients with a catastrophic, irreversible brain injury may progress to brain death [66]. While the concept of brain death is usually clear to most clinicians, it is often very challenging for families to grasp: the brain-dead patient in the intensive care unit does not appear deceased but still feels warm, has a beating heart and vital signs. Key to communication is to be pro-active if at all possible: to have early, honest conversations with the family of a patient with a progressively worsening severe acute brain injury and to prepare them for anticipated developments. If the outcome is clear and hopeless, the family also needs to be given the opportunity to discuss possible organ donation with a representative of an organ donation agency. Families should also be informed that adventitious and often complex movements can occur due to retained lower-level reflexes. In rare occasions, families are unable to accept brain death as death. In addition to providing continued emotional support and repeated conversations with the family, options include continuation of organ support for a few more days while involving the hospital ethics committee, spiritual care specialists if relevant and, eventually, the court [67].

Research Agenda

Educational needs exist for both neurology and palliative care clinicians, and for both trainees and those with an established career. Communication training should be prioritized that teaches clinicians to deliver serious news in an effective and empathic manner, that assists families with difficult treatment decisions and supports them through these. This communication would ideally be somewhat standardized – a common language around severe acute brain injury and prognostic uncertainty as detailed in this chapter may help medical teams and families work together towards a patient-centered approach. Research agenda items include the need for better prognostic models for patients with SABI – enhanced prognostication would make communication easier for clinicians, and would certainly ease some of the decisional burden that surrogates face. We need to identify best ways to integrate primary and specialist palliative care into the care of patients with SABI, especially around shared decision-making and family engagement. Hospice eligibility criteria after SABI have yet to be developed and validated.

Take Home Messages

- SABI is a heterogeneous category of diseases that are characterized by a sudden, catastrophic neurologic event.
- Patients with SABI typically lack decisional capacity in the acute setting, so goals of care discussions typically occur with surrogate decision-makers.
- The initial phase of illness usually occurs in the emergency department and critical care setting: unfamiliar and fast-paced environments which can be uncomfortable for family members suddenly thrust into the role of surrogate decision-maker
- Addressing goals of care in the setting of SABI is best done in a series of conversations, often marked in time by critical decisions that need to be made – around the decision to pursue decompressive hemicraniectomy, and, later, tracheostomy and PEG tube placement.
- Balancing uncertainty and clarity can be a major challenge in communicating with families of patients with SABI.

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Prolonged Coma and Early Disorders of Consciousness

3

Eelco F. M. Wijdicks

Charlie, an 18-year-old man suffered multitrauma after a tractor rollover accident. He was intubated in the field and, on arrival to the ER, is in shock. He was found to have a hemoperitoneum, humerus and pelvic fractures. He does not regain consciousness. CT scan of the brain was initially normal except for cortical subarachnoid hemorrhage, but soon after his life saving surgery he developed a fixed and dilated pupil as a result of a rapidly evolving epidural hematoma. He was transferred urgently to the operating room where a contused brain and large epidural hematoma was found and evacuated. An ICP monitor was placed. After return to the neurosciences intensive care unit he barely opened his eyes to pain and without fixation to the examiner. The right pupil is 7 mm and nonreactive to light, and the left pupil is 3 mm with minimal light response measured with the pupillometer. The corneal reflexes are intact. He has roving spontaneous eye movements. He has no motor response to pain except for some arm flexion. There is marked symmetric rigidity and bilateral Babinski signs.

Two weeks have passed, and the direct family has not left his bedside. The ICP has normalized to single digits. He is overbreathing the ventilator. Information has been provided to the family at various occasions. The primary medical team now plans to discuss the options of tracheostomy and gastrostomy insertion and has invited the full family and all clinicians for a conference in the neurosciences ICU. The family has been prepared that important decisions considering his care need to be made and therefore a full picture will be presented (Fig. 3.1, *showing head CT of patient on admission*).

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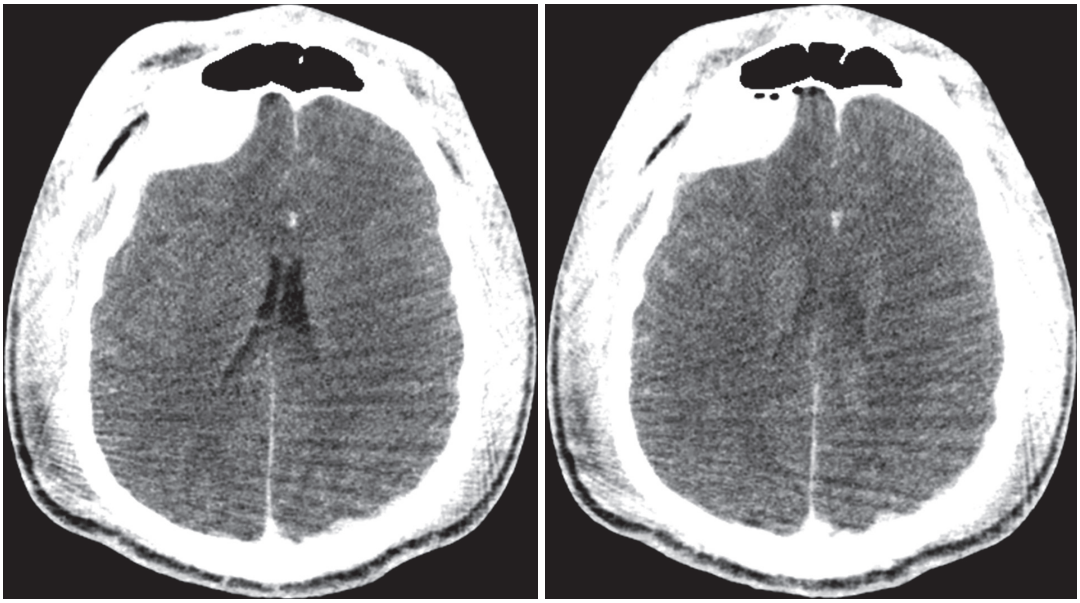

Fig. 3.1 Traumatic brain injury with early swelling from diffuse axonal injury and epidural and subdural hematomas

Clinical scenarios like these constitute a major bioethical, neurologic, neurosurgical, medical and surgical problem in the neuro-intensive care unit (neuro-ICU). Traumatic brain injury (TBI) affects millions of patients including many younger individuals. Clinicians need to assess the degree of injury, type of surgeries, and current neurologic condition, and communicate these to the family members [1, 2]. It is important in this setting to explain why the patient is comatose: Coma results from different types of brain or brainstem injury. Patients often have diffuse axonal shear injuries, bihemispheric cortical damage, or there has been an acute mass effect causing rapid shifts at the brainstem level resulting in pontomesencephalic neuronal injury. In addition, it is important to account for the effects of hypotension and multi-organ injury in polytrauma patients, as is the case in our example. Assessment of the comatose patient must take confounding (and potentially reversible) factors into account [3]. These include the effects of sedative drugs, substance abuse, or polypharmacy, especially in patients who have been on a ventilator in the ICU for a prolonged time; seizures or non-convulsive status epilepticus (rare in TBI) may require a spot EEG, and sometimes continuous EEG monitoring; infections can cloud the sensorium and should be ruled out. MRI scans are often performed to assess the severity of injury but MRI has remained far from reliable as an absolute predictor of poor outcome [4]. Similarly, diffusion-weighted imaging in comatose cardiac arrest survivors may have a good specificity and sensitivity but a number of good recoveries have been reported despite widespread abnormalities [5].

Estimating Prognosis

As this book argues well, discussion of the totality of the clinical findings is critical, and triggers for serious conversation have been identified (Table 3.1). It is important to remember that early prognostication in traumatic brain injury in a

Table 3.1 Triggers for a serious conversation in prolonged coma

General
Major comorbidity
Demonstrated progressive cognitive decline
High surgical risk
Metastatic cancer
Advanced age (>85 years)
Early (weeks)
Tracheostomy and gastrostomy
Neurosurgical intervention
Refractory seizures/status epilepticus
Later (months)
Life-threatening complications
Major surgical interventions
(Surgical) interventions considered medically inappropriate
Recent episode of brief cardiopulmonary resuscitation

young adult is fraught with errors and perhaps even impossible (see Chap. 12 "Prognostication"). Many neurorehabilitation physicians have seen young initially comatose patients in devastating neurological conditions improve to an acceptable physical and cognitive disability years later. It is, therefore, very difficult for a single physician to prognosticate adequately on the basis of his personal experience. One solution is to resort to large databases such as the CRASH and IMPACT databanks that provide estimates of mortality and unfavorable outcome (Fig. 3.2a, b).

In our case example, the CRASH dataset would provide a 75% risk of 14-day mortality and a 92% risk of unfavorable outcome. The IMPACT databank, however, is more optimistic and predicts probability of 6-month mortality (using the CORE, CT, and lab model) at 46%. The probability of 6-month unfavorable outcome is 68%. These databases are very helpful as a screening tool but should never be used as metrics in clinical practice, and when communicating these numbers to families, it is important to 'individualize' them to the specific patient including underlying comorbidities, age and hospital course. One can easily argue not to use these numbers in a conversation at all but use them as an guide rather than an an absolute number.

Charlie's family decides to proceed with the tracheostomy and gastrostomy to allow him full potential for recovery. All caregivers agree. Full resuscitation measures remain in place. Over the next few weeks, his condition waxes and wanes, and he eventually opens his eyes and appears to have developed a sleep-wake cycle. His family has been overjoyed with this development even after compassionate clarifications and a careful attempt to temper enthusiasm. Now, almost 4 weeks after his major multitrauma, his detailed neurologic condition qualifies for a clinical diagnosis of a vegetative state.

From Coma to Vegetative State

The patient has not improved but progressed, and he now seems to fulfill the criteria for vegetative state, meaning the emergence from coma with eye-opening and apparent sleep-wake cycles [6–11]. The diagnosis of a vegetative state requires multiple examinations over time, and the diagnosis should never be made with just one or two assessments. Some have suggested renaming the vegetative state as "unresponsive wakefulness syndrome", but in my experience, family members are very confused by the use of this term and then require far more explanation [12]. Most families know exactly what we mean by a vegetative state and in my experience nobody is offended by this term. Families associate a vegetative state with "being a vegetable" but this term has been used indiscriminatorily and is often coined to denote full dependence on others and no meaningful way of communicating. In a vegetative state, there is no evidence of consciousness, but a preserved capacity for spontaneous or stimulus-induced arousal, sleep-wake cycles, and several reflexive or spontaneous behaviors are present. The cranial nerve examination is preserved. Many

a

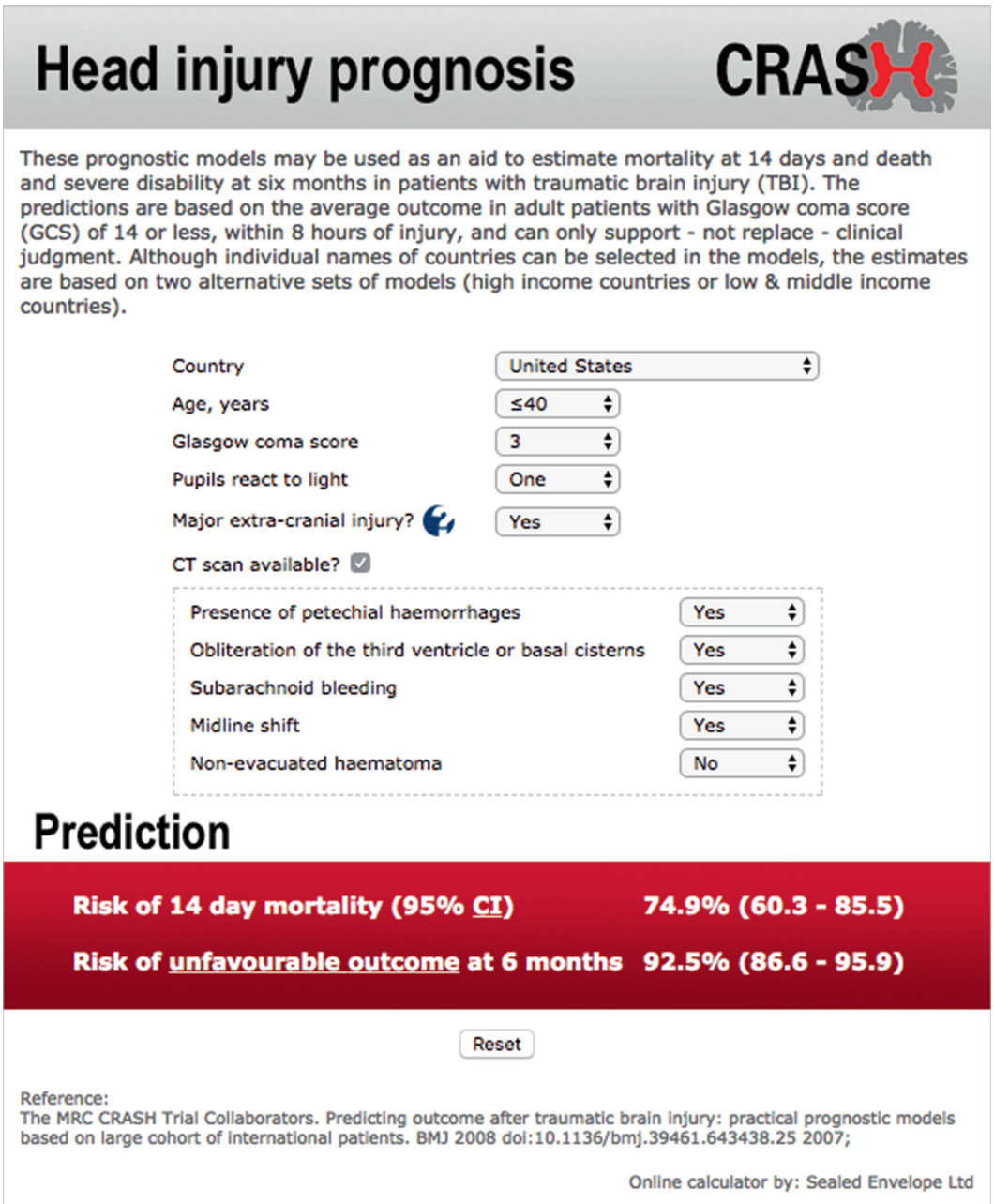

Fig. 3.2 (**a**, **b**) CRASH (http://www.crash2.lshtm.ac.uk/Risk%20calculator/) and IMPACT (http://www.tbi-impact.org/?p=impact/calc) calculations for the case example. ((**a**) With permission of CRASH Head Injury Prognostic Models (**b**) With permission from Steyerberg et al. [27])

b

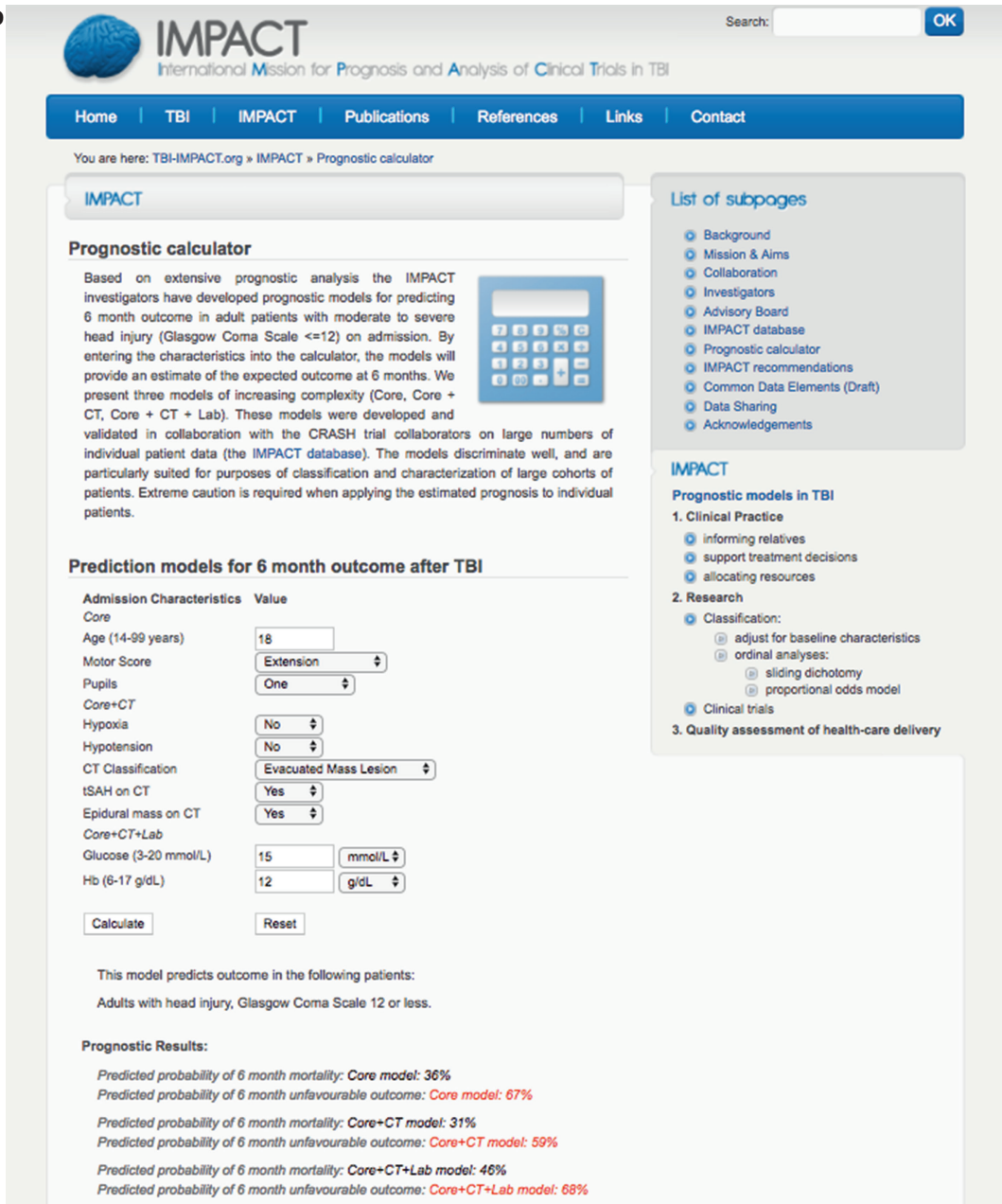

Fig. 3.2 (continued)

patients have roving nystagmoid eye movements; eyes do not track to sound, nor is there reproducible head-turning to sound. There is neither response to imitated gesture nor fixation to any object. Moving a newspaper up and down or tilting a large mirror does not provoke any eye movements or fixation. Often, with rapid head-shaking or noxious stimuli, the eyes may move upward or downward or assume a lateral gaze for 1–2 min. There is no evidence of language comprehension or expression, and there is often marked rigidity, spontaneous clonus,

and snout reflex. With a closer look, there is often spontaneous teeth grinding and sometimes even choreiform movements with shivering or clonus. Patients will not follow commands, for example to lift or turn the head, to blink twice or look up. A loud handclap may startle the patient or cause a myoclonic jitter. Grasp reflexes are present. Tendon reflexes show hyperreflexia. The muscle tone is markedly increased, and many patients have pathological flexion or extensor responses.

As a result of retained tonically active mesencephalon synapsing through sympathetic tracks, there is often the manifestation of some form of dysautonomia with increased bronchial secretions, hypertensive surges, and tachycardia, which can be seen as retained vegetative symptoms of the patient—and explains the name.

Vegetative vs. Minimally Conscious State

A different situation exists if the patient emerges from coma or the vegetative state into a minimally conscious state. In this state, the patient has minimal but clearly noticeable behavioral evidence of awareness of self and environment (See Chap. 4 "Chronic Disorders of Consciousness"). However, there is significant inconsistency in responses, which are mostly prolonged and delayed, and there may be vocalization or gestures that occur in response to questions. Some patients may reach for an object. Some may touch or hold an object as a purposeful behavior. In general, the signs present in minimally conscious state but absent in persistent vegetative state include eyes holding attention momentarily, looking at a person briefly, turning head in the direction of or establishing eye contact with the person speaking, and mouthing words in response to pain. The eyes may follow a person's movements and localize to pain. There may be some intelligent verbalization.

Some rehabilitation physicians have subclassified minimally conscious state into a minimally conscious state with language (MCS+) or a minimally conscious state without language (MCS−), although there is insufficient evidence to support prognostic significance. Preliminary studies, have suggested that MCS+ patients may have a better chance of additional improvement [13]. The degree of functional improvement is not exactly known.

At this point, the nosologic classification of disorders of consciousness is a syndromic one, and therefore relies on the neurologic examination to determine if the patient is in a vegetative state or minimally conscious state [14].

Other classifications could be considered based on the results of imaging studies. For example, studies have looked at diffusion-tensor imaging and found a strong correlation between the structural integrity of white matter in the subcortical thalamic region and the diagnosis of vegetative state and minimally conscious state, providing a good distinction between the two conditions [15]. In addition, there has been categorization on the basis of functional MRI scan, which includes cognitive motor dissociation (CMD). This is a subset of patients who fulfill all the criteria for vegetative state without any behavioral evidence of language function, but show command-following response on functional MRI scan when tested. Other neuroimaging or electrophysiological assessments can also be used to demonstrate such command-following response.

Some have felt that another subset may exist and tentatively called the higher-order cortex-motor dissociation (HMD), which indicates only a response of the associated cortices to auditory stimuli, again in patients who demonstrate no clinical evidence of consciousness. These findings, which on functional MRI scan or other modalities, such as electroencephalography, suggest covert consciousness could influence outcome and suggest recovery by 6 months [16]. The use of functional MRI scan for prognostication is controversial simply because MRI proto-

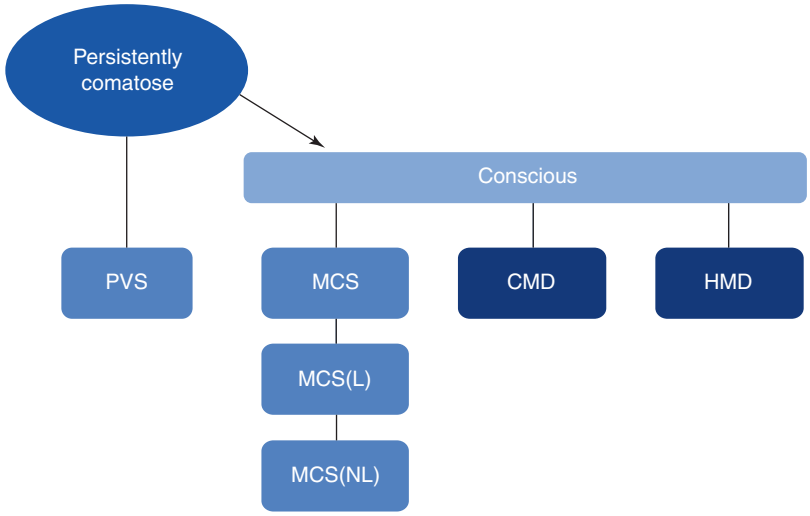

Fig. 3.3 Categories of persistent disorders of consciousness. PVS Persistent Vegetative State. MCS Minimally Conscious State; (L and NL to distinguish language and no language), CMD Cognitive-motor dissociation, HMD Higher-order cortex-motor dissociation

cols and paradigms as well as interpretation may substantially differ across institutions [17]. With more studies by several study groups this categorization of persistent disorders of consciousness is now somewhat in flux and illustrated in Fig. 3.3.

Symptom Detection and Management

Unresponsiveness

Management of patients with prolonged unconsciousness should include at least one trial of enhancement drugs, which could include dopaminergic drugs such as levodopa, amantadine, and bromocriptine or GABAergic drugs such as zolpidem. The data, however, are scarce and difficult to interpret and not subjected to rigorous assessment or prospective studies. The only study that suggested benefit was a randomized controlled trial of amantadine for 4 weeks in patients in a minimally conscious or vegetative state after TBI that showed an accelerated functional recovery compared to patients in the placebo group [18]. Methylphenidate has been found to improve attention and alertness in patients with severe brain injury, but it is unclear if it has any effect in patients with minimally conscious state [19].

The use of deep brain stimulation remains a contentious issue. Some may argue that deep brain stimulation for patients in minimally conscious state is "unethical," creating a situation where the patient becomes more aware of his deficit. In addition, the procedure somewhat violates self-determination, and adequate candidate selection is not known. Most studies are single case reports or case series that have used central thalamic deep brain stimulation. One recent study suggested that patients in minimally conscious state regained consciousness as well as the ability to walk, speak fluently, and live independently but over a long period of time, making it very difficult to distinguish it from natural history [20]. One patient in a vegetative state allegedly attained an improved level of consciousness and could respond to simple commands. Also in this study, three patients in vegetative state died from a respiratory infection or sepsis, and in seven treated patients with persistent vegetative state, there was no noticeable improvement of consciousness after deep brain stimulation. These results are far from encouraging, and thus, at this point, outside of a rigorous clinical trial in a large

group of patients, the procedure should be discouraged.

Pain

The first step in evaluating patients for pain should be the diligent evaluation of their level of consciousness. Patients in a coma or vegetative state do not suffer pain, and this concept is important for family members to understand and can be comforting information for them. Pharmacologic pain management, therefore, is theoretically not necessary including for patients who have facial movements, grimacing, shedding tears, or grunting or groaning sounds. The pain experience is different, however, in patients with minimally conscious state, where neuroimaging has found the possibility of processing pain responses [21]. The threshold to treat pain should be low for all patients with disorders of consciousness so as not to risk under-treatment. For the management of pain in patients with minimally conscious state or ambiguous cases, please see Chap. 4 "Chronic Disorders of Consciousness".

Paroxysmal Sympathetic Hyperactivity Syndrome

Another notable change has occurred. Charlie has developed paroxysmal spells of tachypnea, hypertension, profuse sweating, marked extensor posturing diffuse shivers and rigor like movements, with teeth clenching, all occurring several times during the day. All test results are normal. Fever is often substantial at 39.5 °C or higher, but no infection source is found with CT scans of chest, abdomen and pelvis and cultures have remained remarkably normal.

The patient has now developed paroxysmal sympathetic hyperactivity (PSH) syndrome or sympathetic storming, defined by an expert consensus as a "syndrome, recognized in a subgroup of survivors of severe acquired brain injury, of simultaneous, paroxysmal transient increases in sympathetic (elevated heart rate, blood pressure, respiratory rate, temperature, sweating) and motor (posturing) activity." [22]. PSH can present at all stages after brain injury, from the acute, critical care through the chronic, rehabilitation phase and can last for weeks to several months before it can 'burn out' [23]. The occurrence of PSH may be indicative of a poor outcome and more prevalent in early stages of vegetative state, but often the symptoms go unrecognized, are poorly treated or result in expensive evaluations. Supportive therapy is important because some patients may recover and go beyond this syndrome. This includes physical therapy and careful nutritional management. Many of these patients are admitted to rehabilitation units with paroxysmal sympathetic hyperactivity syndrome and may even have substantial weight loss as a result of the sympathetic overdrive. Various drugs have been proposed to treat PSH, including opioids, betablockers, alpha-2-agnoists and neuromodulators [23]. None is universally effective, and many patients require a combination of drugs. In the critical care unit morphine intravenous infusion can be titrated to effect or, better, a 1–10 mg intravenous bolus can be given. Morphine blocks the opioid receptors in the brainstem and spinal cord and targets in particular the clinical features of hypertension, tachycardia, and allodynia. Oral administration of propranolol (20–60 mg every 4–6 h) may reduce tachycardia, hypertension and diaphoresis. Gabapentin titrating to a maximal of 4800 mg per day can improve these episodes remarkably and should the preferred drug. If there is significant hypertension and tachycardia, clonidine at a maximum of 1200 μg per day but starting 100 every 8 h is effective. Dexmedetomidine may also be helpful, titrating between 0.2 and 0.7 μg/kg per hour. All these drugs are best in patients who have marked hypertension and tachycardia. The experience is limited with use of dantrolene or baclofen, both of which may improve spasticity

and posturing. When temperature is the main concern, Bromocriptine may be helpful. When agitation and posturing are primary symptoms, benzodiazepines can be titrated to effect [23].

End of Life Care

Charlie's physician tells the family that he will never wake up again and suggests withdrawing life-sustaining treatment. While Charlie's sister is interested in 'hearing the options', his parents get very upset and feel that the doctors 'are giving up on Charlie'.

Once a patient has been in a vegetative state for 4 weeks or more with no further clinical improvement, they are typically relatively stable from a clinical perspective with artificial life support including artificial nutrition through a gastrostomy and feeding tube, and sometimes continued need for a tracheostomy with or without mechanical ventilation. How and when to bring up end-of-life care in these situations can be challenging, especially if the family has not been prepared for that conversation from the beginning, and if they have not had a chance to develop a trusting relationship with the clinician or medical team (see Chap. 4 "Chronic Disorders of Consciousness" for additional discussion). While the insertion of gastrostomy tubes and tracheostomies are commonly viewed as time-limited trials, i.e. 'to give him some more time to recover', families are rarely prepared for the follow-up question weeks or months later, and the consideration to end the trial. Pro-active communication is key, and iterative conversations are often necessary. These should always include an affirmation of support from the clinicians, no matter what (see Chap. 2 "Severe Acute Brain Injury", and Chap. 11 "Communicating Effectively").

When the withdrawal or withholding of life-sustaining treatment is brought up, it is important to explain the different processes—for example terminal extubation, discontinuation of artificial nutrition and hydration, do-not-resuscitate, do-not-hospitalize (if discharged), or no further escalation of treatment—and to explain what the process will look like, so that the family can anticipate what will happen. For example, if a patient is ventilator dependent, death is likely to occur within minutes to hours after ventilator withdrawal. If nutrition and hydration are withdrawn, death will occur over the next week or two. These patients are eligible for hospice services and may be able to leave the hospital (see Chap. 16 "Hospice and End of Life Care in Neurologic Disease"). While a comatose patient may not feel discomfort upon withdrawal of artificial nutrition or hydration, it is often difficult to predict and reassure families. Benzodiazepines or opioids can be available if there is doubt about what the patient may perceive and if the patient develops labored breathing or shows significant unrest. These medications should be titrated to comfort before extubation rather than escalating the dose after extubation (see Chap. 14 "Addressing and Managing Requests to Hasten Death"). A challenging situation presents itself when surrogates ask to continue life-prolonging medical or surgical interventions when the clinicians feel that these interventions will not benefit the patient. As discussed in an official ATS/AACN/ACCP/ESICM/SCCM policy statement, the term 'medical futility' should be restricted to the physiologic sense of the term, in other words when the intervention cannot achieve the intended physiological goal (for example performing cardiopulmonary resuscitation in a patient with rigor mortis and livedo reticularis) [24]. More often the intervention may be considered 'potentially inappropriate' and the clinician may refuse to perform an intervention requested by the patient or family. With such value-laden decisions, the goal should always be to *prevent* major conflicts through pro-active and consistent communica-

tion and early involvement of expert consultants rather than trying to resolve conflict when it has become intractable (see Chap. 15 "Withholding and Withdrawing Life-Sustaining"). The policy statement concludes that the "medical profession should lead public engagement efforts and advocate for policies and legislation about when life-prolonging technologies should not be used" [24]. Similar options have been provided by the Neurocritical Care Society [25].

Education and Research Agenda

More research is needed in the area of prognosis after severe acute brain injury and prolonged coma. This will include the investigation of novel biomarkers and imaging studies. Large observational studies are underway [26]; these will be useful for prognosis only if they study patients for prolonged periods of time with all possible resuscitative measures. We will never find 100% accuracy in prognosis and need to realize that most families do not demand that. How to best communicate with families and how to best convey a neurologic prognosis and the uncertainty of prognosis require more research and more education. Finally, much better data is required in the assessment of patients with a minimally conscious state and neurologists should be closely involved in prospective studies of recovery and pharmacologic manipulation of responsiveness.

Take Home Messages

- The palliative care of a patient in a persistent disorder of consciousness is perhaps one of the most important tasks of physicians and includes diagnostic and prognostic acumen as well as effective and empathetic communication skills.
- Various prognostic scales have been published that are helpful to use as frameworks but should be interpreted with caution for each in individual patient.
- Patients in a coma or persistent vegetative state do not suffer pain, and pharmacologic treatment is not necessary *if the diagnosis is clear* and may further cloud their sensorium.
- Paroxysmal hyperactivity syndrome is common, may portend poor outcome but can be effectively managed. Gabapentin, and Opioids, are typically used.
- Providing continued support to families of patients in a prolonged coma also means honest and direct communication about the possibility of withdrawing or withholding life sustaining treatment at a later time point when clinical improvement remains absent.

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Chronic Disorders of Consciousness

4

Sunil Kothari

Persistent Disorders of Consciousness

Case

Mr. K, a 45 year old man who sustained a severe traumatic brain injury 6 months ago, was admitted last night with a diagnosis of aspiration pneumonia. After his brain injury, Mr. K had a prolonged hospital stay but for the last several months has been living at home with his wife. Mrs. K, his primary caregiver, reports that she has been told that her husband was in a vegetative state.

Introduction

Disorders of consciousness (DoC) are neurological conditions characterized by severe alterations in the level of consciousness. They include *coma*, the *vegetative state*, and the *minimally conscious state*. Although DoC can result from congenital disorders (e.g. anencephaly) or represent the end-stage of a neurodegenerative disorder (e.g. advanced dementia), the vast majority occur after severe acute brain injury (SABI) (see Chap. 2 "Severe Acute Brain Injury"). Many patients who sustain a SABI will experience a state of disordered consciousness for a period of time. However, most of these patients will eventually regain consciousness, although they may be left with varying degrees of deficits and disability.

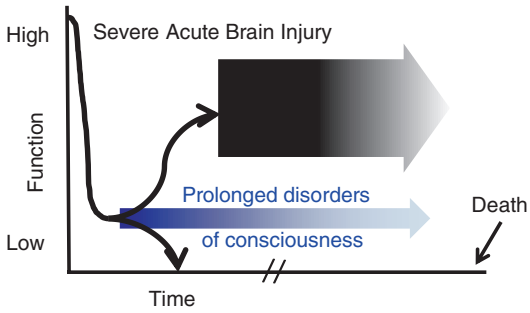

Fig. 4.1 Illness trajectory for prolonged disorders of consciousness after severe acute brain injury. (Adapted by permission from BMJ Publishing Group Limited from Creutzfeldt et al. [124])

For a small portion of patients who sustain a SABI, however, the state of disordered consciousness persists beyond the acute and subacute periods (See Chap. 3 "Prolonged Coma and Early Disorders of Consciousness"). As such, these persistent disorders of consciousness can be thought of as representing a subset of patients in the "fourth illness trajectory" (Fig. 4.1). These patients remain in a vegetative or minimally

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conscious state for months or years after their SABI. Because of challenges in the classification, identification, and tracking of these patients, accurate figures for the incidence and prevalence of persistent DoC in the United States are not available [1]. Keeping these challenges in mind, it has been estimated that there are approximately 35,000 people in the United States in a vegetative state and another 280,000 in a minimally conscious state [2], though it is likely that these figures underestimate the true prevalence of DoC.

Over the last two decades, there has been tremendous growth in our understanding of disorders of consciousness [3], especially with regard to diagnosis and treatment. However, because these developments are fairly recent, there is limited awareness of them, both among neurologists as well as palliative care physicians. As a result, in addition to addressing traditional areas of focus such as symptom management and caregiver communication, this chapter will also emphasize recent advances in the assessment and treatment of patients with a disorder of consciousness.

Nomenclature and Nosology

Although the various states of DoC share many similarities, the distinctions between the categories can have clinical, ethical, and legal significance. Generally speaking, disorders of consciousness are divided into two categories: states of unconsciousness (*coma* and *vegetative state*) and states of consciousness (*minimally conscious state*) (Table 4.1). The differences between coma, vegetative state, and the minimally conscious state can be characterized by the relative presence or absence of *arousal* and *awareness* (Table 4.2). In this context, arousal refers to the overall level of wakefulness. However, by itself, wakefulness is not sufficient for consciousness. Consciousness also requires awareness and, in clinical practice, consciousness has been *defined* as the state of awareness of one's self and/or environment.

Table 4.1 Categories of disorders of consciousness

Unconscious states:
Coma: complete loss of spontaneous and stimulus induced arousal
Vegetative state (VS): return of basic arousal; continued lack of awareness
Conscious states:
Minimally conscious state (MCS): return of awareness; but awareness may be minimal in degree and inconsistent in manifestation

Coma is characterized by the complete absence of spontaneous or stimulus induced arousal, as evidenced by the lack of eye opening. Because there is no arousal, awareness is not present either. It is important to note that coma is a self-limited state, rarely lasting more than 4 weeks (see Chap. 3 "Prolonged Coma and Early Disorders of Consciousness") [4]. After that period, patients will have either died or emerged into at least a vegetative state (although there has been a recent case report of a prolonged coma [5]. In the vegetative state (VS), arousal has returned (although it may fluctuate), and is heralded by the return of eye opening. However, the patient continues to lack awareness. For this reason, the vegetative state has sometimes been referred to as a state of "wakeful unconsciousness". The minimally conscious state (MCS) is characterized by the return of awareness of self and/or environment, although the degree of awareness can be minimal and variable. Unlike coma, both the VS and the MCS can last indefinitely. Therefore, the term *persistent* disorder of consciousness refers almost exclusively to patients who are either in a VS or a MCS.

The transition from coma to vegetative state is usually obvious, given the accompanying eye-opening and the return of apparent sleep-wake cycles. Distinguishing between the VS and the MCS can be more challenging and depends on detecting behaviors that constitute definite evidence of awareness of self and/or environment. While some behaviors, such as following commands, communicating, or manipulating objects, represent clear evidence of consciousness, other behaviors are more ambiguous in their interpretation (Table 4.3). It is important that clinicians be able to identify and distinguish the repertoire of behaviors characteristic of the various DoC, not

Table 4.2 Arousal and awareness in disorders of consciousness

	Coma	Vegetative state (VS)	Minimally conscious state (MCS)	Emerged from MCS
Arousal	–	+/++	+/++	++
Awareness	–	–	+	++

Table 4.3 Repertoire of available behaviors in disorders of consciousness

	Coma	Vegetative state	Minimally conscious state
Response to pain	Posturing	Flexion withdrawal	Localization
Movement	Reflexive	Patterned/involuntary	Nonreflexive/unpatterned
Visual	Eyes closed	Startle	Fixation/pursuit
Affective	–	Random	Contingent
Vocal	–	Non-contingent vocalization	Intelligible verbalization
Response to commands	–	–	Inconsistent
Communication	–	–	Unreliable yes/no[a]
Object use	–	–	Object manipulation[a]

[a]Functional communication and/or functional object use indicate emergence from the minimally conscious state

only to aid in their own assessment of the patient but also to help interpret the observations of family members.

For example, certain behaviors that might otherwise be thought to indicate consciousness may be present in the VS; these include tearing, smiling, yawning, chewing, and vocalization. By themselves, these behaviors do not necessarily imply the presence of consciousness. However, if some of them (for example, *affective behaviors* such as tearing or smiling) reproducibly occur in the setting of an appropriate environmental stimulus, then they may provide evidence of awareness. For example, a patient would likely be considered aware if he tears up only at the mention of his wife's name but not in response to other words or names. Similarly, *vocalization* would imply awareness only if it is contingently related to an appropriate environmental stimulus (for example, grunting that seems to occur only in response to questions but not in response to declarative sentences). Otherwise, only intelligible *verbalization* (i.e. of words) would constitute evidence of consciousness. With regard to the *response to painful stimuli*, it is important to distinguish between generalized flexion withdrawal and true localization. Likewise, although spontaneous *movement* may be present in the VS, it is typically only reflexive or patterned in character. Finally, while it is possible to have *visual* startle in a VS, sustained fixation and/or pursuit is only present in patients who are conscious (Table 4.3).

Patients are considered to have emerged from the MCS if they can demonstrate evidence of *functional communication* and/or *functional object use*. These behaviors were chosen as the "exit criteria" from the MCS because of their relationship to meaningful social interaction and personal autonomy [6]. In the MCS, yes/no responses, while present, are often inconsistent and inaccurate. Functional communication, by contrast, requires the ability to provide accurate yes/no responses to basic questions. Similarly, although patients in a MCS can manipulate objects, functional object use involves the knowledge of the appropriate use of common objects [6].

It is important to note that the term *vegetative state* has, over the years, accrued significant negative connotations. In particular, families often understand the label to imply that the patient is a "vegetable", although the original use of this term was simply meant to convey the preservation of vegetative functions in these patients (such as elimination, digestion, respiration, cardiac function, etc.) [7]. As a result, there have been calls to replace the term vegetative state with an alternate, such as "unresponsive

wakefulness syndrome" or "wakeful unconsciousness". Of the alternatives suggested, the one that seems to have the most support in the field is *unresponsive wakefulness syndrome* (UWS), a term that is already widely used in Europe [8]. Although this chapter will use the term *vegetative state* in deference to clinical usage in the United States, clinicians should consider introducing one of the alternate terms in discussions with family members.

Also, although this chapter uses the term *persistent* DoC, it is only as a shorthand way of identifying those patients who remain in a DoC for a period of months or years. Although terms such as *persistent* or *permanent* have been widely used in the past to imply very specific time frames, the formal use of these terms is now discouraged. Instead, the recommended practice is to describe the patient's condition as well as the duration of time that the patient has remained in that state (e.g. "vegetative state for eight months") [6].

Given the significant levels of disability present in both the VS and the MCS, distinguishing between them may seem of little practical relevance. In fact, the distinction between the two states is often of great importance because the presence of consciousness, which differentiates the MCS from the VS, can have significant clinical, ethical, and legal implications. For example, clinically, because the VS is considered a state of unawareness, patients should not be capable of feeling pain. While this should not imply that clinicians should ignore issues of comfort, it can be reassuring to families to know that patients in a VS should not have the capacity to suffer. On the other hand, knowing that a patient is conscious—even minimally—should reinforce the need to be especially thorough in addressing issues of comfort and quality of life. Apart from implying the capacity to suffer, consciousness is also often of psychological importance to family members because it signifies to them that their loved one is "still there", in however a diminished capacity. This is in contrast to the perceived sense of absence that families often report if they truly believe their loved one is in a vegetative state. The presence or absence of consciousness also has implications for access to care because eligibility for specialized rehabilitation services is much more limited for someone thought to be in a VS. Accurately distinguishing between the VS and MCS also affects prognostication; as will be discussed in the section on outcomes, patients in a MCS have a significantly better prognosis than patients in a VS. Finally, as will be discussed later, the presence or absence of consciousness has significant implications—both ethical and legal—for decisions to limit or withdraw treatment.

Mrs. K states that her husband responds to her and that, despite being told that her husband is in a vegetative state, she believes he is "in there".

Misdiagnosis, Differential Diagnosis, and Assessment

Misdiagnosis

In spite of the importance of accurately assessing the level of consciousness of these patients, numerous studies have documented high rates of misdiagnosis. In particular, patients who are conscious are frequently misdiagnosed as being in a vegetative state [9–11]. The most recent study to date [11] found that over 40% of patients diagnosed as being in a VS (based on qualitative bedside evaluations) were discovered to be conscious when assessed with a standardized behavioral measure. Moreover, 10% of patients diagnosed as being minimally conscious in this study had in fact already emerged from the MCS. These figures are consistent with the earlier studies and underscore the systemic underestimation of consciousness in these patients.

The high rate of misdiagnosis is likely related to numerous factors, which can helpfully be categorized into those related to the patient and those related to the examiner [12]. With regard to examiners, a significant issue is the lack of knowledge about DoC among most clinicians, especially with regard to the distinction between

the VS and the MCS. This increases the likelihood of misidentifying or misinterpreting behaviors. Another factor is the exclusive reliance on bedside qualitative neurological examinations to the exclusion of standardized assessment tools. Finally, the limited number of evaluations that are performed runs the risk of "under-sampling" behavior and thereby missing evidence of awareness (which is often subtle and inconsistent).

In addition to examiner-related factors, the very nature of these disorders poses significant challenges to assessment. For example, superimposed motor, sensory, and cognitive impairments can confound the assessment. These may include sensory deficits (such as impaired vision or hearing), unrecognized paresis or paralysis, and/or unidentified cognitive issues (such as apraxia or aphasia). Additionally, the level of consciousness can be impaired by other factors (sedating medications, concurrent medical problems, etc.). Finally, as previously discussed, the behavioral variability that is the hallmark of the MCS often leads to diagnostic inaccuracy.

Differential Diagnosis

The first step in evaluating these patients is to screen for the presence of conditions that can be mistaken for a disorder of consciousness (Table 4.4). For example, a patient with locked-in syndrome will have difficulty in demonstrating relevant behaviors, but this is due to profound paralysis rather than a deficit in consciousness.

Table 4.4 Confounds in the assessment of consciousness

Conditions that can mimic or overlap with DoC
Locked-in syndrome
Akinetic mutism
Catatonia
Deficits that can mask the true level of consciousness
Bilateral cranial nerve III palsies
Widespread paresis or paralysis (*e.g. critical illness polyneuropathy/myopathy*)
Profound primary sensory deficits (*e.g. deafness, blindness*)
Higher-order sensory, motor, or cognitive deficits (*e.g. apraxia, aphasia, etc.*)

Nonetheless, because these patients can appear behaviorally similar to DoC patients, they may be mistakenly diagnosed with a DoC. The consequences could be catastrophic, for example if decisions are made to limit treatment without realizing that the patient may be fully conscious. Another condition that can be mistaken for a DoC is akinetic mutism. In this condition, the deficit is one of *drive* rather than of consciousness. As with the locked-in syndrome, patients with akinetic mutism often have minimal motor output despite having relatively intact awareness. However, in akinetic mutism this is due to the deficit in initiation rather than paralysis. Finally, catatonia is an important consideration, since its presentation also mimics that of DoC and because it often responds very well to treatment [13].

In addition to general conditions that can mimic (or overlap) with a DoC, the presence of specific deficits can also confound the assessment of consciousness (Table 4.4). These include motor deficits such as widespread paralysis or even focal weakness as seen, for example, in bilateral cranial nerve III palsies (which, by limiting eye opening, may result in a mistaken diagnosis of coma). Sensory deficits, in particular profound deficits in hearing or vision, can also compromise assessment because many of the stimuli or instructions provided to the patient occur through either the auditory or visual systems. Finally, the presence of higher-order cognitive deficits such as apraxia or aphasia can also falsely suggest a lower level of consciousness, either by impairing the comprehension of instructions or the requested motor behaviors [14, 15]. For example, a recent study identified that globally aphasic patients without a DoC could be misidentified as being in a MCS [15].

Finally, clinicians should also investigate and address reversible causes of impaired consciousness (Table 4.5). These include concurrent medical conditions (e.g. infection, metabolic abnormalities, etc.), neurological issues (e.g. subclinical seizures, hydrocephalus, etc.), the use of sedating medications, disturbed sleep-wake cycles, and even a lack of adequate stimulation and mobilization. Searching for and addressing these reversible causes can have a profound

Table 4.5 Reversible causes of impaired consciousness

Disrupted sleep-wake cycles
Under-stimulation and under-mobilization
Sedating medications
Concurrent medical conditions (*e.g. hypoxemia, infection, metabolic abnormalities, etc.)*
Neuroendocrine abnormalities
Seizures (*e.g. non-convulsive status epilepticus, etc.)*
Intracranial abnormalities (*e.g. hydrocephalus, subdural hygromas, etc.)*

impact on a patient's level of consciousness even to the point that a patient may no longer be considered to even have a DoC.

A thorough history and physical examination in addition to routine medical tests can identify many of the diagnoses, deficits, and reversible causes discussed above. More specialized diagnostic tests can also be performed. Structural imaging (such as an MRI) should be reviewed to assess for the presence of lesions that can be associated with these conditions or deficits. Electrophysiological studies can also be useful. For example, an EMG can be used to evaluate for critical illness polyneuropathy or myopathy in patients with limited motor output. Likewise, visual and auditory evoked potentials may be useful in assessing the structural integrity of these sensory pathways. Finally, an EEG can be useful, for example, by demonstrating a relatively normal pattern in a patient who might clinically appear to have a severely altered level of consciousness.

Clinical Assessment

After screening for potential confounds, the patient's level of consciousness can be directly assessed. Currently, clinical (behavioral) assessment remains the 'gold standard' for the evaluation of DoC patients. These behavioral evaluations can either be qualitative, as in the standard bedside neurological examination, or more structured, as with the use of a standardized scale. In either case, the approach should include (1) multiple evaluations over time (2) utilizing different modes of assessment (3) administered by multiple examiners (4) under optimal environmental conditions (5) at various times of day. This approach ensures a large and varied set of observations, which is often required to detect subtle and inconsistent evidence of consciousness. In addition, it is important that patients be examined under conditions of appropriate stimulation to ensure that impaired arousal does not adversely affect the evaluation.

Although exclusive reliance on the bedside neurological examination is associated with high rates of misdiagnosis [11], the clinical bedside assessment remains the starting point in evaluating these patients. However, because behaviors in these patients are ambiguous and inconsistent (if present at all), qualitative evaluations should be supplemented by more formal assessments such as standardized rating scales. An expert panel conducted a review of available scales for assessing patients with a DoC and determined that six of them were appropriate for clinical use [16]. Out of these six, the Coma Recovery Scale-Revised (CRS-R) [17] was recommended for use with only 'minor reservations' (the remainder were recommended with 'moderate reservations'); it is currently the most widely used scale in the United States (Table 4.6).

The CRS-R is a 23-item scale comprised of six subscales that assess function in the domains of arousal, auditory function, visual function, oromotor/verbal function, motor function, and communication. The measure, which takes approximately 15–30 min to administer, is ideally performed at least five times within a 2-week period in order to maximize the chances of detecting signs of consciousness [18]. As with all assessments in this setting, the CRS-R should ideally be administered during periods of maximal arousal. On occasion, clinicians may supplement the use of the CRS-R with another formal method of evaluation: the individualized quantitative behavioral assessment (IQBA) [19, 20].

The assessment process should also take into account the observations of family and caregivers. Families spend a significant amount of time with the patient, often during periods when the clinical team is not present (e.g. evenings, nights). This increases the chances that they will observe behaviors that less frequent observation might

Table 4.6 Coma recovery scale-revised

Auditory function scale
4-Consistent movement to command
3-Reproducible movement to command
2-Localization to sound
1-Auditory startle
0-None
Visual function scale
5-Object recognition
4-Object localization: reaching
3-Visual pursuit
2-Fixation
1-Visual startle
0-None
Motor function scale
6-Functional object use
5-Automatic motor response
4-Object manipulation
3-Localization to noxious stimulation
2- Flexion withdrawal
1-Abnormal posturing
0-None
Oromotor/verbal function scale
3-Intelligible verbalization
2-Vocalization/oral movement
1-Oral reflexive movement
0-None
Communication scale
2-Functional: accurate
1-Non-functional: intentional
0-None
Arousal scale
3-Attention
2- Eye opening w/o stimulation
1- Eye opening with stimulation
0- Unarousable

From Giacino et al. [125], with permission from Elsevier

miss. Moreover, it has been demonstrated that DoC patients are frequently more likely to react to the voice of a family member than a treating clinician [21–23], suggesting that families may actually be better positioned than clinicians to elicit responses from the patient. This again increases the likelihood that behaviors relevant to the assessment of consciousness are detected. Thus, despite the concern that families and caregivers may "over-perceive" and over-interpret behaviors, the advantages of soliciting their observations likely outweigh the potential drawbacks.

Recent empirical evidence seems to support the legitimacy and value of the family's perspective. One study found that families' beliefs about the patient's level of consciousness matched the diagnostic assessment performed by the clinical team 76% of the time. Of note, 17% of families thought the patient had a *lower* level of consciousness than that determined by the clinical team; in only 7% of cases did the family believe their loved one's level of consciousness was higher [24]. Another study found that CRS-R scores were frequently higher when the family collaborated with the clinicians in the administration of the measure. Moreover, in some of these instances, the improvement in score resulted in a patient being reclassified as in a MCS rather than a VS [25].

Mrs. K asks why a "brain scan" can't be done to determine if her husband is conscious or not.

Ancillary Tests

Although behavioral assessments such as the CRS-R represent the current 'gold standard' in the evaluation of patients with DoC, there has been increasing interest in the role of ancillary testing in the assessment of consciousness. This interest has accelerated since the discovery that evidence of consciousness can be detected by diagnostic tests (e.g. functional imaging) in patients who otherwise appear to be in a VS. In a well-known case report, a patient who was determined to be in a VS (based on extensive behavioral assessments) was found to be able to follow commands and answer simple yes/no questions when assessed by fMRI [26]. Specifically, when asked to perform a spatial imagery task (walking through their home while 'looking' around) or a motor imagery task (imagining the swinging of a tennis racket), the appropriate areas of the patient's brain were activated (indicating that the patient was able to follow the mental-imagery commands). Next, the patient was asked a series of questions and was instructed to, for example,

imagine swinging a tennis racket if the answer was "yes" or walking through their home if the answer was "no". In this manner, the patient was able to accurately answer a brief series of simple questions [26].

This and subsequent reports have demonstrated that, even with appropriate and extensive behavioral assessments, the cognitive capacities of a subset of DoC patients are being underestimated, even to the point that patients are being diagnosed as being in a VS when they are, to varying degrees, conscious. A recent meta-analysis of 37 studies (which included over a thousand patients) estimated that roughly 15% of patients with a clinical diagnosis of VS are able to follow commands by modifying their brain activity [27]. This state has been characterized in various ways, for example "covert consciousness", "functional locked-in syndrome" [28], "complete cognitive-motor dissociation" [29].

Despite the significance of the phenomenon of covert consciousness, the use of ancillary technologies in the assessment of consciousness is still not part of routine clinical practice because of concerns about sensitivity, interpretation, technical challenges, etc. As these concerns are addressed over the next several years, it is likely that these techniques will increasingly supplement the clinical evaluation of patients with DoC. Thus, clinicians should begin to familiarize themselves with the available modalities and their limitations. All of these ancillary tests fall into two general categories: those that detect behavioral output (such as subclinical muscle activation) that cannot be detected on bedside evaluation and those that assess brain function directly (for example, in the form of cerebral electrical activity). Examples of the former category include pupillometry [30–33] and surface electromyography [34–36]. Modalities that assess brain activity directly include functional neuroimaging (e.g. fMRI) and electrophysiological measures [27, 37–43]. Examples of electrophysiological measures include global EEG measures (such as complexity or reactivity) [44, 45], EEG paired with transcranial magnetic stimulation (TMS-EEG) [46], and cognitive event-related potentials (ERPs) [38]. Regardless of which of these modalities are eventually incorporated into clinical practice, a multi-modal approach to the evaluation of these patients will likely be considered the standard of care in the future [12, 47, 48].

Mrs. K reports that, since the onset of the infection, her husband's spasticity has significantly worsened; she is worried that he is in significant pain.

Pain Management

The recognition and management of pain is a priority in the care of patients with DoC [49–53]. These patients are at high risk for painful conditions such as neuromusculokeletal complications (e.g. spasticity and contractures), skin breakdown, constipation, etc. as well as to exposure to the discomfort and pain associated with medical interventions. Recent functional neuroimaging studies seem to confirm that—as would be expected—MCS patients are capable of feeling pain [49–53]. And, although it is currently believed that patients who are truly in a VS are incapable of feeling pain, the high rate of misdiagnosis of VS as well as the phenomenon of covert consciousness would suggest that adequate analgesic control be the goal for all patients with DoC, regardless of the presumed level of consciousness. A recently devised scale, the Nociception Coma Scale-Revised, may be a useful tool for identifying pain and monitoring response to treatment in ambiguous cases (Table 4.7) [50].

In addressing pain, it is important to treat the underlying causes. In particular, aggressive management of neuromusculoskeletal complications such as spasticity and contractures is warranted, given their impact not only on pain, but also on positioning, mobilization, and the capacity for voluntary movement. Utilization of treatments such as nerve and muscle blocks, intrathecal baclofen pumps [54–57], and neuro-orthopedic procedures such as tendon lengthenings [58]

should be considered for those patients for whom there are no explicit plans to limit or withdraw treatment. Other potential causes of pain, such as skin breakdown, heterotopic ossification, etc., should be similarly sought and managed. Of course, in addition to addressing potential underlying causes, analgesic interventions must also be implemented.

However, although adequate analgesic control is both a clinical and ethical imperative in these patients, it is recognized that it may sometimes require medications that adversely affect arousal and cognition. In these cases, clinicians and caregivers should discuss the trade-off between improved arousal and optimal pain control. The balance between these two goals may shift over time. For example, it may be appropriate to minimize potentially sedating analgesic medications during the early phases of assessment of consciousness and then introduce them again at a later time. In addition to physical pain, the presence of consciousness implies the capacity to experience psychological distress. Because the presence of such emotional suffering would be even more difficult to detect than physical pain in these patients, clinicians might consider the routine initiation of anti-depressants, even when there is no explicit evidence for psychological distress.

Mrs. K states that she had hoped that her husband would have been "better by now" and wonders aloud "if he would want to live like this". She asks if it is still possible for him to improve after 6 months.

Prognosis and Outcomes

Although prognosis and outcome are clearly key questions in DoC, for both clinicians and families, our ability to prognosticate in individual cases is still limited (see also Chap. 12 "Prognostication"). However, there are several clinical 'rules-of thumb' that can be helpful: (1) patients with a traumatic DoC have a significantly better prognosis than those with a non-traumatic (especially anoxic) DoC; (2) at any given point in time, patients in a MCS have a better prognosis than patients in a VS; (3) the rate of recovery is positively correlated with outcome; and (4) in general, structural neuroimaging (e.g. CT or MRI) is of little value in prognosticating in individual cases.

Our ability to use empirical data to go beyond these general guidelines is limited by the challenges in interpreting the studies in this area. Some of these issues are similar to those encountered in other populations and are addressed in further detail in the chapter on prognostication. Other factors are more specific to studies in patients with DoC. For example, older studies in this area have methodological shortcomings that limit their applicability. In particular, because the distinction between VS and MCS is fairly new, most of these studies did not differentiate between them. This is a significant issue because evidence suggests that prognosis is directly tied to level of consciousness, with patients in a MCS having better outcomes than those in a VS [59]. In addition, the evaluation process for patients was less systematic and comprehensive in the past, raising concerns about misdiagnosis similar to what has been discussed above. Although recent studies have provided more relevant information, they are few in number and—as discussed below—may not fully represent the typical patient with a persistent DoC. These caveats need to be kept in mind in interpreting the findings discussed in the rest of this section.

Studies in this setting have focused on three primary outcomes: mortality, recovery of consciousness, and functional outcome. Most studies have suggested that, as might be expected, *mortality* is relatively high in persistent DoC [60, 61]. A recent study in the U.S. [62] found that patients with a traumatic DoC who were admitted to inpatient rehabilitation approximately 1 month post-injury were almost seven times more likely to die than individuals of similar age, gender, and race in the general population. In addition, they had an average life expectancy reduction of approximately 12 years. Of those that died, over a third died within the 1st year and over half within the

first 2 years. Cardiorespiratory issues were the most common cause of mortality, with pneumonia being the most common diagnosis associated with death. As expected, the mortality rate was higher for older patients and those with a more severe DoC [62].

The most comprehensive review on *recovery of consciousness* in the VS is several decades old [63] and thus subject to the limitations of the older studies described above. However, these conceptual and methodological limitations, while relevant to the actual percentages reported, likely do not affect the general patterns and correlations that were described. Specifically, this review found that outcome in VS was directly correlated both to etiology as well as time since onset. Patients with traumatic VS had significantly better outcomes than patients with non-traumatic VS. And, regardless of etiology, the longer one remained in a VS, the less likely it was that one would recover consciousness (Table 4.8). However, although this review reported a very low incidence of late recovery from VS, it is possible and has since been reported multiple times [60, 64, 65], suggesting that the prospects for late recovery are better than previously thought.

For those who do recover consciousness after post-traumatic VS, *functional outcome* was also found to be directly related to the time that the patient was in a VS [63]. Specifically, for those who were in VS at 1 month, approximately half of those recovering consciousness in a year were *severely disabled* according to the Glasgow Outcome Scale (GOS). The other half were *moderately disabled* or had a *good recovery* by GOS criteria. However, for those who regain consciousness after being in a post-traumatic VS for at least 6 months, the likelihood of *severe disability* (according to GOS criteria) is three times higher than the likelihood of having either a *moderate disability* or *good recovery* [63]. In non-traumatic VS, the overwhelming majority of those recovering consciousness were *severely disabled* (by GOS criteria) [63].

Table 4.7 Nociception coma scale-revised

Motor response
3-Localization to painful stimulation
2-Flexion withdrawal
1-Abnormal posturing
0-None/flaccid
Verbal response
3-Verbalization (intelligible)
2- Vocalization
1- Groaning
0- None
Facial expression responses
3-Cry
2- Grimace
1- Oral reflexive movement/startle response
0- None

From Chatelle et al. [126] with permission from Wolters Kluwer Health, Inc.

Table 4.8 Percentage of patients recovering consciousness at one year if still in a Vegetatve State (VS)

	VS at 1 month	VS at 3 months	VS at 6 months
Traumatic injury	52%	35%	16%
Non-Traumatic injury	15%	7%	0%

Table created from data in: Multi-Society Task Force on PVS "Medical Aspects of the Persistent Vegetative State (Second of Two Parts)". NEJM. 1994;330(22):1574

More recent studies have also examined *functional outcome* in patients with a DoC. One study [66] of post-traumatic DoC patients admitted to a rehabilitation unit approximately 35 days after injury found that, at 1 year, almost half of the patients had achieved recovery to daytime independence at home and close to a quarter had returned to work or school. Another study [67] of patients with post-traumatic DoC admitted to an inpatient rehabilitation program (approximately 1 month post-injury) found that almost 20% of patients were found capable of living without in-house supervision at follow-up (which ranged from 1 to 5 years post-injury). In addition, almost 20% demonstrated employment potential in either a sheltered or competitive employment setting.

Many of the patients in these two studies had emerged from a DoC during their stay in inpatient rehabilitation. Another study examined outcomes in more severely affected patients, namely those who remained in a post-traumatic DoC at the time of *discharge* from inpatient rehabilitation [68]. These patients may more accurately

represent patients in a persistent DoC given the prolonged duration of their impaired level of consciousness. Even in these patients, close to 20% performed independently on basic motor and cognitive subscales of the Functional Independence Measure (FIM) at 2 years.

There are limits to the generalizability of the findings of the recent studies just discussed. As part of a national "model system" of care for traumatic brain injury, these patients likely received care superior to other settings. Also, the fact that these patients were referred to a rehabilitation setting suggests that, despite the fact that they were still in a DoC, they may have had some other promising clinical characteristics that are associated with better outcomes. Finally, these patients were identified at an earlier point in time (approximately 1 month post-injury) than might be the case for many patients with persistent DoC. Even with these caveats, the studies suggest that outcomes from post-traumatic DoC are much better than is commonly believed. With regard to outcomes in persistent DoC due to anoxic brain injury, there are much less data available (in contrast to the large number of studies looking at prognostication in the acute setting). One recent study suggests that, as expected, the prognosis in these patients is worse than that of patients with post-traumatic DoC [69].

As mentioned above, structural neuroimaging has been found to be of little value in prognostication. An exception may be the presence of bilateral brainstem lesions in patients with post-traumatic DoC; this finding has been associated with poorer outcomes [70]. There are other ancillary modalities that may improve our ability to prognosticate in the future. In particular, several of the techniques discussed previously in the section on assessment (e.g. functional neuroimaging, event-related potentials) may identify DoC patients who will have a better outcome. Specifically, those patients who have evidence of covert cognitive abilities appear to recover faster and have better outcomes (than clinically similar patients without such capacities) [42, 71–79]. There are other electrophysiological techniques, not designed to detect covert cognitive capacities, which may also prove to be useful in predicting outcome [80]. Although not routinely in use at the present time, it is anticipated that at least some of these ancillary modalities will play a future role in prognostication in DoC.

Mrs. K also wonders if "everything" has been done to improve her husband's condition. She notes that, before she makes any major decisions about continuation of care, she wants to feel as if she has made every effort to maximize his recovery. She specifically asks about rehabilitation, noting that her husband had been discharged directly home from the hospital after his brain injury, rather than being transferred to a rehabilitation facility. A decision is made to proceed with a time-limited trial of rehabilitation.

Maximizing Neurological Status

In most other palliative care settings, it is assumed that patients have already had access to treatments that can modify the trajectory of the illness. Unfortunately, this is not often the case for patients with DoC, who frequently lack access to services that might significantly impact their clinical condition and, as a result, decisions about the future. For example, a family may decide that a patient with significant spasticity, whose cognitive capacities are limited to visual tracking, would not have wanted continued treatment. However, the family might come to a very different decision if, after receiving appropriate services, the patient's clinical status is optimized such that the tone is minimal and a yes/no system of communication has been established. Thus, it is important to ascertain whether a patient with DoC has received appropriate treatment; if not, there can be lingering questions as to whether the current clinical condition truly represents the patient's maximum neurological and clinical potential.

Unfortunately, the majority of DoC patients lack access to services, such as DoC rehabilitation programs, that might benefit them [2]. This

is partly due to a mindset about these patients that has been characterized as 'therapeutic nihilism' [81]. It is assumed that the prognosis for these patients is uniformly poor and that treatment would not alter the trajectory of recovery. Moreover, clinicians often believe that disorders of consciousness are not compatible with 'quality of life'; this assumption can color, consciously or unconsciously, decisions about the nature and extent of treatment. As a result, the option of referring a patient to a specialized DoC rehabilitation program is unlikely to arise; rather, if the patient survives, plans more often center around long-term placement, either to a nursing facility or home with family. However, even if a clinician wanted to refer a patient to a DoC program, there are systemic barriers to accessing these services. Most notably, many DoC patients do not meet eligibility requirements, set by public and private insurance, for rehabilitation services [82]. And even if these patients are admitted to a rehabilitation facility, their length of stay is often significantly limited.

Clinicians caring for patients with a DoC should have some familiarity with the general goals of these specialized programs so that, if appropriate, they can advocate for and provide a rationale for their patients to access them (Table 4.9). Even when patients can't receive these services, clinicians can still play a role in addressing many of the goals listed. As discussed earlier in this chapter, it is important to perform a thorough assessment of the level of consciousness as well as address reversible causes of impaired consciousness. In addition, clinicians should consider trials of interventions that might actively enhance the level of consciousness. In particular, in addition to non-medical interventions such as sensory stimulation, mobilization, and interpersonal interaction, there is evidence to support the efficacy of at least some medical interventions in improving awareness. The majority of these fall into two large categories, based on mechanism of action: pharmacological manipulation and targeted electrical stimulation. Of these, only medications are currently in routine use.

Pharmacological interventions have long been used in treating patients with a DoC, although the evidence for their efficacy in this setting is still limited [83–85]. Most often used are CNS stimulants, which specifically target catecholaminergic pathways. Of these, amantadine has the strongest evidence base supporting its use, primarily due to the results of a randomized controlled trial investigating its role in post-traumatic DoC [86]. Although this study targeted patients in the subacute setting, it is not unreasonable to consider a trial in patients with persistent DoC. Levo-dopa, bromocriptine, methylphenidate, amphetamine, and modafinil are other possible options, although the evidence supporting their use in DoC is limited and inconsistent [87]; thus, specific recommendations are not possible.

Table 4.9 Goals of specialized doc treatment programs

Consciousness and communication
Accurately assess the current level of consciousness
Address reversible causes of impaired consciousness
Trial interventions to enhance the level of consciousness
If appropriate, establish a system of communication
Medical and neuromusculoskeletal
Identify and augment residual voluntary movement
Minimize restrictions in range of motion
Intensive mobilization and environmental enrichment
Prevent and manage secondary medical complications
Optimize basic bodily functions such as respiration, nutrition, elimination, and skin integrity
Context of care
Provide family education, training, and support
Establish a plan for after-care

In addition to stimulants, GABA agonists, which are usually considered CNS depressants, have been shown to enhance the level of consciousness in some patients with a DoC [88]. In particular, zolpidem has been shown in a placebo-controlled, double-blind single-dose crossover study to improve the complexity and consistency of behavioral responses in approximately 5% of patients [89]. An open-label study reported a higher response rate (approximately 20%) [90]. Although the rate of response is not high, it seems reasonable to consider a trial of zolpidem in all DoC patients (for whom it is not contraindicated) given the relatively low risk associated with the medication. Other than stimulants and GABA agonists, there is some evidence to support the

possible role of other medications such as SSRI's, lamotrigine, and donepezil [83–85]. Although there is not enough evidence available to make specific recommendations, empiric trials with these agents might also be justified, given their relatively low risk profile.

Although pharmacotherapy is currently the mainstay of medical interventions in DoC, more recent studies have investigated the role of electrical stimulation in this population [85, 91]. These interventions include non-invasive treatments such as transcranial direct current stimulation (tDCS) [92–94] and repetitive transcranial magnetic stimulation (rTMS) [88, 95, 96] as well as invasive treatments such as deep brain stimulation (DBS) [97–99] and vagus nerve stimulation (VNS) [100]. Although none of these therapies are currently utilized in routine clinical practice, clinicians caring for patients with a DoC should be aware of them, not only because they may be asked about them by families but also because at least some of them may become part of clinical care in the future.

A few days after admission to the rehabilitation facility, the rehabilitation team determines that Mr. K is, in fact, minimally conscious, although only capable of visual tracking and non-purposeful spontaneous movement. After 6 weeks in the rehabilitation program, Mr. K's medical status has been optimized, his neuromuscular issues have been effectively managed, and his level of consciousness has improved to the point that he will occasionally follow simple commands. However, a yes/no system of communication could not be established. Mr. K is discharged back home with his wife.

Caregiver Experience

The attitudes and beliefs of family members of patients with persistent DoC are often colored by their experiences in acute care. In particular, many of these families faced questions and decisions regarding the continuation of life-sustaining medical treatment early after the SABI (see also Chap. 2 "Severe Acute Brain Injury" and Chap. 3 "Prolonged Coma and Early Disorders of Consciousness"). If they did, families of patients with persistent DoC obviously chose to continue with medical treatment. However, these families frequently report that their experience with the discussions in the acute care setting continue to color their perception of and subsequent interactions with the health care system [81, 101]. Specifically, families have reported that they frequently felt pressured to withdraw treatment in these situations [81, 101]. As a result, they can be resentful and frequently adopt a defensive position, feeling the need to fight for their loved one's life in opposition to the healthcare system [81]. Later, however, some of these families may begin to have doubts and feel guilt about the decision they made to continue with treatment, especially as they realize that the patient is not recovering as expected [101]. When having conversations with families in this setting—especially about goals of care and continued treatment—clinicians should keep in mind both of these dynamics: the initial (often explicit) commitment to continued treatment as well the possibility of later doubt and guilt.

After the initial period of hope and expectation, the central experience of families of patients with persistent DoC is the lack of improvement. While this is similar to the experience of families of patients with other chronic or progressive conditions, the situation is further complicated by features that are more specific to DoC. One is the continued prognostic uncertainty; even after several months, families may not be sure whether to hope for or expect further improvement. This uncertainty can complicate or even suspend the grieving process. In addition, DoC often represents a condition of *ambiguous loss*, a situation without resolution in which their loved one is experienced as 'physically present but psychologically absent' [102]. Traditional approaches to addressing grief may need to be modified in this setting, given the lack of finality and the ambiguity of the patient's status as 'present' or 'absent'.

Compounding the psychological issues just discussed are the cognitive challenges families face in understanding disorders of consciousness.

Consciousness itself is a very abstract concept and there is still disagreement in the field about how to best conceptualize it [103]. Even the clinical categories of DoC (*coma, VS, MCS*) can be difficult to comprehend. This is especially true of the VS, given our everyday experience of the deep relationship between arousal and awareness. Families may struggle to understand how their loved one can be awake and yet remain unconscious. Thus, if not already done, the clinician should ensure a basic level of understanding of the *meaning* of the patient's level of consciousness.

In addition to these emotional and psychological issues, families of patients with persistent DoC face very practical challenges. These include education and training in the care of the patient, especially if the family will be providing care in the home. These families need ongoing material and psychological support throughout this process. Even then, as with families of patients with other severe neurological disorders, these families can experience high levels of burden (and often distress) [102, 104–108]. Clinicians should be sensitive to these issues and be aware of resources—psychological, material, financial—to help support these families (See Chap. 18 "Spiritual Care" and Chap. 20 "Caregiver Assessment and Support").

After 4 months at home, Mr. K is once again hospitalized with another pneumonia. It has been a year since his injury and the wife reports that he has had no further neurological improvement since being discharged from the rehabilitation facility. Although she acknowledges that her husband does not seem to be in pain, she once again indicates that he "would not want to live like this".

Ongoing Discussions About Goals of Care

Discussions about goals of care should be raised at regular intervals and certain triggers should prompt clinicians to initiate these conversations sooner (Table 4.10). Before the initial discussion takes place, clinicians should make every effort to ensure that the diagnosis (e.g. VS vs. MCS) is accurate, given the systematic underestimation of the level of consciousness of these patients. This phenomenon clearly has implications for discussions regarding treatment limitation or withdrawal since, as will be discussed further below, the presence or absence of consciousness plays a significant role in the decision-making for these patients. In addition, as discussed earlier, whether the patient is in a VS or MCS has prognostic implications. Patients in a MCS generally have a much better prognosis than patients in a VS, which will likely impact any decisions that are made about further treatment.

Clinicians should also ensure that patients have received appropriate treatment interventions. As previously discussed, it is likely that treatment can improve the clinical status of the patient as well as possibly modify the trajectory of recovery. If DoC patients have not received appropriate services, as is often the case, decisions that are made about future care may be based on inaccurate perceptions of the patient's current status and future potential.

Table 4.10 Serious conversation triggers

Initial
After a comprehensive diagnostic assessment (to establish actual level of consciousness)
After a trial of appropriate treatment (to ensure that the patient's current status represents their neurological potential)
After a discussion of prognosis
Change in clinical status
Change in level of consciousness (especially worsening but even improvement)
New neurological event
Acute medical illness, especially if it leads to a hospitalization
Subsequent monitoring
Lack of improvement over an extended period of time
Persistent distress despite appropriate intervention (e.g. pain, spasticity, paroxysmal sympathetic activity, etc.)
Other
After questions or concerns raised by the family regarding "quality of life"
At regular intervals depending on the patient; more frequently at first

It should be kept in mind that, in the setting of chronic DoC, families have often made an explicit decision to proceed with treatment in the early stages and may perceive that health care providers are trying to persuade them to limit treatment [81]. This can understandably lead to a sense of defensiveness on the part of the family; if present, this should be recognized and even acknowledged by clinicians. At the same time, studies have shown that families' views evolve [101], highlighting the importance of revisiting the issue of treatment limitation periodically, in case the family's viewpoint has changed over time.

As in other settings, approaching these situations in terms of a de-escalation of treatment can be helpful. Initially one might limit the discussion to do-not-resuscitate (DNR) orders, emphasizing that such orders will not have any impact on the remainder of the care received by the patient. In discussing DNR orders, it is relevant to point out that cardiorespiratory arrest is almost inevitably accompanied by further brain injury and that, should the patient be successfully resuscitated, they will likely have additional neurological compromise. This is often a significant consideration for families who are willing to accept the patient's current level of neurological function but believe that further neurologic decline would be unacceptable.

In addition to DNR orders, surrogates can also be asked about limiting treatment if the patient develops an intercurrent medical illness (usually an infection); ideally, these discussions about "ceilings of care" would take place ahead of time, rather than when the patient is acutely ill. Finally, if appropriate, discussions about active withdrawal of treatment can take place (see also Chap. 11 "Communicating Effectively"). Clinicians should be aware that, as in other settings, families of patients with chronic DoC often have strong beliefs and emotions surrounding limiting medical nutrition and hydration [101]. If they have not already been consulted, palliative care specialists should be strongly considered in any discussions regarding active withdrawal of treatment.

Families may have prior opinions about disorders of consciousness, frequently shaped by media coverage of well-known legal cases such as that involving Terry Schiavo [109]. However, studies suggest that, partially as a result of inaccuracies in the attendant media coverage, families' beliefs may be incomplete or erroneous [109]. Thus, as in other settings, it is important that clinicians inquire as to any prior knowledge and opinions surrogates may have about DoC. Clinicians should also familiarize themselves with the results of empirical investigations into the beliefs of families surrounding treatment limitation in this setting [24, 81, 101]; this knowledge can help anticipate and address concerns that families may not always articulate.

After the clinician elicits the families' prior beliefs and opinions regarding DoC, they should attempt to provide them with additional information about the patient's current status and prognosis. In these discussions, it is important to acknowledge the diagnostic and prognostic uncertainty that may be present. With regard to diagnosis, the phenomenon of covert consciousness implies that, even after comprehensive clinical assessments, a patient thought to be in a VS might actually be conscious, sometimes substantially so. Similarly, prognostication has an element of uncertainty because, as with many other neurological conditions, outcome predictions are often probabilistic in nature. The possible uncertainty in diagnosis and prognosis should be presented in a way that is understandable and not psychologically overwhelming; information on how to do so is found elsewhere in this textbook (see Chap. 11 "Communicating Effectively" and Chap. 12 "Prognostication"). Clinicians should also be aware of the ethical implications of clinical uncertainty in chronic DoC, especially in the setting of conversations about limiting or withdrawing treatment (see Chap. 15 "Withholding and Withdrawing Life-Sustaining Treatments") [110].

To a great extent, the specific content of these discussions will be determined by whether the patient is in a VS or a MCS. For a patient in a VS, the issues—clinical, ethical, legal—are more straightforward, especially if the VS has persisted for a prolonged period of time. Because these patients are unconscious, concerns about suffer-

ing or quality of life are not directly relevant (since the patient is not capable of feeling pain or pleasure). Also, if the VS has lasted for an extended period of time, the likelihood of recovery of consciousness is extremely low. As previously discussed, progression out of the VS is extremely unlikely 12 months after traumatic injury and 3 months after anoxic brain injury, with an intermediate prognosis for other etiologies. Clinically, therefore, there is less ambiguity and uncertainty about prolonged VS.

The same holds true for the ethical and legal status of the VS; there is now a general consensus in the United States that it is permissible to withdraw treatment from patients in a chronic VS, if doing so is consistent with their prior wishes [111]. Of course, ethical dilemmas can still arise in these settings; for example, if the prior wishes of a patient in a VS are not known or if there is disagreement amongst decision-makers [112]. However, these dilemmas occur against a background of general ethical and legal agreement.

This situation contrasts with that of the MCS, where there is legal ambiguity and ethical disagreement. The legal system in the U.S. has rarely explicitly addressed the issue of withdrawal of treatment for patients who are in a MCS. There are no state statutes that specifically mention the MCS, although it is possible that the diagnosis is covered by the triggering conditions that the statutes do address [111]. And there have only been two legal cases to date that directly address withdrawal of treatment in the MCS [113, 114] although, because these were adjudicated in the state court system, these judicial decisions only serve as a precedent in those states. Thus, in most jurisdictions, withdrawal of treatment from a MCS patient is neither explicitly prohibited nor explicitly allowed.

The lack of explicit legal guidance on withdrawal of treatment in the MCS is compounded by a lack of consensus in the bioethics community. In particular, there is disagreement amongst ethicists about the implications of consciousness for decisions to limit or withdraw treatment. Some argue that it should be more difficult to withdraw treatment from someone who is conscious (albeit minimally) than from someone in a VS. Others disagree, arguing that the difference between the VS and MCS is of little ethical relevance since both conditions represent states of severe neurological compromise [115]. Indeed, some have made the point that it might be worse to be in a MCS rather than VS, because consciousness implies the capacity to suffer [116].

Despite the lack of an ethical and legal consensus on treatment withdrawal in the MCS, there is agreement that a patient's prior wishes have a significant bearing on these decisions. Unfortunately, as in other settings, most patients have not expressed any preferences regarding continued treatment in the setting of a persistent disorder of consciousness. If they have, it is almost always in reference to the VS. And clinicians should be wary about extrapolating from a person's wishes about survival in a VS to their wishes about survival in a MCS. One recent study found that almost 65% of people reported that they would want treatment withdrawn if they were in a VS while only about 40% reported the same desire if they were in a MCS [117].

Even if it is determined that a patient would have wanted treatment withdrawn in the setting of chronic MCS, ethical issues have been raised about the force and applicability of these prior wishes. For example, even knowing their prior wishes, it might be difficult to justify withdrawing treatment in such patients if they appear to be free of pain and even seem to smile in pleasure (e.g. when stroked, hearing music, etc.). This dilemma, which occurs in other settings (such as dementia), hinges on whether ethical priority is given to the person as they were (and their prior wishes) or to the person as they seem to be now [118, 119].

The "disability paradox" is relevant in this context. This phenomenon, discussed in more detail elsewhere in the textbook (Chap. 2 "Severe Acute Brain Injury"), refers to the well-documented fact that individuals without disabilities regularly underestimate the quality of life (QOL) of people with disabilities. These attitudes likely influence the family members of patients with severe brain injuries as they are deciding on future treatment. It is also known to impact the decisions of health care providers [120, 121].

And, importantly, it is likely to affect the preferences for treatment that people might express *prior* to their injury. Some might argue that the disability paradox should lead us to place less weight on prior wishes for treatment limitation because those wishes were likely based on a misperception or misunderstanding of the QOL possible after disability. On the other hand, it might be that the disability paradox, while applicable to most conditions of disability, may not be relevant to conditions as severe as the MCS.

Ethical debate continues regarding the moral status of prior wishes in cases of severe neurological impairment; however, from a clinical and legal point of view, the patient's prior wishes are still accorded significant weight. But in most cases the patient's specific wishes are not known. In these cases, the clinician should attempt, in collaboration with those who know the patient best, to obtain an understanding of the patient's goals, values, and even life-narrative. This process is described elsewhere in this textbook (see Chap. 2 "Severe Acute Brain Injury" and Chap. 11 "Communicating Effectively"). This general knowledge about the patient can be supplemented with information regarding the family's preferences, the patient's current clinical status (e.g. whether the patient seems to be in distress), awareness of phenomena such as the "disability paradox", etc. In effect, the clinician is creating a mosaic from these various sources of information with the hope that the 'image' that results will help guide decision-making in situations where there is no definitive evidence of the patient's prior wishes [122].

Another ethical issue that has implications for treatment withdrawal is the impact that factors such as financial and material resources play in determining a patient's quality of life. For example, an impoverished MCS patient who is discharged to a suboptimal nursing facility will likely face diminished quality of life or frank suffering because of possible skin breakdown, contractures, social isolation, etc. Is it appropriate to consider withdrawal of treatment for this patient even if the suffering in question is more a result of social circumstances rather than clinical status? Allowing such non-clinical factors to play a role in decisions to withdraw treatment might lead to treatment being withdrawn disproportionately from patients of lower socioeconomic status, which is clearly troubling. On the other hand, some would argue that it is the fact of unremediable suffering itself, rather than its cause, that should ultimately drive these decisions.

This dilemma highlights how intertwined matters of access to appropriate care are with questions of treatment withdrawal. Ideally, the palliative care approach in persistent disorders of consciousness would address both issues. As one commentator has summarized it, an ethic of palliative care for these patients would "preserve the right to die AND affirm the right to care" [123]. For those for whom treatment is withdrawn, clinicians should attempt to ensure a peaceful and dignified death (See Chap. 16 "Hospice and End of Life Care in Neurologic Disease"). But for those who survive, the palliative care approach entails a commitment to providing care that is medically appropriate and that maximizes quality of life for the patient and their caregivers.

Research Agenda

Despite the significant recent advances in our understanding of disorders of consciousness, there are still important barriers in providing appropriate neuropalliative care to these patients. Most obviously, there is a need for disseminating knowledge of these advances to all those caring for these patients: neurosurgeons, neurointensivists, neurologists, primary care physicians, physiatrists, palliative care clinicians, etc. Widespread understanding of the issues discussed in this chapter would significantly enhance the quality of care provided to patients with a DoC. But there is also important work that needs to be done in furthering our understanding and even generating new knowledge about DoC, especially in the areas of diagnosis, prognosis, and treatment.

For example, much more research needs to be done in determining what role the ancillary diagnostic modalities discussed earlier (functional neuroimaging, electrophysiological studies, etc.) should play in the assessment of patients with a

DoC, especially those thought to be in a vegetative state. Questions to be answered include characterizing the sensitivity/specificity of these tests, establishing guidelines for interpretation of results, specifying the appropriate level of technical expertise required to administer them, etc. The recognition of the phenomenon of covert consciousness and cognition makes work in this area even more pressing.

Similarly, more studies are needed to determine the efficacy, if any, of the newer modalities that might be used to enhance arousal and awareness in these patients, especially those interventions that rely on electrical stimulation such as rTMS, tDCS, etc. Finally, it is clear that our ability to prognosticate in individual cases is quite limited and based on very limited evidence. Many more studies are needed to better characterize the long-term outcome of these patients as well as the prognostic factors that will enable clinicians to more precisely counsel families regarding which of the possible outcomes is most likely.

There are also opportunities for improvement with regard to issues that are more specific to palliative care. As discussed in the last section, there is still a significant amount of ethical and legal uncertainty regarding the limitation or withdrawal of treatment in minimally conscious patients; it is hoped that the bioethics and legal community will help clarify the issues involved. For those patients for whom treatment is continued, more thought needs to be given to the determinants of quality of life for minimally conscious patients. Clinicians should look beyond simply minimizing pain in these patients and consider ways to enhance pleasure and meaning by increasing the opportunities for pleasurable sensory and tactile experiences, expanding opportunities for social contact/interaction, improving communication, maximizing control over one's body and environment.

Take Home Messages

- There have been dramatic improvements in our understanding of the pathophysiology, diagnosis, treatment, and prognosis of disorders of consciousness; clinicians caring for these patients should make an effort to familiarize themselves with these advances.
- There is a significant underestimation of the level of consciousness and cognitive capacities of these patients, resulting in high rates of misdiagnosis of the vegetative state. In particular, the phenomenon of "covert cognition" is likely to be more common than was previously recognized.
- There is growing evidence that prognosis for improvement is much better than previously thought, especially for patients with post-traumatic DoC.
- In the future, newer technologically based modalities should enhance our ability to diagnose, treat, and prognosticate for these patients.
- Despite the fact that specialized DoC rehabilitation programs are likely to improve care for these patients, most patients with a DoC lack access to these services.
- An ethic of palliative care for these patients should "preserve the right to die AND affirm the right to care" [123].

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Parkinson's Disease and Related Disorders

5

Janis M. Miyasaki

Case

John is a 75 year-old man with 10 years of PD. He attends clinic with his wife. John responded well to Levodopa/Carbidopa 100/25, two tablets five times a day, but is noticing more time when his medications wear-off early or don't kick in fully. Unfortunately, he is also lacking motivation and is not exercising or socializing. He is vague in his answer, whereas previously, he provided histories with rich details and precision. When asked about constipation he confirms that he has a bowel movement only twice a week. He is fatigued throughout the day and has stumbled when rising from a chair, but has not passed out. His wife is concerned about leaving him at home alone. He often will forget to take medications and then will be quite impaired from a motor symptom standpoint. His wife lets him manage medications independently, but wonders now if this is wise.

His exam is notable for orthostatic vitals with a lying blood pressure of 160/90 that falls to 85/60 after standing for 3 min. He is very tremulous with marked rigidity and bradykinesia. John's wife looks exhausted and she confesses that she doesn't know how much longer she can manage.

Parkinson disease (PD) has a prevalence of approximately 0.3% of the entire population, 1% for those over 60 years, and 4% for those over age 80 [1]. Therefore, as the population ages, physicians and healthcare providers will increasingly encounter those with PD either as a primary diagnosis or comorbidity. While traditionally characterized by motor symptoms, attention to non-motor symptoms in PD has increased over the past two decades [2]. While some non-motor symptoms may be present early in the illness or even precede motor symptoms, other non-motor symptoms such as cognitive impairment increase with disease duration and complicate treatment decisions [3]. This complexity along with its progressive nature, impact on mortality and the need to prioritize patient values makes application of palliative principles to PD a natural solution [4]. Although this chapter focuses primarily on PD, other related movement disorders such as Multiple System Atrophy, Progressive Supranuclear Palsy and Corticobasal Syndrome

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have similar palliative care needs, including symptom burden, and may respond to a similar approach [5].

Mortality and Estimating Prognosis in PD

A common myth heard by those with PD is that people "do not die ***of*** PD, they die ***with*** PD". Unfortunately, the myth of dying "with" PD results in patients not being referred to palliative care or adopting the palliative care principles that may improve their quality of life.

Across multiple study designs, mortality is consistently increased beyond age-matched non-PD controls, and PD is listed by the Centers for Disease Control as the 14th leading cause of death in the United States [6]. The 50% survival rate from PD is approximately 15 years after diagnosis [7]. The range however is quite broad with those diagnosed prior to age 40 frequently having survival of 30 years while those with onset in the 70s or 80s might have survival of only a few years [8–10]. Risk factors predicting higher rates of mortality include: dementia, postural instability, older age of onset, postural instability gait disorder subtype, falls and psychosis [11–13]. Hence, while it is true that those with PD can live long and productive lives, having PD does increase the risk of mortality particularly when other non-motor symptoms become evident.

Common causes of death attributed to PD are aspiration pneumonia and falls resulting in injury such as hip fractures, head injury or other injuries requiring hospitalization) [14–17]. Studies varying in time from 2010 to 2015 reveal that the majority of patients with PD die in the hospital (43–55%) or in a nursing home (36–66%) with only 9% dying at home [6, 10, 16, 18]. Hospice utilization varies widely among studies, with one UK study citing 0.6% of all PD decedents [16], and one US study reporting hospice involvement in over half of nursing home residents with PD (54.2%); this rate was even higher if a neurologist was involved in the patient's care [19]. Among those dying in hospital, the most common cause listed was PD (29%) followed by malignancy (12%), ischaemic heart disease (12%), pneumonia (11%), and cerebrovascular disease (9%) [17].

Recognizing that patients with PD may benefit from hospice, current Medicare guidelines for referral to hospice of Medicare recipients with PD or other neurologic disorders are: Critically impaired breathing (including dyspnea at rest, vital capacity <30%, O2 need at rest) AND refusal of artificial ventilation or rapid progression (to bed-bound status, unintelligible speech, need for pureed diet and/or major assistance needed for ADLs) with either critical nutrition impairment and refusal of artificial feeding methods or life-threatening complications in the prior year (including recurrent aspiration pneumonia). If using the dementia criteria, the patient must be Stage 7C or higher on the Functional Assessment Staging Test which translates to speech ability limited to use of a single intelligible word in an average day or course of an interview and ambulatory ability lost (See Chap. 6 "Dementia" and Chap. 16 "Hospice and End of Life Care in Neurologic"). These guidelines do not capture all patients with PD who may benefit from hospice, and clinicians are encouraged to document other factors that support a predicted survival of 6 months or less such as weight loss or decreasing benefit of dopaminergic therapies [20]. Table 5.1 highlights clinical scenarios that may trigger conversations about goals of care and consideration for referral for hospice or other palliative care services.

A cohort of 130 PD patients followed from 2007 to 2012 at the University of Toronto team-based outpatient palliative care clinic had 43 deaths: 29 (67%) died at home and received community palliative care, 4 in a nursing home (9%), 4 in an inpatient palliative care unit (9%) and 6 in an acute hospital (14%) (1 due to lack of a palliative care inpatient bed). This (unpublished) data suggests that an ambulatory palliative care program can impact location of death in a manner congruent with the wishes of patients and families.

Table 5.1 Potential triggers for palliative conversations in PD

Bothersome or disabling pain not responsive to PD medication management
Behavioral complications of PD requiring reduction in motor control (through reduced medications)
Caregiver distress or burnout
Recent or Repeated hospitalization (for infections, falls, fractures)
Loss of ability to drive
Loss of ability to perform activities of daily living without assistance
Recurrent falls or need for gait assistance device
Cognitive impairment or Dementia
Behavioral issues including hallucinations, delusions or wandering
Significant dysphagia
Hospitalizations from aspiration pneumonia or falls
Weight loss (may be due to increased metabolism, decreased appetite or dysphagia)
Existential distress: loss of hope, feelings of despair
Acceleration in changes in functional status

Defining Advanced PD

Advanced PD is loosely defined in the neurology community. To those focusing on motor symptoms, advanced PD may refer to any time after the development of motor complications of treatment. This includes motor fluctuations (having early, sudden or unpredictable wearing-off of benefit from dopaminergic therapy) and dyskinesias (abnormal involuntary movements that are typically rocking and writhing). However, even after first development of motor complications, many patients will have many years if not decades of very good or excellent motor function, and surgical interventions (such as lesions or deep brain stimulation) may help many retain very good or excellent quality of life. As time passes, patients become more encumbered by non-motor symptoms (Table 5.2) [21]. From a palliative care perspective, the concept of advanced PD often means a time when non-motor symptoms surpass motor symptoms in severity, where motor disability cannot be controlled with best medical or surgical management, or if motor control may need to be compromised by reducing medications in order to increase cognitive clarity.

Table 5.2 Pharmacologic treatments for PD nonmotor symptoms

Symptom	Treatment	Dose range
Dementia	Donepezil	10 mg daily
	Rivastigmine	3–12 mg daily
	Memantine	10–20 mg daily
Psychosis	Quetiapine	12.5–100 mg daily
	Clozapine	12.5–150 mg daily
RBD	Melatonin	3–15 mg
	Quetiapine	12.5–50 mg
Parasomnia nonREM	Clonazepam	0.25–2 mg qhs
Insomnia	Melatonin	3–15 mg
	Yang-Xue-Qing -Nao granules	4 g tid
Restless Leg syndrome	Levodopa	Varies
Sialorrhea	Candies, gum	
	Atropine drops	0.1%
	Botulinum toxin injection	15–40 units/side
Constipation	PEG 3350	14 mg 1–4 times daily
	Senokot	8.5–34 mg qhs
Orthostatic hypotension	Fludrocortisone	0.1 mg qam
	Midodrine	10 mg Morning, noon, dinner
	Droxidopa	100–600 mg daily
Urinary frequency	Pelvic floor exercises	
	Mirabegron	25–50 mg once daily
	Botulinum toxin injection	Refer to urologist
Pain	Range of motion exercises	
	Acetaminophen	250–300 mg tid
	Oxycodone/ naloxone	5/2.5 mg bid
	Botulinum toxin injection	Varies

The multitude of non-motor symptoms that require balance with motor symptom control represent the diffuse nervous system involvement in PD: impaired blood pressure control (supine hypertension and orthostatic hypotension), fatigue, daytime wakefulness, dementia, anxiety, depression, delusions, hallucinations, pain, constipation or bowel incontinence, urinary symptoms (frequency, nocturia, incontinence),

insomnia (both primary and secondary to other sleep disorders), REM sleep behavior disorder, restless legs, leg swelling, excessive sweating, dysphagia, weight loss (due to anorexia or dysphagia). A quick tool to assess these symptoms is the Non-motor symptoms questionnaire [22].

The incidence of dementia seems to be most strongly associated with the patient's age, rather than the duration of illness [23]. The challenges of dementia in PD, arising as Lewy Body Dementia (dementia onset prior to motor symptoms or within 1 year of motor symptoms) or PD dementia (any time after 1 year) include apathy, reduced autonomy, depression, anxiety and psychosis [24]. Other longitudinal studies found that dementia, psychosis and other non-motor symptoms such as orthostatic hypotension, urinary symptoms (nocturia or frequency to frank incontinence), constipation and pain are significant issues in advanced stages [7, 11, 25–27].

Symptom Burden, Needs Assessment and Triggers for Palliative Referral in PD

Symptom Burden in Parkinson's disease should be assessed at every visit. We recommend using the patient completed Edmonton Symptom Assessment System revised for Parkinson Disease (ESAS-PD) that adds Confusion, Constipation, Stiffness, Dysphagia to the traditional ESAS scale (Fig. 5.1) [28]. The ESAS-PD can be used even by very disabled patients or their family members, correlates with the Health Utility Index and is responsive to improvements in symptom burden associated with outpatient team-based palliative care [28, 29]. When used in the team-based ambulatory palliative care program for PD and related disorders ESAS-PD was 56/140 (indicating high symptom burden comparable to patients with metastatic cancer) at baseline and improved to 40/140 ($P < 0.0001$). Pain, tiredness, depression, anxiety, drowsiness, poor feeling of wellbeing, stiffness, constipation, dysphagia and confusion were the most frequently endorsed symptoms. Symptoms that responded most to interventions were dysphagia, constipation, anxiety, pain, and drowsiness.

The Needs Assessment Tool-PD has been used to assess palliative needs. Patient, caregiver and family members indicate whether there are potential or significant symptoms, psychiatric symptoms, problems with activities of daily living, existential distress, financial needs or health beliefs, cultural or social factors making care delivery complex [27]. This requires intimate knowledge of the patient and caregiver or a semi-structured interview and thus may not be feasible in busy ambulatory practices or private medical offices. Palliative care clinics for PD established at the University of Toronto and University of Alberta use the following general referral guidelines: (1) motor symptoms are less well controlled due to cognitive or neurobehavioral complications, (2) psychosis, (3) pain or (4) any other unresolved symptoms, (5) existential distress (6) caregiver burnout or concerns or (7) requiring coordination of care and community resources.

Managing Symptoms in Advanced PD

In approaching the overwhelming list of symptoms present in advanced PD, the patient's and family's values should be paramount. Neurologists may easily fall into the trap of attempting only to maximize motor function. We recommend a balanced approach presenting options and emphasizing available choices and trade-offs. As an example, for those with marked orthostatic hypotension, despite maximal therapy, reducing levodopa may improve blood pressure control with a possibility of reducing motor benefit.

Simplifying Medication for Motor Symptoms in Advanced Illness

One of the most challenging aspects of advanced PD is the balance between cognitive decline and control of motor symptoms since medications

Edmonton Symptom Assessment System Revised: Parkinson's Disease (ESAS-R: PD)

Please circle the number that best describes how you feel NOW:

No Pain	**0**	**1**	**2**	**3**	**4**	**5**	**6**	**7**	**8**	**9**	**10**	Worst Possible Pain
No Tiredness *(Tiredness = lack of energy)*	**0**	**1**	**2**	**3**	**4**	**5**	**6**	**7**	**8**	**9**	**10**	Worst Possible Tiredness
No Drowsiness *(Drowsiness = feeling sleepy)*	**0**	**1**	**2**	**3**	**4**	**5**	**6**	**7**	**8**	**9**	**10**	Worst Possible Drowsiness
No Nausea	**0**	**1**	**2**	**3**	**4**	**5**	**6**	**7**	**8**	**9**	**10**	Worst Possible Nausea
No Lack of Appetite	**0**	**1**	**2**	**3**	**4**	**5**	**6**	**7**	**8**	**9**	**10**	Worst Possible Lack of Appetite
No Shortness of Breath	**0**	**1**	**2**	**3**	**4**	**5**	**6**	**7**	**8**	**9**	**10**	Worst Possible Shortness of Breath
No Depression *(Depression = feeling sad)*	**0**	**1**	**2**	**3**	**4**	**5**	**6**	**7**	**8**	**9**	**10**	Worst Possible Depression
No Anxiety *(Anxiety = feeling nervous)*	**0**	**1**	**2**	**3**	**4**	**5**	**6**	**7**	**8**	**9**	**10**	Worst Possible Anxiety
Best Wellbeing *(Wellbeing = how you feel overall)*	**0**	**1**	**2**	**3**	**4**	**5**	**6**	**7**	**8**	**9**	**10**	Worst Possible Wellbeing
No _____ Other Problem *(for example constipation)*	**0**	**1**	**2**	**3**	**4**	**5**	**6**	**7**	**8**	**9**	**10**	Worst possible _____

Patient's Name _____

Date _____ Time _____

Completed by (check one):
- □ Patient
- □ Family Caregiver
- □ Healthcare professional caregiver
- □ Caregiver assisted

Fig. 5.1 Edmonton symptom assessment system

Edmonton Symptom Assessment System Revised: Parkinson's Disease (ESAS-R: PD)

Please circle the number that best describes how you feel NOW:

No Stiffness	**0**	**1**	**2**	**3**	**4**	**5**	**6**	**7**	**8**	**9**	**10**	Worst Possible Stiffness
No Constipation	**0**	**1**	**2**	**3**	**4**	**5**	**6**	**7**	**8**	**9**	**10**	Worst Possible Constipation
No Swallowing Difficulties	**0**	**1**	**2**	**3**	**4**	**5**	**6**	**7**	**8**	**9**	**10**	Worst Possible Swallowing Difficulties
No Confusion	**0**	**1**	**2**	**3**	**4**	**5**	**6**	**7**	**8**	**9**	**10**	Worst Possible Confusion

Please mark on these pictures where it is that you hurt:

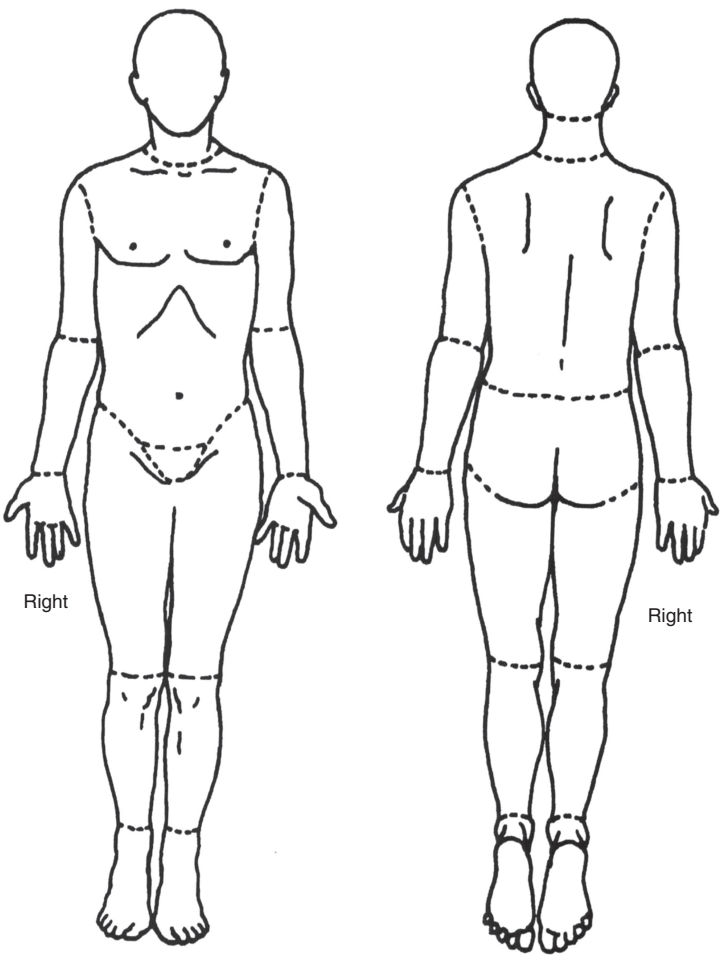

Fig. 5.1 (continued)

that treat motor symptoms may exacerbate cognitive and behavioural symptoms. In general principle, minimizing the complexity of the treatment regimen by eliminating PD meds other than levodopa will reduce the risk of cognitive side effects while maximizing motor benefit. Levodopa remains the most effective medication for the relief of motor symptoms with the least likelihood of inducing delirium/psychosis, impulse control disorder, hypomania, anxiety, orthostatic hypotension, nausea or vomiting [30]. Therefore, reducing other dopaminergic medications (e.g. dopamine agonists) very slowly and substituting an equivalent amount of levodopa is generally preferable in advanced stages. Rapid discontinuation of dopamine agonists may result in dopamine agonist withdrawal syndrome (DAWS) marked by dysphoria, fatigue, motor worsening and anxiety that may last months to 1 year [31]. Therefore, if patients are on maximal doses of dopamine agonists, expect to withdraw the medication (while simultaneously substituting levodopa) over 6 months or longer. In general, pramipexole 4.5 mg/day is approximately equivalent to 450 mg of levodopa, ropinirole 5 mg = 100 mg levodopa, rotigotine 3 mg = 100 mg levodopa. In withdrawing dopamine agonists, encouraging the patient and family with respect to the hoped for outcomes (improved blood pressure control, improved cognition, reduced impulsive behavior, reduced psychosis) is important since this is often an uncomfortable process and support from the spouse or family is crucial for successful discontinuation.

Reducing amantadine may also be necessary to improve cognition. Again, withdrawal of amantadine should be conducted slowly and may require use of liquid amantadine to further slow the discontinuation process to 50 mg per week or 25 mg per week as amantadine withdrawal psychosis is reported [32]. If patients remain on anticholinergic medications for tremor benefit, these too should be discontinued to improve cognition. Further, medications with significant anticholinergic profiles including antidepressants, sleep medication with diphenhydramine, or medications for urinary function should be discontinued if possible prior to considering specific treatment for dementia.

Dementia

If dementia is significant and concerning to the patient and family, cholinesterase inhibitors may be employed [33–35]. While donepezil, galantamine and rivastigmine have been studied in PD dementia and are commonly used, evidence is most consistent for rivastigmine and this is the only medication approved for use in PD dementia in the US [33, 35]. Patients and families should be counseled that cholinesterase inhibitors may benefit cognition, but will not stop the process of cognitive decline. Further, patients may experience worsening of motor symptoms. In particular, tremor may increase or become bothersome and was the commonest cause for discontinuation of rivastigmine in a large study [35]. Memantine has also been studied in PD and demonstrated improvement as determined by the Clinical Global Impression of Change and prolongs survival [34]. This study followed 75 patients over 36 months (N = 42) and therefore, needs to be replicated in a larger cohort.

Psychosis

Psychosis (hallucinations and delusions) is common and disabling for patients occurring in up to 75% of individuals [35, 36]. Psychosis may result in dangerous behavior and breakdown of the family unit as delusional thoughts may include paranoia about theft, affairs or being involuntarily committed. Occurrence of psychosis is difficult to predict, but recognizing signs early is important as such thoughts and resulting behavior is a common cause of nursing home placement. Treatment of psychosis in PD includes ensuring that infection (urinary tract infection or pneumonia) is ruled out and treatable causes such as vitamin B12 deficiency and hypothyroidism are addressed. Medication lists, including nonprescription medications which may contain anticholinergics, and actual pill bottles should be

scrutinized and adherence to the medication schedule should be ensured. Use of cholinesterase inhibitors and memantine is reported to improve neuropsychiatric symptoms, but based on population studies and clinical experience, the benefits are mild. Antiparkinsonian medications should be simplified to reduce effects on cognition and maximize motor benefit as discussed above. If further reduction of levodopa results in unacceptable worsening of motor symptoms, then neuroleptic medications may be entertained. The only neuroleptics that do not worsen motor symptoms are quetiapine, clozaril and pimavanserin [35, 37]. Quetiapine has conflicting data surrounding efficacy, but does not require neutrophil monitoring and thus, has been preferentially used at doses of 12.5 mg up to 150 mg/day in divided doses. Clozaril may be used at 6.25 mg qhs up to 10–50 mg/day. Clozaril requires blood monitoring due to the risk of neutropenia and physicians should comply with regulations in their respective jurisdiction of practice. Pimavanserin is recently available for treatment of psychosis in PD at 40 mg/day but does have a 10% risk of worsening psychotic symptoms and was assessed in those with psychosis and no dementia [37]. Quetiapine, clozaril and pimavanserin require a baseline ECG for prolonged QTc risk prior to initiation. No other neuroleptic or atypical neuroleptic should be used in PD or related disorders without considerable discussion and monitoring for worsening of motor symptoms.

Sleep Disorders, Daytime Sleepiness and Fatigue

Sleep disorders including restless legs syndrome (RLS), obstructive sleep apnea (OSA) and rapid eye movement behaviour disorder (RBD) are common in PD and sleep studies should be considered, particularly if patients report nonrestorative sleep. It is important to note that obesity and neck size are often absent in PD patients with OSA. In RBD, patients will mumble, shout or be physically active during dreaming. This may result in injury to the patient or the bed-partner as the patient acts out often violent dreams. The treatment of REM sleep behavior disorder (RBD) can improve energy, night-time safety and quality of life. A review of treatments for RBD, melatonin 3–15 mg may be used but quetiapine was found to be superior [38]. Historically, clonazepam may be used cautiously as benzodiazepine medications are also associated with confusion and increased risk of falls in the elderly.

Excessive daytime sleepiness and fatigue are frequent problems and may worsen with cognitive decline. This is problematic for patients and families since there is less participation in social activities, diminished ability to exercise, and prolonged or incomplete meals. Practical suggestions are to minimize levodopa as sleepiness may occur 1 h after dosing; reducing and stopping dopamine agonists which are known to cause excessive daytime sleepiness; ensuring that blood pressure is maintained since orthostatic hypotension may cause cognitive fluctuations and daytime sleepiness or fatigue; and use of short naps (<60 min). Exercise during the day can be helpful and anecdotal evidence suggests that day light exposure may be helpful. A systematic review found insufficient evidence to support the use of caffeine to improve wakefulness although one study did demonstrate improvement of the Epworth Sleepiness Scale by 1 point and that doxepin, Yang-Xue-Qing-Nao (YXQN) granules or rivastigmine did not improve sleep quality [39]. However, a subsequent study found improved sleep with YXQN [40] and there is also some evidence supporting the use of methylphenidate for fatigue [41].

Dysautonomia

Constipation is a common problem that reduces efficacy of levodopa due to delayed gastric emptying, reduces appetite, increases abdominal bloating and may result in intestinal obstruction. Therefore, it is important to maintain an excellent bowel routine. Sufficient water intake, a healthy diet of vegetables and fruits and less dairy products can improve bowel function sufficiently in some patients without the need to resort to

medications. A systematic review found that polyethylene glycol was effective in the treatment of constipation in PD [42]. Polyethylene glycol may be used up to four times daily for severe constipation and may be used safely for prolonged periods of time. Senokot may be necessary to improve intestinal contraction for those with severe constipation not responding to polyethylene glycol. If constipation is severe (no bowel movement for 1 week or more), the use of magnesium citrate 150–300 mg followed by 250 ml of water should result in a bowel movement in approximately 30 min to 6 h and should only be used for short-term effect and in those with normal kidney function.

Orthostatic hypotension is defined as a postural drop of 20 mmHg systolic from lying to standing after 3 min of standing. Absolute hypotension is a systolic blood pressure less than 90 mmHg. Orthostatic hypotension occurs in 30% of PD patients [42]. Adequate hydration is important in treatment and may be challenging due to concomitant urinary frequency, urgency and incontinence. Reducing and stopping dopamine agonists may improve blood pressure control. Reducing and stopping antihypertensives becomes important in maintaining a safe blood pressure to allow sitting, standing and walking in those who had hypertension prior to the diagnosis of PD. However, frequently PD patients will have early supine hypertension resulting in vigorous antihypertensive medication initiation. The key is monitoring orthostatic blood pressure to ensure that patients are safe to stand and walk. There is insufficient evidence to recommend the use of fludrocortisone for orthostatic hypotension in PD although the mechanism of action is plausible and historically, it has been used to treat orthostatic hypotension [42]. Potassium monitoring is required since fludrocortisone may cause hypokalemia. Midodrine 2.5 mg starting first thing in the morning and 1 h prior to lunch up to 15 mg three times a day (1 h prior to each meal and no later than 6 pm) can be used [42]. Droxidopa is a norepinephrine prodrug for use in primary autonomic failure from PD, Multiple System Atrophy and pure autonomic failure [43]. Droxidopa is taken three times a day in doses from 100 to 600 mg. Pressure stockings need to fit up to the axilla in order to be sufficiently effective and given problems with manual dexterity and urinary frequency is impractical for patients.

Urinary symptoms are frequent in PD. Conservative management by restricting fluids after 6 pm, ensuring that daytime blood pressure is sufficiently high to avoid orthostatic hypotension (which results in nocturnal diuresis), and bladder training (going to the bathroom on a schedule) can be helpful. A study of pelvic floor exercises (Kegl maneuver) was effective in the treatment of urinary urgency [42]. Anticholinergic medications should be avoided since urinary retention may occur in some patients and confusion/delirium/psychosis may occur in others. Mirabegron is a β3 adrenergic agonist that helps nocturia and urinary urgency and may raise blood pressure as a welcome side effect for PD patients [44]. Alternatively, urinary retention may also occur in PD [44, 45]. Ensure that medications (anticholinergics or drugs with anticholinergic properties) are not causing urinary retention. Referral to a urologist or multidisciplinary incontinence clinic may be helpful and patients may require intermittent or permanent urinary catheterization. Detrusor-sphincter dyssynergia may also occur in PD. Botulinum toxin injections by a urologist after confirmation of the diagnosis with urodynamics can be helpful [44].

Dysphagia and Sialorrhea

Dysphagia is often problematic and may respond to simple, step-wise interventions. General instructions include: do not eat while watching the television or any other distractions including talking while eating. Put your fork down in between mouthfuls. Chew thoroughly and then take a small sip of water to help swallow. Impulsive eating (shovelling food quickly before being able to swallow) is common in PD. Putting down the fork can be helpful. Also, when patients cough with drinking or eating, this is a sign of probable aspiration. With progression of dysphagia, avoiding dry bread, nuts and putting sauces on food can aid in swallow safety. Eventually

mincing or pureeing food becomes necessary. Bedside assessment of swallowing in PD is inadequate as patients typically have silent aspiration even when this is not evident at the bedside [46]. A Cochrane review of percutaneous gastrostomy tube feeding did not find improved wound healing or survival for those with dementia [47]. Whether this holds true for PD without dementia is unclear.

Sialorrhea is common in PD and is most often due to impaired swallowing, but in some individuals may also be due to over production of saliva in addition to abnormal posture [42, 48, 49]. Treatment of sialorrhea is complicated since ability to lubricate food is often impaired as well hence limiting the use of approaches that only dry the mouth. Using sugar-free candies, chewing gum can be effective if symptoms are mild to remind the patient to swallow. Atropine drops under the tongue and botulinum toxin injections have been used to treat sialorrhea [46, 49].

Pain

Pain is under-recognized in PD. Pain may have several sources including rigidity, contractures, painful dystonia and central pain. Musculoskeletal pain from arthritis or immobility is also common. Attempting to optimize medical treatment of PD is the mainstay of addressing pain. Thus, it follows that discontinuation of levodopa is not advised if at all possible. A study of botulinum toxin for dystonia and pain in 160 patients treated with PD and related disorder, 50.6% reported pain as a predominant symptom. Eighty-one percent reported significant reduction in pain with injections that was maintained over many years [48]. A combination of low dose oxycodone with naloxone (5/2.5 mg bid) was studied in 16 PD patients with pain over 8 weeks and found effective using the Clinical Global Impression of Change with no significant changes in sleep or bowel function [50]. Central pain (not related to PD) may possibly be relieved by oral cannabis extract and tetrahydrocannabinal but the effects on cognition are not known [51].

Withdrawing Levodopa

Withdrawal of levodopa should only be done with extreme caution, very slowly and with a clear discussion about goals of care with the patient and family. There is evidence that even delaying levodopa more than 30 min may be sufficient to cause delirium in very sensitive patients [52]. There is no role for abrupt withholding or discontinuation of levodopa as this may result in neuroleptic-malignant syndrome (also called parkinsonism hyperpyrexia syndrome in this setting) and death. Withholding levodopa to "see where the patient is" or whether dementia or delirium will clear is not appropriate and in fact, may result in worsening delirium and has on occasion resulted in death [53–59]. The concept of the drug holiday has largely been abandoned given these risks and as the purported benefits of a drug holiday were reduced dyskinesias, which upon longer follow-up, inevitably return. Levodopa doses should only be reduced slowly and with careful monitoring.

While abrupt cessation of medication without a conscious goal is never appropriate, reducing and stopping dopamine agonists (extremely slowly to avoid dopamine agonist withdrawal syndrome) may improve cognitive status [11]. In very advanced stages with refractory behavior changes (violent or threatening behavior), reducing levodopa slowly may improve agitation and behavior. Depending on the dose of medication, reductions may take place over weeks to months. Every change in levodopa requires approximately 2 weeks to become steady state. It is common that patients nearing end-of-life or hospice may have levodopa dose may lowered potentially due to weight loss or diminished benefits from medications [22].

Caregiver Burden

PD patients often survive for decades with progressive decline in motor and frequently cognitive function. Spouses are often the same age and have their own health issues. Providing physical care in the face of neurobehavioral complications

such as depression, anxiety and psychosis can be challenging, if not impossible, without outside, professional, paid assistance. Multiple studies document caregiver burden associated with PD [30, 37, 60]. Strain occurs from reduced social interactions since the PD patient needs constant supervision in the advanced stage and maneuvering a wheelchair is complex and straining. Caregivers also report feeling as if the person with PD relies on them too much, yet feeling simultaneously that they should be doing more and uncertain that they are "doing it right" [61].

Improving sleep for the person with PD and bladder function to reduce nocturia can allow the caregiver to sleep well and thus improve resilience. Identifying psychosis and improving cognition and resolving psychotic symptoms can improve strain. Enrolment in adult day programs sensitive to the needs of those with cognitive and physical challenges improves socialization for the PD person and respite for the caregiver. Encouraging the person with PD and their caregiver to broaden their social network and accept help in moderate stages can set the stage for better support in advanced stages. Engaging adult children in care is also important where possible. Finally, considering hospice enrolment for those with a life expectancy of 6 months or less can provide many in home services and access to a hospice palliative care provider to address unmet needs [62, 63] (see Chap. 20 "Caregiver Assessment and Support").

Education and Research Agenda

Palliative care education should include PD and related disorders as this patient population is increasing. The treatment of advanced symptoms is complex and requires understanding of disease trajectory in addition to specific treatment of symptoms. In addition, neurology and movement disorders training should address the impact of these disorders on mortality incorporate palliative care principles and specific approaches to PD and related disorders in advanced stages.

Palliative care research concerning PD should address: (1) Appropriate triggers and needs assessment tools for referral to specialist palliative care; (2) Palliative care interventions for improving the quality of life of the patient and caregiver; (3) The economic impact of palliative care interventions from both a patient and health system perspective; (4) Clinical trials to improve our evidence base of effective therapies for complex nonmotor symptoms; and (5) Interventions focused on end-of-life care and advanced PD.

Take Home Messages

- PD and related disorders are associated with increased morbidity and mortality compared to age-matched controls.
- Weight loss, accelerated decline in function, dementia and diminishing benefit of medications may indicate a time to consider hospice.
- Nonmotor symptoms including pain, depression, dementia, psychosis, fatigue and autonomic dysfunction contribute substantially to quality of life and can benefit from intensive management.
- Levodopa and dopamine agonists may need to be reduced as the disease progresses due to diminished benefit to side effect ratio but should never be abruptly stopped.

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Dementia

6

Thomas V. Caprio and Nicole Kosier

Case

Mrs. Sebor is an 81 year old woman with Alzheimer's Dementia who until recently resided in an assisted living facility. She was diagnosed with Alzheimer's seven years ago. At that time, she was still living in the community with help from her children. Over time, she had increasing difficulty maintaining the home, preparing meals, and often forgot her medications, at which point she transitioned to an assisted living community. Over the next 2 years, her disease slowly advanced with bladder incontinence and difficulty ambulating. Two weeks ago, she was hospitalized for pneumonia, after which it became clear she needed more support and she was transitioned to a nursing home. She continues to struggle with progressive difficulty in swallowing, even with hand feeding, and has been losing weight; her family asks about a feeding tube. Mrs. Sebor is also becoming increasingly confused and agitated at night, resulting in several falls. She has been aggressive and combative with care and was recently started on quetiapine as needed for this agitation behavior. Her family wants to know what stage of dementia their loved one is at and what her prognosis is. They ask when hospice would be appropriate and if anything more can be done for her confusion and agitation.

Dementia is an umbrella term encompassing many distinct syndromes and diseases associated with cognitive and functional impairment. These syndromes can be static, as is the case with traumatic brain injury, progressive like Alzheimer's disease (AD), or potentially reversible, as may occur with vitamin B12 deficiency. Progressive dementia syndromes, which is the focus of this chapter, can be caused by primary neurodegenerative conditions, such as AD and related dementias, or secondary to other neurologic conditions, such as multiple sclerosis. This decline in cognitive function occurs over one or more domains of cognition, most commonly memory, but also executive function, language and visuospatial abilities [1]. All of the progressive

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neurodegenerative conditions lead to functional dependence, debility, progressive symptom burden, and ultimately death.

Dementia is quite common with global estimates suggesting that 35.6 million adults suffer from dementia, a number which is expected to double by 2030 [2]. In a prevalence study of adults 71 and older in the United States, 13.9% had dementia with Alzheimer's disease accounting for 70% of cases [3]. All told, one out of every three older adults will die from or with dementia [4]. This also represents a major burden on the healthcare system. While some are able to live at home with most care provided by family and friends, many need additional support. More than half of all nursing home residents have dementia, and 2/3 of patients who die of dementia do so in a nursing home. Aggregate healthcare cost for those with dementia is estimated at 226 billion in 2017. Most of these costs are paid for by Medicare and Medicaid, but significant out of pocket costs are also incurred [5].

Common Types of Dementia

AD remains the most common dementia, accounting for an estimated 60–80% of all cases [6–8] and is currently estimated to affect 5.3 million Americans [9]. The incidence rapidly increases with age. While one in ten people over the age 65 have the disease, one in three over the age of 85 are afflicted [9]. With 93,541 deaths in 2014, AD ranks as the 6th overall cause of death in the United States [10]. It is marked by prominent difficulty with memory, particularly short term memory, and the processing of new information [11]. Cognitive decline tends to begin later in life, in the seventh decade and beyond, and progresses slowly over the course of years to more significant impairment in all areas of cognition. The time course varies by age at symptom onset but tends to lead to death within 3–10 years [12–14].

Vascular dementia occurs as a result of clinical or subclinical ischemia in the setting of cerebrovascular disease. It shares the same risk factors for cardiovascular disease including hypertension, diabetes, and hypercholesterolemia. Vascular dementia can be secondary to large vessel strokes or pervasive small vessel damage, and accounts for an estimated 10–20% of all dementias, but frequently contributes to other dementia subtypes, creating a mixed pattern of pathology [6, 7, 15]. Patterns of cognitive loss tend to associate with the area of damage and often occur with focal neurologic deficits, particularly with larger vessel involvement. Small vessel disease often presents with memory retrieval deficits, slowed information processing, and subtle neuropsychiatric changes and executive dysfunction [15]. Vascular dementia has been described as having a "step-wise" pattern of cognitive and functional loss as opposed to the slow and progressive nature of AD. This step-wise pattern has periods of steep decline followed by more quiescent periods in which cognitive function may plateau, followed again by an acute worsening in function, presumably due to new areas of evolving ischemia. Vascular dementia may have a shorter overall survival, generally 3–5 years, with death often occurring due to underlying cardiovascular disease [14, 15].

Dementia with Lewy bodies (DLB) is estimated to account for 5–20% of cases, but estimates vary greatly between studies and some experts assert the prevalence may actually be much higher and under recognized [16, 17]. It should be suspected in patients with prominent visual hallucinations, especially if it is early in the disease course and out of proportion to other cognitive deficits. Parkinsonism and fluctuating levels of attention and alertness, similar to that seen in delirium are also hallmarks of the disease. Phenotypically similar, Parkinson's disease dementia (PDD) is defined by cognitive deficits which begin to evolve at least 1 year after onset of the typical motor symptoms of Parkinson's disease. Both DLB and PDD also tend to have prominent psychiatric disturbance, sleep disorders, autonomic instability, and marked sensitivity to antipsychotics in terms of motor side effects (see Chap. 5 "Parkinson's Disease and Related Disorders") [18]. DLB tends to have more rapid cognitive decline and shorter time from diagnosis

to death than AD, with average survival from symptom onset of DLB being 5–7 years [16].

Frontotemporal dementia (FTD), which is the underlying etiology of 5–10% of cases results in prominent decline in executive function and language abilities, usually beginning at a younger age than other dementia syndromes [6]. The prevalence is higher in those with early onset dementia and approximately 60% of cases of FTD occur between the ages of 45 and 64 [19]. This most often manifests as behavioral issues, loss of social graces, and personality changes in patients with relatively intact memory. This can often delay diagnosis as it may be initially misdiagnosed as a primary psychiatric disorder. Other forms of FTD include primary progressive aphasia and semantic dementia, which are defined by gradually progressive expressive or receptive aphasia, respectively. Survival varies by subtype, but is generally 6–10 years after symptom onset [19].

The common dementias have distinct early stages, which facilitates clinical diagnosis, and may provide helpful insight into expected progression and prognosis. As disease progresses into more moderate and severe phases, resulting in significant functional and cognitive debility, the clinical distinction is less, and determining the underlying cause becomes difficult. At autopsy there are often mixed patterns of disease with multiple underlying pathologic patterns of disease present, with concomitant AD and vascular dementia being particularly common [7].

Alzheimer's Disease Phenotype: Early Stages

The early stages of AD are marked by changes in memory and this remains the most frequent presenting symptom (Table 6.1). This usually begins with subtle difficulty with short-term memory and retaining of newly learned information, which often begins months or years prior to formal diagnosis. At this point, many patients are able to compensate for these cognitive deficits with the use of reminders or aides and these deficits are often attributed to normal aging. During this phase, patients often begin to have noticeable deficits in other cognitive domains as well as changes in mood and personality, which often manifests as social withdrawal, apathy, or loss of interest, often times appearing very much like depressive type symptoms.

These changes generally become evident to others as the patient begins to have difficulty with more challenging tasks, such as failure to maintain work performance and difficulty with complex tasks and instrumental activities of daily living (e.g. managing finances, cooking, and med-

Table 6.1 Dementia stages

	Mild	Moderate	Severe
Cognitive	Short term memory loss- difficulty learning new information, trouble remembering names, misplacing objects	Disorientation, development of cognitive decline in other domains; visuospatial ability, executive function, verbal abilities	Significant impairment in most or all domains of cognition, decreased verbal fluency, long term memory loss
Functional	Impaired performance of complex tasks (IADLS[a]) -work, finances, event planning	Requiring assistance with some daily tasks (ADLS[b])- picking out clothing, taking medications	Impaired mobility and require significant assistance with all ADLS[b] (feeding, dressing, bathing).
Mood/ behavioral	Apathy, social withdrawal	Disinhibition, poor judgment, agitation, wandering, hallucinations, delusions	Variable- may continue to have behavioral disturbances, but may fade away with time

Domains of cognition: memory, visuospatial, executive function, attention/concentration, verbal abilities
[a]IADLs (instrumental activities of daily living): needed for successful independent living, Examples include money management, food preparation, transportation, shopping, and medication management
[b]ADLs (activities of daily living): fundamental for caring for one's self. Examples include eating, toileting, grooming, bathing, dressing

ication management). At this point, long-term memory and verbal fluency are generally intact.

Alzheimer's Disease Phenotype: Advanced Stages

As the disease advances, everyday tasks (basic activities of daily living) become increasingly difficult and patients may require assistance with bathing, dressing, and eating. Incontinence and failure to maintain personal hygiene are also common. Declines also begin to occur in language abilities; maintaining a conversation is difficult. By now, the symptoms are generally obvious even to casual acquaintances. Throughout this process, memory continues to decline and long-term memory may begin to erode. Mobility decreases, falling is common, and parkisonism may arise as the dependence on others for basic care increases. In the final stages, sufferers are bed bound, unable to communicate verbally, and are totally dependent on others for all care needs. At this stage patients may need to be hand-fed to maintain oral intake.

Throughout the course of disease, but especially common in later stages, are changes in personality and behavioral patterns. These behavioral and psychological symptoms of dementia (BPSD) are challenging to treat and frequently a source of distress for caregivers. Early changes of loss of interest and depressed mood often give way to angry outbursts, restlessness, and frank agitation. As long as mobility is maintained, wandering is a potential issue, especially for those still living in the home. Sexual disinhibition combines with poor judgment and impulsivity, often leading to social situations that are distressing to caregivers and families. Insight, both to the cognitive decline and personality changes is generally minimal, especially in later stages.

Estimating Prognosis

Trajectories of Death

The timeline and trajectory of functional decline and, ultimately death, generally occurs over many years (See Chap. 1 "Neuropalliative Care: Introduction", *illness trajectories*). The pervasive pattern is that of gradual and inexorable decline in function punctuated by periods of rapid deterioration. These rapid declines may occur as part of the primary disease process (new infarcts in vascular dementia), or secondary to other acute events, such as a hospitalization for hip fracture or pneumonia. Function after these acute declines may recover slightly but generally does not reach prior baseline, and may not occur at all. Dementia in general tends to follow a less predictable course than other terminal conditions, such as malignancy, with some prolonged phases of very gradual decline, or plateauing of function, which may confer a longer life span than expected. Conversely, acute illnesses and hospitalizations often trigger a downward spiral of functional decline, leading to death in a much quicker fashion than would be predicted from stage of dementia and baseline function alone. To further complicate matters, prognosis may be altered by treatment decisions and care planning, depending on a family's goals of care. While some aggressive interventions, such as feeding tube placement, have not been shown to extend life [20], other interventions may impact survival such as the decision to not treat pneumonia with antibiotic agents [21].

Prognostication

In the final stages of all dementia, most afflicted are completely dependent and bedbound. With diminished appetite and difficulty feeding, malnutrition sets in. This is often accompanied by the development of skin breakdown and chronic wound formation. Common recurrent infections are urinary tract infections, wound infections, and pneumonia; aspiration is particularly common and often ultimately leads to death. Multiple staging systems and criterion exist to help identify those patients at high risk of mortality and disease related complications, as well to assist with timely referral to hospice services.

The Functional Assessment Staging (FAST) (Table 6.2) is a seven-stage framework for standardizing the categorization of the stage of

Table 6.2 Functional assessment staging (FAST)

Stage	Assessment
1	No difficulties, either subjectively or objectively
2	Complains of forgetting location of objects; subjective work difficulties
3	Decreased job function evident to coworkers; difficulty in traveling to new locations. Decreased organizational capacity[a]
4	Decreased ability to perform complex tasks (e.g., planning dinner for guests), handling personal finances (such as forgetting to pay bills), difficulty marketing, etc.
5	Requires assistance in choosing proper clothing to wear for the day, season, or occasion, e.g. patient may wear the same clothing repeatedly unless supervised[a]
6	6a – Improperly putting on clothes without assistance or cuing (e.g. may put street clothes on overnight clothes, or put shoes on wrong feet, or have difficulty buttoning clothing) occasionally or more frequently over the past weeks[a]
	6b – Unable to bathe (shower) properly (e.g., difficulty adjusting bath-water temperature) occasionally or more frequently over the past weeks[a]
	6c – Inability to handle mechanics of toileting (e.g., forgets to flush the toilet, does not wipe properly or properly dispose of toilet tissue) occasionally or more frequently over the past weeks[a]
	6d – Urinary incontinence (occasional or more frequently over the past weeks)[a]
	6e – Fecal incontinence (occasional or more frequently over the past week)[a]
7	7a – Ability to speak limited to approximately a half dozen intelligible different words or fewer, in the course of an average day or in the course of an intensive interview
	7b – Speech ability limited to the use of a single intelligible word in an average day or in the course of an interview (the person may repeat the word over and over)
	7c – Ambulatory ability lost (cannot walk without personal assistance)
	7d – Cannot sit up without assistance (e.g., the individual will fall over if there are no lateral rests [arms] on the chair)
	7e – Loss of the ability to smile
	7f – Loss of ability to hold head up independently

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FAST Scoring: The FAST stage is the highest consecutive level of disability. For clinical purposes, in addition to staging the level of disability, additional, non-ordinal (nonconsecutive) deficits should be noted, since these additional deficits are of clinical relevance
[a]Scored primarily on the basis of information obtained from knowledgeable informant

dementia for an individual, and is often used in the determination for hospice eligibility (See Chap. 16 "Hospice and End of Life Care in Neurologic Disease") [22]. It focuses more on an individual's level of functioning and activities of daily living versus cognitive decline. The progression of functional and cognitive impairment in this staging model is primarily based on AD, but the staging also is used in other dementia subtypes, particularly in the late stages of disease. FAST scale 7 and subsequent substages (7A-7F) represent severe dementia, characterized by urinary and fecal incontinence, limited or no intelligible speech, inability to walk (or even to sit up unsupported in later phases), and ultimately inability to smile or hold up head.

Once this degree of debility exists, the prognosis is quite poor. In an 18-month longitudinal study of nursing home residents with advanced dementia, 25% of residents had died within 6 months, with a median survival of 1.3 years. Disease-related complications also became common; in the same study, the majority of patients developed nutritional problems and nearly half developed pneumonia or febrile episodes. Once these complications developed, 6-month mortality substantially increased, to nearly 50% [23].

Under the current Medicare guidelines, patients are eligible for hospice services when they have signs of both severe functional impairment (FAST stage 7) as well as disease-related complications including aspiration pneumonia, sepsis, multiple advanced stage (stage III/IV) pressure ulcers, recurrent fevers, or significant malnutrition and weight loss. There is evidence that the current guidelines are relativity poor at accurately predicting 6-month mortality, which may contribute to under referral to hospice

services [24]. Other scoring systems can also be useful in predicting mortality and guiding hospice referral. Based on patient demographics in conjunction with functional status, presence of disease-related complications, and serious medical comorbidity, the ADEPT criterion were developed to help better guide prognostication for nursing home residents with dementia [25]. This has demonstrated improved, albeit modest accuracy in prognostication and can also be used to guide hospice referral [24].

The Palliative Care Approach Across Dementia Stages

Being a progressive and terminal disease, without effective disease-modifying treatments available, it is important to recognize the need for ongoing symptom management and support, as well as the transition ultimately towards end-of-life care. Early palliative care intervention, whether it be through a specialist or primary provider, is essential in high quality care for both the patient and family. The ideal palliative care services for these patients encompass a multifaceted approach; anticipating care needs and exploring goals of care, identifying and managing symptoms, and providing support to the patient and their family and caregivers. While a palliative care approach is certainly helpful throughout the course of the disease, symptom burden tends to increase with progressive decline and each major decrement in cognition or function should trigger revisiting of all the critical components of palliative care. The nature of dementia, with both functional and cognitive decline, presents unique challenges at all of these stages as the patient's needs are changing. Table 6.3 provides triggers for serious conversation in dementia based on disease stage.

Table 6.3 Triggers for serious conversations in dementia

Stage/trigger	Palliative care interventions
Mild (early) dementia Time of diagnosis with early memory loss New behavioral symptoms such as sadness, boredom, withdrawal	Advance directives/goals of care Health Care Proxy/Power of Attorney Treatment of depression Consider medications for cognitive symptoms Caregiver assessment/ support
Moderate dementia New or increasing agitation (agitation, violence, wandering, disinhibition) Increased dependency in dressing, bathing, meals, and mobility	Screen for and treat BPSD[a] Safety evaluation (screening for abuse, driving concerns, managing finances) Caregiver support and referral to community services Assess care needs and setting (home, assisted living, nursing home)
Severe (advanced) dementia Incontinence Decreased ability to ambulate, frequent falls Decreased ability to have a conversation Choking, dysphagia Pneumonia Weight loss Hospitalizations	Symptom management (BPSD, pain, skin integrity) Reassess goals of care and therapeutic interventions (including future hospitalizations) De-prescribing medications of limited benefit or those with high burden/risk Consider hospice referral

[a]*BPSD* Behavioral and psychological symptoms of dementia

Mild Dementia

As significant cognitive changes begin in mild dementia, advance care planning should be addressed promptly. It is critical to have open discussion regarding anticipated decline and lack of curative therapy when the patient's own decision-making is intact. Basic questions to establish who they trust most to manage their finances or to make medical decisions also function to identify critical caregivers and partners in care. This is the ideal time to open goals of care discussion. Establishing an advance directive that is in line with the patient goals while they are able to participate offloads burden from family and helps to avoid unwanted medical interventions down the line. Encouraging early involvement of surrogate decision makers in this discussion is also crucial. While a patient with dementia may want aggressive medical treatment early in the course of their disease, many wish to forgo life prolonging measures in the advanced stages [26], at a time they will depend on others, usually family or caregivers, to voice those wishes. Given the estimated

prognosis of 3–10 years from diagnosis (based on dementia type, age, and comorbidities) it is also appropriate to discuss cessation of medical interventions requiring a prolonged time horizon to benefit, such as screening mammography and colonoscopy [27].

Moderate Dementia

The progression from mild to moderate dementia (FAST scale 5–6) is characterized by increasing care needs, development of new symptoms, particularly behavioral and psychological symptoms of dementia (BPSD), and more difficulty with decision-making (often leading to both loss of medical decision making capacity and safety concerns). Patients and their families should be carefully screened for difficulty in all of these areas.

Directly inquiring about behavioral and psychological symptoms, particularly wandering, agitation, mood changes, and aggression, can guide further evaluation and treatment. If not already done, progressive cognitive decline can also trigger evaluation for trial of pharmacologic therapy, such as an acetylcholinesterase inhibitor. Similarly, if not addressed previously, advance care planning and goals of care should be explored as the patient is still likely able to provide some guidance and input into their wishes, even if they are unable to fully understand the terminal nature of their disease.

Safety becomes a paramount concern as disease progresses, and counseling patients and caregivers in an attempt to maintain maximal safe level of independence is key. While many patients with mild dementia continue to drive safely, as the disease progresses driving ability becomes significantly impaired, with lower scores on road-testing and more motor vehicle collisions. Patients with dementia are also more likely to continue driving despite prior accidents [28]. Clinicians should directly inquire about accidents, or near accidents, and discuss safety concerns with family and caregivers. If there remains a question regarding driving safety, or if the patient is hesitant to stop driving, it can be helpful to refer them to a local resource for a formal driving evaluation. Clinician reporting of suspected unsafe driving practices varies by state and should be reviewed through the state department of motor vehicles.

Older adults with dementia are also at elevated risk of abuse; psychological, physical, financial, and neglect, with psychological abuse and financial exploitation being the most common [29, 30]. Most perpetrators are caregivers, either an adult child or spouse, which may impact self-reporting but patient physical, verbal or sexual abuse of their caregiver is not uncommon [30–32]. Multiple screening tools and questionnaires exist, but there is not an evidence-based consensus on a preferred screening method [33, 34]. Medical providers are morally obligated (and legally mandated in most states) to report suspected abuse. Information about local resources and contact information for Adult Protective Services can be found through the National Center for Elder Abuse.

As care needs and caregiver burden are increasing, the transition to moderate dementia should trigger referral to social work or local agencies if not already done earlier in the disease. This can help in identifying patients whose needs cannot be met in the current setting and who need more care in the home or a more supportive environment such as assisted living or nursing home placement. They can also function to connect patients and their families to local resources for both physical assistance and emotional support.

Severe (Advanced) Dementia

The transition to severe dementia (FAST scale 7) is characterized by markedly impaired cognition, functional dependence, as well as the development of disease-associated secondary complications, such as pneumonia and pressure ulcer development. Focus should continue on identifying and managing symptoms that are present, with particular emphasis on evaluation of pain as the ability to localize symptoms becomes severely impaired. Ongoing caregiver evaluation and support should also continue, as most patients with severe dementia require intensive 24-hour supervision.

As disease progresses and life expectancy becomes limited, how best to approach medical care to meet a patient's needs and goals shifts. While continuing attempts at life prolonging and preventive measures, such as a statin medications for hypercholesterolemia and bisphosphonates for osteoporosis, is reasonable initially, this should be revisited over time. As disease progresses, burdens of continuing treatments mount; patients are often more resistive to taking medications, frequently have concomitant dysphagia, have difficulty remembering to take medications, may take them incorrectly, and are more sensitive to side effects of polypharmacy. It is important at this point to revisit the time horizon for benefit for any therapeutic interventions, including the sum total of medications prescribed. A patient with severe dementia whose prognosis is months to 1–2 years are unlikely to benefit from medications requiring prolonged periods of time to see positive clinical outcomes. Given this, prime considerations for "de-prescribing" efforts in advanced dementia such as the lipid-lowering agents, antihypertensive, bisphosphonates, and acetylcholinesterase inhibitors. Nonetheless, prevalence of prescribing these medications near end of life remains high, nearly 50% in one study of Medicare beneficiaries [35].

Throughout the course of disease, revisiting goals of care is critical, shifting focus from prolonging life to maintaining quality of life and personal dignity is appropriate, especially in the terminal stages of disease. Those patients with severe functional impairment (FAST stage 7) and evidence of secondary complications related to their disease are eligible for hospice services.

Capacity Evaluation

The changes which begin in mild cognitive impairment, even prior to the development of frank clinical dementia impact the patient's ability to understand and process complex medical decisions, particularly if deficits in verbal fluency and executive function are present [36, 37]. While most patients with mild dementia retain decision-making capacity [38] as disease progresses this is lost, making the identification of a surrogate decision maker and establishment of advance directives early in the disease a clinical imperative. Capacity should be evaluated on initial diagnosis and also with progression of disease. Demonstrating capacity requires that a patient show understanding of the information they have been given, are able to apply that understanding to their own health, manipulate this in a logical fashion consistent with their values, and express a choice. This should be decision specific; while a patient may be able to name a health care agent more complex decisions such as forgoing hospitalization for acute illness may need to be made by a surrogate decision maker. Even when a patient does lack capacity they should be involved in discussions as much as is plausible and still may be able to provide insight into their values, hopefully taking some of decision-making burden off of their surrogate decision maker.

Symptom Assessment and Management

Cognitive Treatment

Symptoms can be challenging to assess in a patient with dementia and also difficult to target with safe, effective treatment. Effective symptom management is important throughout the spectrum of disease but becomes especially critical as patients enter the final stages of disease. Treatment of cognitive symptoms of disease is both complex and patient specific. While several pharmacologic treatment options for dementia exist, their efficacy is limited and true benefit is likely small for most patients. The first class of medications, acetylcholinesterase inhibitors (donepezil, rivastigmine, galantamine) are associated with small improvements in cognition and functional status for some patients. Unfortunately, this does not translate to demonstrable effects on disease progression, entry into the nursing home setting, or overall prognosis [39, 40]. There is no clear consensus as to how long to continue these medications and at what point to discontinue, but there is little evidence supporting the continuation of

these agents once disease is severely advanced. Side effects upon initiation of medications are common with acetylcholinesterase inhibitors (nausea or diarrhea), but longer-term side effects can be potentially life threatening such as bradycardia or complete heart block. For those with moderate to severe disease, memantine can also be used for treatment of cognitive symptoms. Similar to the acetylcholinesterase inhibitors, there is some small improvement in scores on testing of cognition and function, but the margin of benefit is small and may not be overly clinically significant [39]. In both cases, it is reasonable to reassess patients for cognitive improvement after a therapeutic trial, with taper and discontinuation if no significant clinical improvement is noted.

Whether or not a patient is started on pharmacologic treatment, ongoing non-pharmacologic management of cognitive symptoms is needed. Early in the disease course, reminders and notes may be helpful to allow patients to cope with cognitive deficits and declining memory. As the disease progresses, working with the patient and family (or care facility) to provide the highest level of independence without adding undo risk of harm is critical.

Dysphagia and Weight Loss

Particularly in advanced disease, weight loss and dysphagia become apparent. This is often distressing to family and caregivers; addressing this as an anticipated disease complication early on can be helpful in managing expectations going forward. The dysphagia that develops is not reversible; dietary consistency modifications help to some degree but do not prevent aspiration and often the change in texture may not be palatable to some patients and contributes to decreased nutritional intake at meals. Similarly, feeding tubes do not decrease or prevent aspiration pneumonia or pressure ulcers in advanced dementia and are not indicated for the treatment of dysphagia and weight loss in this setting [20, 41]. Progressive weight loss also occurs from a combination of dysphagia, functional decline, difficulty with feeding, and cognitive decline with decreased appetite and drive to eat. Careful hand feeding remains the standard treatment to maintain nutritional status and prevent aspiration for as long as possible. Oral nutritional supplements are also frequently recommended for caloric supplementation, and do lead to weight gain [42], although it is unclear what impact this has on clinical outcomes, such as prognosis or pressure ulcer formation.

Behavioral and Psychological Symptoms

Particularly early in the disease or soon following the diagnosis of dementia, a patient may experience grief, frustration, guilt, boredom, and other difficult mood or behavioral symptoms, which may be normal emotional reactions to a diagnosis of dementia. Depression and suicide risk screening as well as ongoing psychosocial support for the patient and caregiver are critical elements. Perhaps the most troubling type of symptom, particularly with moderate-severe dementia, is the behavioral and psychological symptoms of dementia (BPSD). These symptoms can be especially problematic for caregivers and can be a trigger for entry into long term care. BPSD will affect the vast majority of those with dementia at some point in their disease. The most common symptoms are apathy, depression, agitation, and wandering. While less common, frank psychosis with hallucinations and delusions, as well as violent or aggressive behavior, are especially problematic [43, 44].

The first step in evaluation of BPSD is screening for a source of distress. Often an unmet physical need: pain, hunger, thirst, the need to urinate or defecate, triggers behavioral symptoms as the patient is unable to make this known in any other way [45]. Psychological distress or the need for emotional connection can also be a trigger. A patient with a history of past trauma, such as physical or sexual abuse is likely to feel threatened with personal care and responds in the only way they can; with agitation and violence. Patterns of behavior tend to manifest over time and with careful observation and history, and

modifications to environment can often be sufficient to manage behavioral symptoms.

Clinical evaluation of patients with BPSD is also critical, particularly if this is a new or progressively worsening symptom. In addition to unmet physical or emotional needs, injury or acute illness is another common trigger. Pain is an especially important factor to evaluate for, but can be difficult to assess and localize in dementia. While self-report is considered the standard for pain assessment, many patients with dementia do not reliably report pain when compared to objective pain measurements [46]. For most patients, pain evaluation includes a history with screening questions for pain, as well as for recent falls, medical procedures, or changes in condition. For patients with moderate-severe dementia, direct observational tools should be employed to screen for pain. While no single gold standard test exists, multiple scales such as the PAINAD (Table 6.4), Abbey score, and the CNPI scoring system can be used [47]. While there have been very few high quality studies regarding the blanket use of analgesics in agitation, what evidence there is does support their use. In a study of nursing home residents the addition of analgesics in a stepwise approach, based on the American Geriatric Society guidelines (generally acetaminophen followed by a low dose opioid) resulted in significant decreases in pain scores, behavioral disturbances, and agitation, particularly verbal agitation [48, 49]. Most of these patients (70%) were treated with acetaminophen alone and did not require the addition of opioid agents to achieve this response. Once therapy has been initiated, close follow-up for improvement in behavioral symptoms and subjective or objective signs of pain is warranted.

Behavioral management and environmental modifications should always be the first line intervention when addressing troubling symptoms. When no medical trigger or other reversible cause is identified and non-pharmacologic interventions have failed, medical management of behavioral or psychological symptoms can be considered. Although the effect is modest, acetylcholinesterase inhibitors and memantine can be helpful in some cases to treat BPSD [50, 51]. Citalopram or sertraline have also been used to reduce agitation and treat BPSD [52] and should also be strongly considered, especially when underlying anxiety or depression is suspected. Trazodone has also been shown to increase nocturnal sleep time in patients with dementia and insomnia [53]. Other medications are often used but with less evidence, such as are mirtazapine and divalproic acid [53]. Benzodiazepines and anticholinergics should generally be avoided in the management of behavioral or psychological symptoms due to

Table 6.4 Pain assessment in advanced dementia (PAINAD)

Observation	0	1	2	Score
Breathing (Independent of vocalization)	Normal	Occasional labored breathing. Short period of hyperventilation	Noisy labored breathing. Long period of hyperventilation. Cheyne-Stokes respirations	
Negative vocalization	None	Occasional moan or groan. Low-level speech with a negative or disapproving quality	Repeated troubled calling out. Loud moaning or groaning. Crying	
Facial expression	Smiling, or inexpressive	Sad. Frightened. Frown	Facial grimacing	
Body language	Relaxed	Tense. Distressed pacing. Fidgeting	Rigid. Fists clenched. Knees pulled up. Pulling or pushing away. Striking out	
Consolability	No need to console	Distracted or reassured by voice or touch	Unable to console, distract or reassure	
Total:				

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PAINAD is a Five-item observational tool for pain assessment. Total scores range from 0 to 10 (based on a scale of 0 to 2 for each of the five items), with a higher score indicating more severe pain (0 = "no pain" to 10 = "severe pain")

their potential for precipitating delirium and worsening cognitive symptoms.

As antipsychotics have only modest efficacy in the treatment of agitation and aggression, and significant risk of adverse events, their use should be restricted to those with evidence of significant psychosis (often manifested by delusions or hallucinations) causing distress or danger to the patient or caregiver [54, 55]. The efficacy of antipsychotics even in the treatment of delirium has been called into question, with a recent study investigating their use in patients receiving palliative care services revealed no reduction in delirium severity or symptom burden [56]. These medications, both typical and atypical, should be initiated at low doses and to target a particular symptom, such as paranoid or persecutory delusions causing distress to the patient. They should be tapered and discontinued if there is no improvement, or the patient has remained stable for several months. Doses are typically much lower than for primary psychiatric disorders. Antipsychotics are associated with serious side effects and increased risk of death in patients with dementia, although their causal role in hastened death remains controversial. Important caveats include patients with underlying severe mental illness, such as schizophrenia or bipolar disorder with mania, for whom coordination with psychiatric providers is helpful.

DLB is associated with high rates of BPSD with psychotic symptoms, particularly visual hallucinations. It also confers high risk of severe neuroleptic sensitivity; parkinsonism, increased confusion, autonomic dysfunction, neuroleptic malignant syndrome, and even death. Most typical and atypical antipsychotics should be avoided in patients with a known or suspected history of DLB. For these patients, when possible, reduction of any psychoactive medications should be a first step for managing psychotic symptoms, starting by eliminating dopamine agonists, anticholinergics, and MAO-inhibitors. Then reducing or eliminating carbidopa/levodopa if the patient is receiving, especially considering that classically the motor symptoms related to DLB is less responsive to the dopaminergic medications compared to idiopathic Parkinson's disease. Quetiapine or clozapine are considered first line antipsychotics for patients with DLB, as they have a significantly lower antidopaminergic profile than other typical and atypical antipsychotics and may be used if symptoms are refractory to all other interventions or motor symptoms worsen with reductions in dopaminergic therapy. Pimavanserin is a newer serotonergic atypical antipsychotic that may also be considered in this population but has been associated with a worsening of psychotic symptoms in approximately 10% of patients and high mortality [57].

Caregiver Support

Dementia is also very distressing for family members and caregivers. Nearly half of the estimated 6.5 million Americans who are providing substantial assistance to an older adult are faced with caring for a loved one with dementia [58]. Caregivers often feel the burden of progressive cognitive and functional loss more than the patient themselves, which is associated with poor health outcomes for the caregiver (both psychological and physical) as well as early nursing home placement for the patient. Caregiver burden generally increases as disease progresses and is particularly high in patients experiencing the BPSD including wandering, agitation, or aggression [59]. Assessing caregiver burden is critical in providing good patient and family centered care.

Multiple screening tools exist to assess caregiver burden, including the Zarit Burden Interview and Caregiver Strain Index, which attempt to quantify the amount of financial strain, emotional distress, and the impact of caregiving on their social and family life [59–61]. During medical evaluations of the patient, questions targeting the hopes and fears of not only the patient, but also the caregiver are helpful. The progression from mild to moderate dementia is characterized by the loss of independence and an emergence of new symptoms. Care needs in this transition point also increase, so realistic expectations and frank discussion with family and caregivers is critical in identifying patients whose

needs cannot be met in the current setting and who need more care in the home or a more supportive environment such as assisted living or nursing home placement. Questions can be as specific and identify practical concerns for the future, such as: "How will you be able to care for your mother when she is no longer is able to use the toilet on her own?" "What if your father falls at home and is unable to contact anyone for help?" Providing anticipatory guidance for the future and encouraging proactive planning can allay caregiver anxiety and burden. An in-office social worker or outside referral to community resources, such as the Alzheimer's Association, can be extraordinarily helpful for patients and their families. These services can provide educational resources and help caregivers become connected with support groups, respite, or day care services. They can also help with assessment of the patient and their caregivers' financial situation and guidance for the future. Referral to home care and physical/occupational therapy can also help make environmental changes, such as the addition of a commode, which can foster safety and decrease burden of providing care. These steps to support caregivers are necessary to keep patients in the home as long as is feasible (see Chap. 20 "Caregiver Assessment and Support").

End-of-Life Care

Patients with dementia are frequently subjected to aggressive treatment at the end of life, with 40% being subjected to burdensome treatments, such as hospital evaluation or tube feeding in the last 3 months of life [23]. This can be mitigated by ongoing evaluation and referral to hospice for those with severe dementia and evidence of disease related complications. For those patients whose goals align with their philosophy, hospice provides the most robust support services to augment care and keep patients at home when possible. Whether end of life occurs in the home, a nursing home, or hospital, attention should be paid to identifying and treating underlying symptoms. As discussed above, pain should be evaluated and treated based on observational tools, not just patient or caregiver report. As pneumonia and cardiovascular disease are very common causes of death, dyspnea should be monitored and treated if bothersome to the patient, generally with opioids in addition to any appropriate adjuvant agents (such as diuretics in the treatment of congestive heart failure). Dehydration is also common, and may be the underlying cause of death, so attention to oral care with liberal use of oral lubricants is indicated. As opposed to earlier in the disease, in the imminently dying patient, it is reasonable to trial benzodiazepines for refractory anxiety or dyspnea, and anticholinergic agents, such as scopolamine, for secretions (see Chap. 16 "Hospice and End of Life Care in Neurologic Disease").

Education and Research Agenda

Given the extremely high prevalence of neurodegenerative dementias in older adults and the common occurrence of cognitive deficits and dementia due to other neurologic disorders (e.g. multiple sclerosis, stroke, glioblastoma) there is a great need for primary palliative care education in neurology to address the effects of dementia on symptom assessment, caregiver distress, goals of care discussions, advance care planning and end-of-life care. Fellowships in behavioral neurology, neuropsychiatry, geriatric medicine, and geriatric psychiatry should also plan to cover these issues in depth.

There is a pressing need for better tools to assist in prognostication in advanced dementia which could facilitate earlier hospice referral and be utilized to coordinate home, community, and specialty-based services to meet patient needs. More attention needs to focus upon the level of the patient and caregiver, to develop evidence-based interventions to decrease caregiver stress/burden and maintain and enhance care at home in order to avoid or delay the need for institutional based care. Improved pharmacologic options for BPSD would be helpful for management of distressing symptoms, however the nonpharmacologic interventions and identification of a patient's unmet needs will remain as a gold

standard for quality person-centered care. Given the considerable prevalence of these conditions, there is need for cost-effectiveness, implementation, dissemination and healthcare policy research to develop best practices for caring for patients with dementia and care coordination to ensure the best outcomes for these vulnerable patients. These approaches must consider workforce issues, as palliative care specialists, and even general neurologists, will not likely fill all the gaps in the current system.

Take Home Messages

- Alzheimer's disease and other dementias are leading causes of disability, institutionalization and death in older adults.
- Severe limitations of functional abilities, recurrent infections, weight loss and impaired mobility and communication abilities should suggest consideration for hospice referral.
- Safety must be assessed when developing plans of care including driving safety, wandering, falls, and potential for physical, verbal/emotional and financial abuse.
- Goals of care and advance care planning should be completed as early as feasible while patients have decision-making capacity and can meaningfully contribute to discussions regarding goals of care.
- For patients with behavioral issues, such as agitation, treatable causes (e.g. pain) and environmental triggers should be considered before utilizing pharmacologic treatments.

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Multiple Sclerosis

7

Ludo J. Vanopdenbosch and David J. Oliver

Case

Irene was 28 years old when her son Michael was born. In the peripartum period, she noticed a numb feeling in her left foot that eventually resolved. She was diagnosed with Multiple Sclerosis (MS) 2 years later, when she was hospitalized with optic neuritis. She started weekly intramuscular injections with interferon beta-1-a but was admitted twice more during the same year for high dose intravenous methylprednisolone because of generalized pain and urinary dysfunction. Over the next 15 years, Irene's course has been marked by relapsing-remitting progressive disease unresponsive to first-line therapies. She has become increasingly more disabled due to spastic gait and needs to self-catheterize her bladder due to urinary incontinence. She had to stop her work as a receptionist. She is now 43 and living at home with Michael, her 15-year-old son, and her husband who works full time.

Her neurologist has realized that her pain is not controlled by a variety of oral pain medications, and plans to talk to Irene about intrathecal baclofen at their next visit. When she shuffles into his office with her walker, he has 2 other concerns on his list to discuss with her that day: first, current immunomodulatory treatment seems to be no longer working and he is concerned that she has entered the phase of secondary progressive MS. Second, he is worried that Irene is not fully accepting of her disability and her need for more help at home.

Multiple sclerosis (MS) was well described clinico-pathologically over 150 years ago, but it remains unclear to this day what causes it. The current understanding is that of an interplay of a genetic and epigenetic background of susceptibility, with environmental triggers and protective factors [1]. In addition to an overactive immune system and autoimmunity, there is an insufficient activity of the innate anti-inflammatory system and also a deficiency of the macrophage cleanup system and the oligodendrocyte repair system [2, 3]. The prevalence of MS varies from 80 to 140/100,000 – with a higher prevalence in countries with higher latitude [1].

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Given its variable and often long course, the heterogeneity of symptoms, and the impact on both physical and cognitive function, the palliative care needs of patients and families are high [4]. While new neuro-immunomodulating treatments have dramatically changed the therapeutic landscape, patients with MS and their caregivers need access to both exceptional primary palliative care through a multidisciplinary team and access to specialist palliative care when complex situations arise. Communication with patients and families is both important and difficult, and clinicians caring for patients with MS should acquire additional skills regarding effective communication (see Chap. 11 "Communicating Effectively"). In addition to learning to support the caregiver (see Chap. 20 "Caregiver Assessment and Support"), there is also evidence that clinicians will need to support themselves to cope with the continual loss and increasing issues of patients with MS and their families. Clinician burnout and withdrawal may occur and ongoing supervision and support will allow these issues to be addressed and improved (see Chap. 19 "Clinician Self-Care").

Presentation and Disease Stages

The median onset for MS is 31 years with a male to female ratio of about 1:2 [1]. Common presentations include visual disturbances with optic neuritis or diplopia; difficulty walking with weakness or ataxia; dysuria and frequent bladder infections; sensory complaints with pain and numbness.

Three core phenotypes of MS are defined by their disease course:

- Relapsing-remitting MS (RRMS) accounts for 85% of patients and is characterized by clearly defined relapses with full recovery or with residual deficits. The intervals are variable but over time leave the patient with increasing disability.
- Secondary progressive MS (SPMS) is the chronic phase of RRMS with continuing gradual decline over decades without obvious exacerbations.
- About 15% of patients have primary progressive MS (PPMS) characterized by progressive accumulation of disability, often with long plateaux and gradual deterioration. Over half of patients with progressive MS have very slow progression and only mild handicap [5, 6].

This classification has been challenged recently and many MS specialists prefer a newly proposed clinical classification as relapsing (the patient experiences exacerbations) or progressive (the patient does not experience exacerbations) AND active (measurable disease activity either on MRI or clinically) or not active [7]. This classification is easier to use, as the older term of SPMS is a retrospective diagnosis which is not helpful in planning neuro-immunomodulating therapies.

Treatment and Multidisciplinary Team-Based Care

There are now treatments with proven efficacy on relapse rate and disease progression. In milder forms, injections with interferon-beta or glatiramer acetate have been used for decades. Side effects include flu-like symptoms, diarrhea, hair loss, flushing in up to 50% of patients. Oral therapies with dimethyl fumarate and teriflunomide are replacing these injections. More active MS is treated with alemtuzumab, ocrelizumab, natalizumab, cladribine and fingolimod, with known and manageable treatment related risks. Readers wanting a more detailed review of currently used MS treatments may find the review by Trojano helpful [8]. The use of neuro-immunomodulatory therapy has advanced considerably in the last decade with an increasing proportion of patients treated meeting the definition of No Evident Disease Activity (NEDA) over several years: no relapses, no change in handicap score, and no change in MRI lesion load [9].

Given the wide variability in disease trajectories and the wide range of needs for patients with

MS and their families including physical, psychosocial and spiritual needs, a multidisciplinary approach to their care is very helpful, with a team including a social worker, psychologist, neurologist, nurse, administrator, and therapists [10]. A recent study using a clinic based multidisciplinary team for patients with amyotrophic lateral sclerosis suggested not only improved quality of life but also increased survival compared to historical controls [11]. A similar effect of a multidisciplinary approach to MS care is likely.

Palliative care is increasingly seen as a needs based approach, responding to the specific needs of each patient and their family [4]. The involvement of palliative care specialist services typically varies by patient, by trajectory, by needs and over time [12]. Therefore, close collaboration and co-operation of neurological, rehabilitation and palliative care services is recommended to provide the most appropriate care for patient and family and support all involved, including the professional caregivers as suggested in Fig. 7.1 [13].

Prognosis

Patients with multiple sclerosis live on average over 40 years after diagnosis. Their life expectancy compared to the general population is reduced by 7 years and the life expectancy of someone with primary progressive MS is 7 years less than patients with relapsing disease [14]. Approximately half of patients with MS who die, are registered as having died from their disease, whereas cancer and cardiovascular disease are less common causes of death compared to the general population [15]. The difference in life expectancy compared to the general population is diminishing in recent years due to the availability of dramatically effective treatments and improvements in supportive care [14].

Prognostication is one of the main challenges in managing patients with MS. There are patients who progress rapidly early but do well in the long term and vice versa. A small percentage (approximately 5%) become bedridden, with incontinence, blindness and dementia within 2 years after diagnosis ("malignant" MS). Other patients

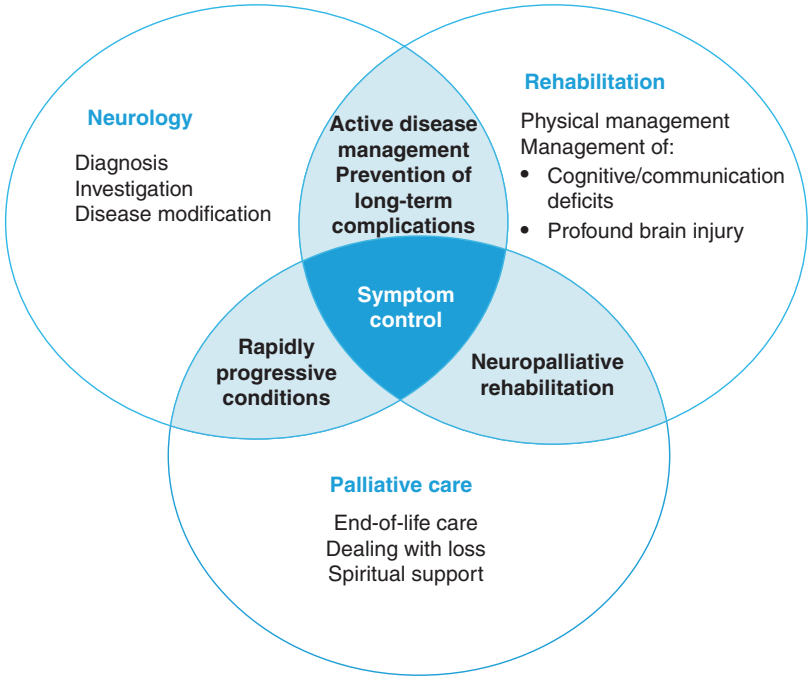

Fig. 7.1 The interaction between neurology, rehabilitation and palliative care services in the management of patients with long-term neurological conditions. (From Turner-Stokes et al. [13], Fig. 1 with permission of the Royal College of Physicians)

have only minimal disability with disease duration of 35 years ("benign" MS) [16].

The Expanded Disability Status Scale (EDSS) is universally used to express the level of handicap of a person with MS and ranges from 0 (no signs or symptoms) to 9 (bedridden) and 10 (dead). The scale is nonlinear and in the mid-range relies mainly on walking functioning. The progression from 0 to 3 (moderate disability but fully ambulatory) can take anywhere from months to decades, while the evolution from 3 to 6 (wheelchair) is rather linear over years, reflecting differential effects of inflammation early on and neurodegeneration later in the disease course [17]. While group level factors may predict progression and treatment response, for the individual MS patient, there is actually less certainty of who will do well, who will respond to therapy, or who will have progressive disease and require greater assistance.

Communicating this uncertainty with patients recently diagnosed with MS is challenging (see below). With present therapeutic options it is projected that for around 80% of patients the disease will be well-controlled, allowing them to start families and have a working career; a figure of 93% with no disease activity at 2-years in a selected population treated with highly active therapy was recently published [18]. Unfortunately, we still do not have accurate means to prognosticate, particularly at the time of diagnosis.

What Is Severe MS?

Traditionally, patients with severe MS are those experiencing many debilitating relapses, with high levels of handicap reflected in high EDSS scores and MRI scan showing high lesion load and atrophy. The EDSS score relies heavily on motor function and ambulation but does not reflect psychosocial issues, fatigue and cognitive decline. While group statistics show a 30% decline in overall quality of life when progressing from EDSS 0 to 3 and another 30% from 3 to 7, the EDSS in itself does not reflect quality of life. MSQOL is a disease specific quality of life questionnaire commonly used in clinical trials. In a subjective perception study in a large group of patients with mainly secondary progressive MS with an average EDSS of 6, 64% of participants reported having severe MS. Reasons for the patients to call their MS 'severe' were loss of mobility, fatigue, autonomic disturbances (incontinence, impotence), loss of autonomy, social isolation, loss of future, and pain. Patients who scored their MS as severe also identified the highest needs, especially in the categories of funding services, social integration and medical support. 'Severity' did not correlate with EDSS, which is therefore not a good factor to identify patients with the highest needs [10].

Communication Challenges

Telling a patient he or she has MS is rarely straightforward and should allow more than one visit to include education on what we know of MS, what treatment options we have and how to deal with uncertainty. The UK NICE Guidelines recommend that the diagnosis should be given by a neurologist, who should provide both oral and written information and engage family or caregivers, if agreeable to the patient. This information should include information about (1) the disease, (2) treatment options, including disease-modifying therapies, (3) symptom management, (4) the organization of and how to reach support groups, local services, social services, legal authorities and national charities [19]. In addition, we recommend tailoring the information to the individual patient as discussed in Chap. 11 "Communicating Effectively".

The progressive nature of MS leads to many times when a more serious conversation is necessary – such as discussing difficult treatment options or the discussion of future care plans (Table 7.1). The content of this communication needs to be adapted to disease stage: in the early stages there will be a greater focus on goals of rehabilitation and therapy, and the very realistic potential of a slow progression with the opportunity of a good quality of life, even if there are limitations due to the disease. Later, especially in

Table 7.1 Potential serious conversation triggers in patients with advancing multiple sclerosis by different stages of disease

Early stage triggers
Time of diagnosis
Malignant multiple sclerosis
Hospitalization or treatment for relapse
Escalation of immunomodulatory therapy to more aggressive therapies with more risk for complications
Advancing disease triggers
Having to stop or change work because of growing disability
Loss of ability to drive
Development of chronic pain
Marital/relationship crisis and loss of caregiver support
Loss of ambulation and adaptation to wheelchair
Urinary incontinence and consideration of catheterization
Cognitive and/or communication dysfunction noted or anticipated
Later stage disease triggers
Advancing cognitive dysfunction and dementia
Transfer from home care to residential care
De-prescribing neuro-immunodolatory agents
Dysphagia, risk of aspiration and reduced nutritional intake
Recurrent Infections and repeated hospitalizations for co-morbidity or complications

advanced stages and with loss of autonomy about wishes and preferences, there will be a greater consideration of symptom control, revisiting advance care planning, and more intensive goals of care discussions. Opportunities to address patient's or families concerns or to recognize a change in the disease course or patient preferences should not be missed. Timing and content of serious illness conversations need to be tailored to the needs of individual patients and their families. Certain signs or events as presented in Table 7.1 can trigger clinicians to offer a conversation – to provide anticipatory guidance including a 'big picture' and what to expect; to consider starting, stopping or continuing a treatment; to consider disease progression and planning for end of life care.

The discussion of the future is always difficult, particularly in the early stages of disease. Given the prognostic uncertainty, it is important to stress that multiple sclerosis is highly variable and the patients all have an individual disease progression. Patients will differ in how much they want to know (See Chap. 12 "Prognostication"). In the earlier stages, discussion of serious handicap with patients who will not experience this for decades and who will have to work and care for their families for many years may not be the best practice. However some patients and families want to discuss these issues, perhaps based on their own experience of others with MS, and the provider should offer the conversation. A personalized approach with honesty and realism, that is tailored to the particular information needs of the patient is necessary.

In patients with highly active, 'malignant' MS, advance care planning is mandatory early on in the disease course. The completion of an advance care plan can be helpful for any patient, as they may then feel more in control of the future, knowing that their wishes will be upheld. Some patients want to talk through everything which will come their way, while others prefer to live in the now and not think about hypothetical undesirable events. Discussion about "hoping for the best, while planning for the worst" may facilitate discussion about the future, including ways to reframe hope and manage uncertainty (See Chap. 11 "Communicating Effectively" and Chap. 12 "Prognostication") [20].

Symptoms and Management

There are many symptoms that may occur and the possible therapies that have been used in the treatment of MS [21]. Important MS-related symptoms include:

Pain

Pain is a common symptom and found in up to 80% of patients [22]. Careful assessment of the cause is important as this may be related to spasm, spasticity, neuropathic pain, or skin pressure pain from immobility. The use of analgesics should be according to the WHO Analgesic

ladder.(see Chap. 17 "Pain Assessment and Management") If there appears to be a neuropathic component, antidepressants or anticonvulsants may be needed. Trigeminal neuralgia occurs in up to 6% of patients with MS [23]. Treatment of trigeminal neuralgia is slightly different in MS than in the non-MS population, and includes the use of high dose steroids and carbamazepine (or other anticonvulsants) or misoprostol, baclofen and rarely invasive procedures, such as neuro-ablation.

Spasticity

Careful assessment by a physical therapist is essential, aiming to maintain mobility and reduce the risk of contracture. Passive stretching and medication such as baclofen and tizanidine can be helpful. Less evidence exists for the use of dantrolene, gabapentin and cannabis [24]. The injection of botulinum toxin may be considered if there is severe spasm [25]. Continuous intrathecal baclofen by an implanted pump system should be considered for advanced stages and wheelchair bound patients [26].

Fatigue

Fatigue is a common symptom and may be seen in up to 80% of patents, particularly in the later stages. Exercise, including strength-training and yoga, may be helpful for patients to build endurance, and cognitive therapies, including teaching energy management strategies and mindfulness, can help patients successfully work with and cope with this symptom [27–29]. Avoidance of heat and cooling therapies may also be helpful. Amantadine, methylphenidate and modafinil are frequently used in clinical practice although the evidence supporting their effectiveness is not strong [19, 30].

Tremor and Ataxia

These symptoms may be due to cerebellar involvement and can be very disabling in a minority of patients, reducing hand movements and balance, leading to falls. Physical therapy may be helpful in developing techniques to compensate for ataxia. MS tremor tends to be refractory to medications, and deep brain stimulation (DBS) surgery may be considered for patient with severe disabling tremor [31].

Dysphagia

Speech and language therapy assessment is important if there is evidence of dysphagia. Careful feeding, with food of the correct consistency, often soft solids, is important and support for patient and caregivers. Severe dysphagia, particularly if it is interfering with nutrition or quality of life, may prompt a conversation about artificial nutrition with a gastrostomy [32]. This decision should be carefully considered within the goals of the patient and family, as evidence from other neurologic conditions suggests that it does not prevent aspiration and can be associated with increased risks of morbidity and mortality from the procedure. Survival benefit has not been studied specifically in Multiple Sclerosis and likely depends on other neurological and medical comorbidities. For troubling sialorrhea, anticholinergic medications (glycopyrronium bromide or scopolamine) or botulinum injections into the salivary glands may be helpful.

Dysarthria

Speech and language therapy assessment is essential; augmentative and alternative communication systems, ranging from simple spelling boards to more complex computer based systems may be needed.

Seizures

Seizures occur in 2–5% of patients with MS and can be the first manifestation of the disease. Early age of onset and aggressive disease are risk factors. It is reasonable to use the drugs for partial

and generalized seizures as are used in the non-MS population with seizures and epilepsy.

Vertigo and Dizziness

Involvement of the cerebellum and vestibular system may cause vertigo. Repositioning and vestibular rehabilitation therapy may be helpful. Medication such as gabapentin and baclofen can be tried but are often not very effective. Oscillopsia can be very troublesome and often responds to gabapentin or memantine.

Urogenital

Urinary incontinence is one of the most frequently encountered problems in MS, can present as urge, stress or mixed pattern incontinence, and significantly impacts patient's quality of life [33]. A variety of non-pharmacologic (e.g. pelvic exercises, behavioral/lifestyle interventions) and pharmacologic (from oxybutynin to botox) treatment options exist for all types of incontinence [34]; in some patients with MS, urinary catheterization becomes necessary, including intermittent catheterization, or chronic urethral or suprapubic catheterization. Sexual dysfunction is common, with failure of erection and ejaculation in men and loss of orgasm in women. Sildenafil may be helpful to help but counselling and support of patients and their partners is essential.

Bowel Dysfunction

Constipation may occur in up to 50% of patients, due to immobilization, medication and reduced eating and drinking. Careful assessment and the use of laxatives/aperients, and sometimes regular suppositories or enemas may be needed [19].

Psychological

MS is a disease where there is progressive loss but with continual uncertainty – of relapse or recovery. Patients and families have many losses to cope with over time – mobility, independence, hope, employment, relationships, cognition – and may need support and counselling to help (see Chap. 18 "Spiritual Care"). Engaging the family is important and should be encouraged, so that they can share these issues and make the most of the patient's abilities, and maintain quality of life [35].

Depression occurs in up to 60% of patients with MS including a higher prevalence of suicide (see below). The presence of depression is not necessarily related to duration of illness, degree of disability or cognitive impairment but seems to be more common during relapses. Some patients experience psychological decompensation early on, possibly with a role of limbic MS localizations [10]. Medication, such as steroids, may increase depression. Many patients with MS do not receive adequate treatment for depression and antidepressants and cognitive behavioral therapy should be offered. Mood stabilizers, such as sodium valproate or lamotrigine, may be needed if there are mood swings associated with bipolar disease, which is twice as common in MS as in the general population. If there is severe anxiety benzodiazepines may also be helpful [35].

Suicide

Suicide is more common than in some other neurological diseases, and studies have shown hazard ratios of up to four times the risk for people with MS compared to the general population. Uncertainty of the disease course, psychiatric manifestations of relapses, the lengthy disease duration with social isolation, pain, incontinence, and social or financial factors may all contribute to a feeling of helplessness [36]. Care is needed when using SSRI antidepressants in this population at risk for suicide because of the potential of causing activation, with a consequent higher suicide risk with SSRI in younger patients.

Requests for hastened death – by euthanasia or physician assisited suicide (see Chap. 14 "Addressing and Managing Requests to Hasten Death") – are more frequent in patients with MS than in the general population where these

practices are permitted. For instance in Belgium, where euthanasia in patients with MS is allowed by law, MS patients are four times more likely than the general population to die by euthanasia [37].

Approaching End of Life Care

The timing of and triggers for serious illness conversation is influenced by stage of disease (Table 7.1). As MS often progresses slowly it may also be important to ensure that the whole multidisciplinary team is aware of these conversations that may initiate a change in priorities or in the emphasis of medical care. There are general triggers for all progressive neurological disease including MS suggesting patients are entering the final stages of diseases: swallowing problems, recurring infection, marked decline in functional status, first episode of aspiration pneumonia, cognitive difficulties, weight loss and significant complex symptoms [38]. Specific triggers have been suggested for MS – dysphagia with associated choking attacks and poor hydration and nutrition, frequent infections, cognitive decline with reduced communicationand fatigue with profound, fatigue and a reduced response to the environment [38].

The number of triggers increases as death approaches (most often aspiration pneumonia) and the terminal phase of illness can be recognized by providers in the majority of patients [39]. Depending on the needs of the patients and family and the skill set of the multidisciplinary team, this may include consideration of a formal specialist palliative care consultation.

There are a number of approaches to alerting clinicians when patients are entering the terminal phases of illness, including in patients with MS. These include the use of the surprise question "Would you be surprised if the patient were to die in the next 6–12 months?", the use of specific signs or symptoms (progressive deterioration in physical and/or cognitive function despite optimal therapy, speech problems with increasing difficulty communicating and/or progressive difficulty with swallowing, recurrent aspiration pneumonia and breathlessness), the use of various performance scales, or more multi-decisional approaches to identify patients approaching the end of life: SPICT-tool [40]. Although these are not directly aimed at a person with MS the presence of these factors may again suggest that the end of life phase is approaching.

By being vigilant and attentive to the needs of the patient and family, the multidisciplinary care team will be best positioned to transition the patient and family to appropriate terminal care. This may include referring to a hospice if in the appropriate jurisdiction, ensuring care is provided in the preferred place (e.g., home), education about the course of expected terminal signs and symptoms, adjusting medications and treatments as appropriate, addressing spiritual and cultural concerns, preparing the family for death, and providing the appropriate support. For more information, see Chap. 16 "Hospice and End of Life Care in Neurologic Disease".

Supporting the Caregiver

Every clinician caring for a patient with MS should assess and involve a patient's caregiver, if they have one. This includes considering the relationship of the caregiver: for example, a parent may experience the stresses differently than a spouse or child; a spouse may be juggling their additional responsibility of caring for children, or continuing to work. It may be helpful to find out the caregiver's health status – physical, emotional and mental, as their own health issues may affect their ability to care long term for their loved one with MS.

Studies have shown increasing feelings of burden among caregivers, particularly in advanced MS. This burden increases with disease duration and increasing handicap. Themes affecting caregivers include coping with frequent and repeated change and loss, challenges of MS, caregiving demands, burden of care, and concerns about the future [41]. Bowel and bladder symptoms can be troublesome with frequent catheterizations and frequent awakenings in the night causing exhaustion [42]. Almost 90% of caregivers state being

happy to help and two thirds report finding caregiving rewarding [43]. Moreover support was found to be helpful and helped in developing strtaegies to manage the caregiving role [41]. A caregiver of a person with MS will face a number of challenges throughout the course of the illness, and careful and iterative assessment of their health, knowledge, skills and resources is essential as is a continued show of support by their clinician.

Unmet needs of patients with severe MS and their family include a strong need for qualified personnel who know about MS, care coordination in day-to-day home care, a supportive network and the preservation of patient and family roles within both the family and community [44]. Further discussion on supporting the caregiver may be found in Chap. 20 "Caregiver Assessment and Support".

Education and Research Agenda

An increasing number of studies are surfacing that suggest that early integration of palliative care may lead to improved symptom management and quality of life, and support for caregivers. Given the long and uncertain time course of MS, it is likely that MS specialists will be providing the majority of palliative care to their patients. Therefore, MS specialist training needs to include palliative care skills, especially effective communication and specific symptom management.

More research specific to patients with MS is needed. One small trial in London randomized 52 severely affected patients with MS to a multiprofessional palliative care team at diagnosis vs. after 3 months. At 3 months, the early intervention group improved in five key symptoms (pain, nausea, vomiting, mouth problems and sleeping difficulties), in caregiver burden as well as costs [45, 46]. A recent Italian trial examined the effectiveness of a limited palliative care intervention with palliative care training and support of specialist MS 'teams' (a neurologist, nurse, psychologist and social worker) [47]. Seventy eight patients and caregivers were randomised and the symptom burden was significantly reduced but there was no change in quality of life or other patient or carer outcomes.

There is a need for further research evaluating the most effective way for providing ways to manage symptoms and provide support for MS patients, including the most appropriate timing of specialist palliative care [12, 48]. This includes the need for further research to identify predictors of disease progression and functional prognosis. Finally, research is needed to better understand the issues faced by those caring for people with MS and how to best help them.

Take Home Messages

- People with MS have many needs and issues which may be helped by palliative care, provided by a multidisciplinary team
- Communication is often complex – in coping with the discussion of future deterioration and advance care planning
- People with MS have many symptoms which may need careful multidisciplinary team assessment and management
- Awareness of the later stages of the disease progression ad preparation for end of life care is important and the consideration of triggers, which may suggest that end of life is close, may be helpful
- Support of family and caregivers is very important in all stages of the disease progression

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Neuromuscular Diseases

8

Maisha T. Robinson and Danny Estupinan

Case

John is a 68-year-old man with a 1-year history of diffuse muscle twitching and right leg weakness. Recently, he has been tripping over curbs and he feels unsteady enough when he is walking that he has begun using a cane. Over the past few months, his family has noticed that it is more difficult to understand him when he is talking and his wife worries that he is not breathing well at night. He subsequently sought evaluation with a neurologist and after laboratory studies, imaging, and electrodiagnostic studies, he was diagnosed with Amyotrophic Lateral Sclerosis (ALS).

During the clinic visit, John and his family described the progression of his symptoms and they primarily focused on his recent respiratory distress. He and his family are worried that he will be gasping for air as his disease progresses. He expresses that he does not want to be put on a ventilator and be "hooked up to a breathing machine without being able to have some level of independence". He was a former Vietnam War veteran and he has seen human suffering first hand in combat. He doesn't want the end of his life to be traumatic for him or for his family. He state that he wants to die a "natural death" and that he doesn't want to suffer. He understands his condition is progressive and terminal, but he wants to have the best quality of life until the end of his life.

Affecting either central motor neurons, the neuronal pathways, the muscles themselves or a combination of those, neuromuscular diseases are marked by progressive disability due to muscle weakness. Motor neuron disease (MND) includes Amyotrophic Lateral Sclerosis (ALS), primary lateral sclerosis, progressive muscular atrophy, progressive bulbar palsy, pseudobulbar palsy, and spinal muscular atrophy. The most common type of MND is ALS. Rarer forms of MND such as progressive muscular atrophy and primary lateral sclerosis may have a slower rate of progression [1]. This review will describe a few types of neuromuscular diseases that are particularly appropriate for a neuropalliative care approach. We will focus on ALS as the primary

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example as it has the best evidence base for palliative care management.

Amyotrophic Lateral Sclerosis

Amyotrophic Lateral Sclerosis (ALS) is a chronic and degenerative motor neuron disorder (MND) that selectively affects motor neurons, the cells that control voluntary muscles of the body. Although it is the most common MND, ALS is a rare condition with an incidence of two new cases per 100,000 people each year [2]. Approximately 30,000 Americans are affected by the disease [3]. The age of onset is usually between 55 and 70 years, and men are more commonly affected than women. There is an ethnic predilection toward Caucasians [4].

ALS classically presents with muscle weakness, wasting, cramps and stiffness of arms and/or legs, difficulty with speech and/or swallowing or, more rarely, with respiratory impairment. Limb onset ALS is the most common presentation followed by bulbar onset ALS. Motor symptoms include weakness, muscle atrophy, spasticity, and fasciculations. Sensation, bladder function, and extraocular muscles are usually spared [1].

The disease involves a combination of upper motor neuron (UMN) and lower motor neuron (LMN) signs and symptoms progressing from one of four body segments – brainstem, cervical, thoracic, and lumbosacral [5]. UMN findings such as spasticity, increased muscle tone, incoordination of limbs, increased deep tendon reflexes, and pathologic reflexes including Babinski, Hoffman, crossed adductor, and snout may be present depending on the site of involvement. LMN signs and symptoms include weakness, atrophy, muscle fasciculations, cramps, and depressed deep tendon reflexes [5].

Common non-motor symptoms include mood disorders such as depression, and anxiety. Pseudobulbar affect or emotional incontinence can also occur. It is characterized as uncontrollable crying or laughter that is inconsistent with the patient's mood. Pseudobulbar affect is thought to be caused by dysfunction of the corticobulbar tracts, resulting in an involuntary display of emotion [6]. Cognitive dysfunction including frontotemporal or executive dysfunction and dementia can occur in 45–55% of people with ALS [7]. Pain is also a common but underrecognized and undertreated symptom in patients with ALS.

Median survival in ALS is about 3–5 years from symptom onset [8–10]. A small subset of patients with slowly progressive ALS variants live upwards of a few decades. These patients may actually have other forms of Motor Neuron Disease such as primary lateral sclerosis (PLS), progressive muscular atrophy (PMA) or other ALS mimickers such as Kennedy's disease (spinobulbar muscular atrophy) [1].

Estimating Prognosis

Estimating prognosis in motor neuron disease, especially ALS, can be challenging given that the prognosis is variable and it can be measured in terms of a few months to a few decades. Accurate prognostication for survival is extremely important to help patients, families, and their caregivers in designing a plan of care that meets their goals and that allows patients to focus on living with the best quality of life possible.

Factors associated with reduced survival in ALS include bulbar onset, a body mass index of less than 25, and age greater than 75 [10, 11]. Prognostication can be aided by disease-specific scales in ALS, such as the ten-item ALS Functional Rating Scale (ALSFRS, Table 8.1) and a revised version that incorporates respiratory function, the ALSFRS-revised scale [12, 13]. The 12 item ALSFRS-R questionnaire (score 0–4 per item) assesses speech, salivation, swallowing, handwriting, cutting food and ability to use utensils, dressing and hygiene, turning in bed, walking, climbing stairs, dyspnea, orthopnea, and respiratory insufficiency. These 12-items provide subscores for the following four health domains: bulbar symptoms, fine motor function, gross motor function, and breathing function. A 25% decline in the ALSFRS-R score is thought to be clinically meaningful [14]. (Also see Chap. 12 "Prognostication", for more information).

Table 8.1 ALS functional rating scale

Symptom/activity of daily living	Grading
Speech	4 Normal
	3 Detectable speech disturbance
	2 Intelligble with repeating
	1 Speech combined with nonvocal communication
	0 Loss of useful speech
Salivation	4 Normal
	3 Slight but definite excess of saliva in mouth
	2 Moderate excessive saliva
	2 Marked excess of saliva
	0 Marked droling
Swallowing	4 Normal eating
	3 Early eating problems
	2 Dietary consistency changes
	1 Needs supplemental tube feeding
	0 Nothing by mouth
Handwriting	4 Normal
	3 Slow or sloppy
	2 Not all words are legible
	1 Able to grip pen but unable to write
	0 Unable to grip pen
Cutting food and handling utensils	4 Normal
	3 Somewhat slow and clumsy
	2 Can cut most food, some help needed
	1 Food must be cut by someone
	0 Needs to be fed
Dressing and hygiene	4 Normal
	3 Independent and completes self-care with effort
	2 Intermittent assistance needed
	1 Needs assistance for self-care
	0 Total dependence
Turning in bed and adjusting bed clothes	4 Normal
	3 Somewhat slow and clumsy
	2 Can turn alone/adjust sheets with difficulty
	1 Can initiate but unable to turn/adjust sheets alone
	0 Helpless
Walking	4 Normal
	3 Early ambulation difficulties
	2 Walks with assistance
	1 Nonambulatory functional movement only
	0 No purposeful leg movement
Climbing stairs	4 Normal
	3 Slow
	2 Mild unsteadiness or fatigue
	1 Needs assistance
	0 Unable to do
Breathing	4 Normal
	3 Shortness of breath with minimal exertion
	2 Shortness of breath at rest
	1 Intermittent ventilator assistance
	0 Ventilator dependent

Disease Modifying Therapy Affecting Overall Prognosis

Riluzole

Riluzole was the first disease-modifying pharmacologic agent in ALS, providing a modest survival benefit of approximately 3 months. Approved in 1995, the drug likely works via inhibition of glutamate release [15]. The cost can often be prohibitive and it does not palliate any ALS-associated symptoms or improve quality of life. In fact, side effects such as fatigue can be significant enough to warrant discontinuation [15]. Given these factors, it is reasonable to discontinue the medication at the time of hospice enrollment (or when a patient becomes ventilator-dependent), although there are no published guidelines regarding these considerations [16].

Edaravone

Edaravone was recently FDA-approved based on a randomized controlled Phase III trial involving 137 ALS patients. Treatment slowed a decline in a 48-point clinical test of daily function that assessed fine motor, gross motor, bulbar, and respiratory functions of patients. After 24 weeks of treatment, the scores of edaravone-treated patients fell around 2.5 points less from baseline than those of placebo-treated patients [17]. Common side effects included bruising and gait

disturbance. It remains unclear what effect, if any, the drug has on survival times or quality of life. A further post hoc analysis questions whether the general ALS population would benefit from this drug [18]. More research remains to be done to determine the potential long term benefits of the medication as well as its safety and efficacy.

Spinal Muscular Atrophy

Spinal muscular atrophy (SMA) is a hereditary neurodegenerative disorder of lower motor neurons which leads to progressive muscle weakness and atrophy [19]. The incidence of SMA has been estimated at 7.8–10 per 100,000 live births and at 4.1 per 100,000 live births for type I SMA [20].

SMA subtypes are classified as types 0–4 depending upon the age of onset and clinical course [19]. SMA is an autosomal recessive disorder and the clinical severity is determined by subtype, which is based on SMN gene copy numbers. Disability can range from a patient being unable to achieve any motor milestones with congenital/prenatal SMA (Type 0) to potentially reaching all motor milestones until adulthood in Type III/IV SMA [21]. The prognosis varies considerably, but the mortality rate with Type 0 is usually less than 6 months, Type I (infantile or Werdnig-Hoffman disease) less than 2 years without respiratory support, Type II (intermediate form) can survive into early adulthood with respiratory support, Type III (least infantile form) can usually have near normal to normal life expectancy and Type IV (adult onset form) is normal life expectancy [22–25].

SMA treatment has typically been supportive including helping provide adequate nutritional support, physical, occupational therapy and adaptive equipment to maintain best quality of life until the end of life. However, in December 2016 the FDA approved the first treatment available, nusinersen, for the treatment of infantile onset SMA; it can also be used for SMA type II and III [26].

Myopathies

Duchenne's Muscular Dystrophy

Duchenne (DMD) and Becker muscular dystrophies (BMD), X-linked recessive diseases, are caused by mutations of the dystrophin gene thus are known as dystrophinopathies. Duchenne's muscular dystrophy has an estimated incidence of 1 in 3802–6291 live male births. The data suggest that Becker's muscular dystrophy is about one third as frequent as Duchenne's Muscular dystrophy [27].

The classic presentation of DMD is proximal greater than distal symmetric muscle weakness, sometimes with calf pseudohypertrophy, cardiomyopathy/cardiac conduction abnormalities, bone fractures, scoliosis, and progressive decline. Physical exam findings might include lumbar lordosis, a waddling gait, shortening of the Achilles tendons and hyporeflexia or areflexia. The typical course of illness leads to significant functional impairment and disability by adolescence. Usually most patients with Duchenne's muscular dystrophy die by early adulthood due to complications of respiratory insufficiency or cardiomyopathy [28, 29].

As opposed to Duchenne's muscular dystrophy, Becker's is typically a milder form of the disorder with >20% dystrophin protein expression.

There is slowly progressive decline, usually a more benign and variable course. The typical age of onset is during childhood or adolescence. Patient's usually remain ambulatory into adulthood and life expectancy is usually well into adulthood with much better overall quality of life [27].

Glucocorticoid treatment is beneficial in the treatment of Duchenne muscular dystrophy (DMD) for improving motor function, strength, pulmonary function, reducing the risk of scoliosis, and possibly by delaying the onset of cardiomyopathy [27, 30, 31]. For children with DMD age 4 years or older whose motor skills have plateaued or declined, glucocorticoid treatment is recommended. The preferred regimen is prednisone 0.75 mg/kg per day or alternatively deflazacort at dose of 0.9 mg/kg/day which has been associated with less weight gain and poten-

tially fewer complications than prednisone [32]. The only FDA approved drug for DMD is Eteplirsen [33].

Advance Care Planning and Goals of Care

When a patient is diagnosed with motor neuron disease, it is important to address the typical trajectory of the disease and to engage in a discussion regarding a patient's preferences with regard to life-prolonging measures. Given the common sypmtoms of dysphagia and respiratory distress, artificial nutrition and mechanical ventilator support should be specifically addressed [34]. Goals of care discussions with patients and their surrogate decision makers should occur routinely at clinic visits and when clinical decline occurs.

Novel approaches such as a computer based advance care planning decision-aid may help clinicians feel more confident in having advance care planning and goals of care discussions with their patients. This can improve clinicians 'understanding of ALS patients' wishes with regard to end-of-life care and promote goal concordant care [35]. Patients report high satisfaction and low decisional conflict suggesting that formal training and preparation of clinicians for this conversation can lead to better overall advance care planning discussions without affecting a patient's ability for self determination in the decision-making process.

Case continued…

As part of his evaluation for respiratory symptoms, John had pulmonary function testing which revealed he had a Forced Expiratory Volume (FEV1) of 40% of predicted and a Forced Vital Capacity (FVC) of 49% of predicted.

John's forced vital capacity (FVC) is less than 50% predicted which overall is strongly correlated with shorter survival. Independent predictors of poor prognosis in ALS include age of onset, respiratory symptoms or bulbar onset, and a rapid rate of change in FVC or in the ALS Functional Rating Scale.

Based on his level of respiratory distress and his FVC, Non-invasive positive pressure ventilation (NIV) is recommended. NIV can improve fatigue, sleep, and overall quality of life as well as prolong life expectancy in ALS.

The option of tracheostomy was also discussed as a means to prolong his life but given the expected continued functional decline and poor quality of life associated with it, he decided against a future tracheostomy. He did not want any other forms of life-prolonging measures and in the setting of his terminal illness, his Advance Directive was consistent with that. His family was supportive of his decision.

Common Symptoms and Management

In this section we will review the common symptoms associated with ALS/chronic progressive motor neuron disorders and their management based on current evidence. Table 8.2 provides a summary of the medical and non-medical approaches to symptom management in ALS.

Dysphagia

Dysphagia is denoted in ALS patients by difficulty chewing and swallowing, nasal regurgitation, or coughing when drinking liquids. These symptoms should prompt a formal swallow evaluation by a certified speech pathologist to determine the degree of dysphagia and to assess dietary needs including dietary modification in food preparation and to discuss the possibility of percutaneous endoscopic gastrostomy (PEG) tube placement. There are no randomized controlled trials comparing PEG tubes and oral

Table 8.2 Symptomatic management of ALS summary table

Symptom	Medications	Non-medication options
Dysphagia	None	PEG tube
		Dietary modification
Dyspnea	Opioids (see prior sections on opioids and symptom management for more)	Non-invasive ventilation
		Invasive ventilator support if FVC <50% or MIP <−60 cm
Pseudobulbar affect	Neudexta (Dextromethorphan (20 mg)/ Quinidine (10 mg)	None
	Selective Serotonin reuptake inhibitors (SSRIs)	
	Selective Serotonin Norepinephrine inhibitors (SRNIs)	
	Tricyclic Antidepressants (TCAs)	
Spasticity	Baclofen (both orally and intrathecally), tizanidine, benzodiazepines, botulinum toxin, dantrolene, and Levetiracetam	Physical therapy
		Stretching
		Occupational therapy
Weakness	None	Physical therapy
		Adaptive equipment
		Ankle-foot orthotics
Mood disorders	Tricyclic antidepressants, selective serotonin reuptake inhibitors, and serotonin- norepinephrine reuptake inhibitors	Psychotherapy
		Meditation/Stress and relaxation techniques
		Cognitive behavioral therapy
		Biofeedback
Cognitive dysfunction	Cholinesterase inhibitors (donepezil, rivastigmine, galantamine)	Cognitive behavioral therapy
	NMDA receptor antagonist (memantine)	
Pain	NSAIDs	Physical therapy
	Botox for spasticity/spasms, Gabapentin	Massage
	Opioids, Muscle relaxants, quinine sulfate or mexilitine for muscle spasms, steroids, etc	Stretching
Cramps	Vitamin E, Baclofen, Gabapentin	Massage
Dysarthria	None	Writing boards
		Letter boards\referral to a speech-language pathologist at least annually for an augmentative/ alternative communication evaluation
Insomnia	Antidepressant medications (i.e. mirtazapine at 15 mg qhs)	Durable medical equipment such as a hospital bed.
	Anxiolytic medications (i.e. benzodiazepines to induce sleep (low doses may be used to reduce the risk of respiratory depression)	An alternating pressure air mattress or gel overlay mattress
	Melatonin	Noninvasive ventilation
Sialorrhea	Atropine, tricyclic anti-depressants, and scopolamine patches	To minimize drooling, portable suction devices can be used to clear excess secretions
	Botulinum toxin injections	For treatment refractory sialorrhea, salivary gland irradiation delivered over 1–5 fractions may improve symptoms within 24 h
		Laryngectomy is used for secretion management and prevention of aspiration in patients whose speech is already severely compromised, as the procedure completely eliminates a patient's ability to speak

feeding in ALS patients but studies suggest that PEG tubes may help to stabilize weight and offer a survival advantage in dysphagic patients of 3–8 months depending on the site of disease onset [36, 37]. PEG tubes may also allow for the delivery of medications for symptom management as the disease progresses [38].

Dyspnea

Dyspnea due to respiratory failure is common in the later stages of ALS, occurring in up to 85% of patients [39]. Pulmonary function tests should be performed every 3 months to assess respiratory function and to determine potential eligibility for noninvasive ventilation (NIV) [40]. As the respiratory status declines in ALS patients, reversible causes such as respiratory tract infections or increased secretions should be assessed for, particularly in the setting of an acute decline. Noninvasive ventilation is recommended if the patient experiences orthopnea, or if the FVC is <50% predicted or if the maximal inspiratory pressure is <−60 cm. NIV has demonstrated a positive impact on quality of life and it may be considered at the earliest sign of nocturnal hypoventilation, as determined by nocturnal oximetry or symptoms. Non-invasive ventilation may improve median survival in people with respiratory insufficiency and normal to moderately impaired bulbar function, compared to standard care, and it improves quality of life but not survival for people with poor bulbar function [38, 41]. Mechanical insufflation and exsufflation may be used to clear secretions.

ALS patients typically die from their disease as a consequence of progressive involvement of respiratory muscles. Common signs and symptoms of respiratory impairment include early morning headaches, vivid dreaming, dyspnea on exertion, an inability to lie flat (orthopnea), and nocturnal hypercapnea [42]. A 2017 Cochrane review on symptomatic treatment of ALS showed insufficient evidence to recommend any one specific treatment based on lack of randomized controlled trials for the treatment of dyspnea in ALS [38]. In addition to non-invasive ventilation, opioids are commonly used to treat dyspnea. One small, non-randomized prospective study demonstrated that low dose morphine appears to be both safe and effective in this patient population [43]. Also see Chap. 16 “Hospice and End of Life Care in Neurologic Disease”, for more specific recommendations of managing dyspnea at the end of life.

At some point during the disease course, NIV may no longer provide sufficient respiratory augmentation. Ideally, the conversation regarding the option of tracheostomy and mechanical ventilation would have already been had and it should be readdressed at this time. This decision should be made in advance of acute respiratory distress. The conversation should include the logistics regarding 24-hour care and ventilator support. Specific instructions should be outlined as to when the person would want to discontinue the ventilator. Family and caregiver burden should also be discussed. Given the known progression of disease and overall poor quality of life, fewer than 10% of people with ALS pursue tracheostomy and mechanical ventilation in the United States, but this varies greatly across countries and by provider [44].

Spasticity

Spasticity is muscle stiffness affecting one or more whole limbs and it can be painful in nature. Controlled trials for treatment for spasticity are lacking. Medications used based upon their benefits in other disorders associated with spasticity or in open label trials in ALS include baclofen (both orally and intrathecally), tizanidine, benzodiazepines, botulinum toxin, dantrolene, and levetiracetam [38]. As these medications are titrated, it is important to ensure that mobility is not reduced secondary to increasing muscle weakness.

Physical and occupational therapy, with a focused exercise program that aims to help maintain joint range of movement, prevent contractures, reduce stiffness and discomfort, and optimize function and quality of life, should be employed. Exercise programs should be

appropriate to the person's level of function and tailored to their needs, abilities, and preferences.

Weakness

As an ALS patient develops progressive weakness in the lower extremities, typically, the ability to ambulate unassisted becomes increasingly impaired. There is no evidence to support the use of a pharmacological treatment for muscle weakness in people with ALS. It is treated primarily with physical and occupational therapy with associated adaptive equipment provided to help maintain the best quality of life as possible as the disease progresses. Bracing with ankle foot orthotics may increase gait stability for a prolonged period [45]. However, as patients become more prone to falling, evaluation by physical therapy is imperative to determine the need for assistive devices such as a walker or power wheelchair. The 2013 AAN quality measures specify that screening for falls is recommended at least annually to prevent traumatic injury [16].

Pseudobulbar Affect

Pseudobulbar affect affects 20–50% of patients with ALS, especially in patients with bulbar onset [46]. Patients experiencing uncontrolled crying are more common than those with uncontrolled laughter. These symptoms can result in significant disability, limiting social interactions and impairing quality of life. Selective serotonin reuptake inhibitors, tricyclic antidepressants and some serotonin-norepinephrine reuptake inhibitors have been used for treatment of pseudobulbar affect [6]. Additionally, the combination of dextromethorphan (20 mg) and quinidine sulfate (10 mg) has been shown to be effective in a large phase three multicenter randomized trial [6, 47]. Patients taking dextromethorphan/quinidine sulfate reported significantly less emotional lability, improved quality of life, and improved quality of relationship scores [47]. Side effects included dizziness, nausea, and somnolence. These side effects can be minimized by initiating the dose at one tablet at bedtime for 7 days followed by twice a day dosing. The American Academy of Neurology (AAN) Practice Guidelines recommend that if side effects are acceptable, dextromethorphan/quinidine should be considered for pseudobulbar affect in patients with ALS [16]. Selective serotonin reuptake inhibitor (SSRI) medications may also be helpful though they have not been studied in the ALS population in a randomized fashion.

Mood Disorders

The prevalence of depression in ALS patients varies in the literature from 4% to 56% [48]. Compared to the general population, patients with ALS have a higher overall likelihood of developing depression. It is most common after their diagnosis and perhaps also prior to their diagnosis [49]. In ALS patients, approximately 0–30% of patients experience anxiety and the presence of it may be related to the stage of the disease [50]. Routine screening at clinic visits is encouraged.

The treatment of depression and anxiety for patients with ALS can involve both pharmacological and non-pharmacological interventions. Neither has been demonstrated to be superior to the other and a combined approach is recommended. Patients may benefit from a range of psychotherapy approaches, including relaxation strategies such as meditation and biofeedback [50]. Cognitive behavioral therapy improves a patient's ability to cope with their diagnosis and to adapt to the progressive decline in function. Antidepressant medication, including tricyclic antidepressants, selective serotonin reuptake inhibitors, and serotonin- norepinephrine reuptake inhibitors may assist with mood elevation, appetite stimulation, and sleep. Antidepressants are selected based on their side effect profile. Referral to a psychiatrist, clinical psychologist, or palliative medicine specialist may be warranted for patients with severe or persistent symptoms. Counseling should also be offered to depressed spouses and other family members.

Cognitive Dysfunction

Frontotemporal dementia (FTD) is apparent in approximately 5–10% of patients with ALS, although nearly 50% of patients may have some cognitive impairment [7]. Cognitive dysfunction can increase the level of care needed, affect a patient's medical decision-making capacity, and make communication with others including caregivers and healthcare providers challenging. The 2013 AAN quality measures suggest that screening for cognitive and behavioral impairment using tools such as the ALS Cognitive Behavioral Scale (ALSCBS) should be performed at least once annually given the strong correlation and potential impact on overall quality of life and mortality [45].

Pain

Pain is reported in 57–72% of patients with ALS and may involve the extremities, neck, back, or trunk [51]. Descriptions of pain include burning, aching, cramping, and shock-like. Limited range of motion in joints, immobility, spasticity, cramps, and skin breakdown related to immobility are all potential sources of pain in ALS, which occurs in the later stages in up to 80% of patients [52]. The etiology of musculoskeletal pain in ALS may be relatd to muscle atrophy with subsequent strain on bones and joints [53].

While nonsteroidal anti-inflammatory drugs are frequently used, a number of therapies are prescribed including non-opioid analgesics, opioids, muscle relaxants, quinine sulfate, gabapentin, steroids, botulinum toxin, and physical therapy [54]. Massage therapy may also be useful to patients. A Cochrane review found no controlled or quasi-controlled studies of treating pain in patients with ALS [38]. However, identifying the etiology and the characteristics of the pain may aid the clinician in developing a rational approach to devising a treatment plan.

(Please refer to the section on spasticity and cramps for further discussion regarding pain in ALS; for a comprehensive approach to pain management, see Chap. 17 "Pain Assessment and Management").

Cramps

Muscle cramps are sudden, involuntary, painful contractions of muscles. Electrophysiologically, this is represented as a burst of a group of lower motor neurons firing spontaneously together. It is relieved by stretching the muscle and it may be aggravated after exercise. Cramps improve spontaneously after a few seconds or minutes. Muscle cramps are common in ALS, poorly responsive to treatment, often debilitating, and unrelated to the severity of disease [55, 56]. There have been a number of randomized treatment trials addressing this frequently disabling symptom but most have been unsuccessful [56]. To date, there is no high quality evidence regarding treatments for cramps, although Baclofen, Vitamin E, and Gabapentin may be helpful [38]. Anecdotally, quinine sulfate taken orally may be helpful for symptomatic relief of muscle cramps, though the drug is no longer available in the United States due to safety issues. The cardiac antiarrhythmic medication mexiletine has been demonstrated to reduce the frequency and severity of muscle cramps in ALS in a dose dependent manner [57]. For mexiletine and quinine sulfate, an electrocardiogram should be performed to ensure no evidence of QT prolongation given the risk of long QT with both. In addition to medication, a daily stretching program can be helpful.

Dysarthria and Communication Issues

Dysarthria is a motor disorder of speech where speech articulation or intelligibility is impaired [58]. If the speech is unintelligibile but motor function in the upper extremities is present, maintenance of communication can be achieved through writing or using a letter board. Conventional articulation training is ineffective;

however, some adaptive strategies taught by a speech-language therapist may be useful [59]. As the disease progresses, alternative methods of communication may become necessary, such as eye tracking technology and other augmentative/alternative communication (AAC) devices. Caregivers of patients report that AAC including speech generating devices are helpful to stay connected, to respond to patients' needs, and to discuss complex important issues, including medical information [60]. As emphasized by the 2013 AAN quality measures, dysarthric patients should be offered a referral to a speech-language pathologist at least annually for an AAC evaluation [16]. An emphasis on maintaining a patient's ability to communicate can enhance patient and caregiver quality of life.

Insomnia

Sleep disruption in patients with ALS is frequently multifactorial in etiology and may be due to respiratory muscle weakness, difficulty repositioning in bed, anxiety, depression, and pain [42]. Nocturnal hypoventilation results in frequent arousals and decreased total sleep time which contributes to daytime fatigue and poor concentration, which can affect quality of life and overall prognosis [42].

Possible treatments for a disturbance in sleep may include durable medical equipment such as a hospital bed, an alternating pressure air mattress or gel overlay mattress, or NIV. In some patients, there may also be a role for anxiolytic or antidepressant medications such as low dose benzodiazepines or mirtazapine. If anxiety or depression is the underlying cause of insomnia, addressing these symptoms through pharmacologic and non-pharmacologic strategies is recommended [61]. A dietary supplement such as Melatonin may also be useful.

Fatigue in ALS is a very common symptom and it should be differentiated from insomnia. It relates to whole body tiredness or exercise-induced muscle weakness that may be partially reversible with rest [62].

Sialorrhea

In ALS, sialorrhea is caused by difficulty clearing secretions secondary to bulbar weakness, spasticity, or dysphagia. Drooling may occur as a result of pooled secretions which can lead to social stigmatization [61]. Additionally, difficulty with secretion management also increases the risk of perioral skin irritation and aspiration.

There are a number of treatment options for sialorrhea. A portable suction device can be used to clear excess secretions and pharmacologic management with anticholinergic medications such as atropine and scopolamine patches, tricyclic antidepressants, or Botulinum toxin injections can also be used [63, 64]. For treatment of refractory sialorrhea, salivary gland irradiation delivered over one to five fractions may improve symptoms within 24 h. Xerostomia is a potential side effect of radiation treatment but if it occurs, it is usually temporary as salivary function often returns after 3 months [65]. A laryngectomy is used for secretion management and prevention of aspiration in patients whose speech is already severely compromised, as the procedure completely eliminates a patient's ability to speak. This approach can be used independent of a patient's decision regarding long-term mechanical ventilation [66].

Withdrawing and Witholding Life Sustaining Treatments

Early in the disease course a patient's preferences for non-invasive and invasive ventilation should be discussed and re-addressed iteratively (*see serious illness conversation triggers below).* If life-prolonging care is pursued, detailed communication between the patient, caregiver, and medical team is necessary to ensure that there is no ambiguity surrounding if and when to discontinue respiratory support [67]. Symptom management, including the use of pharmacological treatments for breathlessness, should be explored with the person with MND [67].

ALS patients present the unique and often challenging experience of potentially removing

artificial ventilation once it has been started. Patients may be at home under the care of a primary care provider, a neurologist, a palliative care provider or a hospice team. If a terminal withdrawal is planned, personnel with the relevant skills and expertise should be identified to assist in a number of areas: practical expertise and knowledge of the ventilator machine, familiarity with the use of palliative medication, and supportive services for all of the people involved in the process including the patient, caregivers, and family members [67].

Requests for a Hastened Death

Numerous studies have attempted to determine the factors that predict whether a patient is likely to request a hastened death. Common factors cited associated with a request for a hastened death include feelings of being a burden, a loss of hope, a loss of control, and depression [68]. In a review of the Oregon experience with physician aid in dying, ALS was the second most common terminal condition and the primary reasons for pursual of death with dignity were a loss of autonomy and an inability to engage in activities [69]. Please see Chap. 14 "Addressing and Managing Requests to Hasten Death", for more detailed discussion on this topic.

Serious Illness Triggers

It is useful to keep in mind disease milestones that may serve as reminders to initiate or review goals of care with patients. Suggested triggers include a decline in functional status, which may be indicated by a change in the ALS functional rating scale score, progressive weight loss, and recurrent hospitalizations [70]. Evidence of disease progression may also include respiratory decline with FVC <50% or MIP <−60 cm H_2O and bulbar dysfunction such as worsening dysarthria or dysphagia. These are important markers of advancing illness and shortened survival.

Caregiver Burden

Caregivers of patients with ALS may experience significant distress as the patient's functional status deteriorates and more assistance is required [71, 72]. As the disease progresses, communication may become more limited, which may increase the strain on providing care and it may also lead to increased isolation [72]. Additionally, a decline in cognition for an ALS patient may place an increased burden on caregivers and it can lead to mood disorders and stress in this population [73, 74]. The impact of respiratory failure and the decision regarding whether to pursue a tracheostomy and mechanical ventilation affects not only the patient but perhaps more importantly, the caregiver. Quality of life for caregivers is reduced when they are caring for a ventilated patient due to the increased daily responsibilities [40, 75]. The provision of palliative care in ALS should also incorporate the caregiver given the potential for high caregiver burden.

EOL Care and Hospice

In a study of the last month of life in ALS patients, the most common symptoms were difficulty communicating, dyspnea, choking episodes, insomnia, and pain. Caregivers reported depressed mood (40%), anxiety (30%) and confusion (10%) in patients [2]. Many of these symptoms were often inadequately controlled [2]. For patients opting for a comfort-oriented approach, hospice is an excellent option.

In the United States, hospice refers to specialized end-of-life care for people who have a terminal condition and who have a prognosis of 6-months or less, according to Medicare guidelines [76]. Hospice organizations provide high-quality care for patients at the end of life and they are available for the management of terminal symptoms in patients with ALS. They can assist with optimizing the care and increasing the likelihood of a peaceful and dignified death. Despite the advantages of hospice care, the services are generally underused or they are initiated too late in the disease course [3].

In ALS, signs and symptoms of a 6th-month life expectancy include a rapid progression of disease and significant nutritional compromise or a rapid progression of disease and life-threatening complications, significant respiratory distress, a vital capacity less than 30% of predicted, dyspnea at rest, a need for supplemental oxygen, and a decision to not pursue tracheostomy and mechanical ventilation [77]. Hospice referral guidelines for Medicare in patient's with ALS are shown in McCluskey and Houseman's discussion in the Journal of Palliative medicine on hospice referral criteria for ALS [77].

In preparation for the end of life, support from an ALS team, a palliative medicine service, or a hospice team can be very beneficial to patients and caregivers. Adequate methods of communication should be utilized to allow patients to express their needs and to maintain the ability to exercise choice and control regarding the end of life. Additionally, appropriate equipment such as suction machines, riser-recliner chairs, hospital beds, bedside commodes, and hoists may also be needed. Medications for symptom management including opioids and benzodiazepines to treat breathlessness and antimuscarinic and anticholinergic medications to treat sialorrhea and respiratory secretions should be available. Bereavement support should be offered to caregivers and families of ALS patients. (See Chap. 16 "Hospice and End of Life Care in Neurologic Disease", for further discussion).

Education Agenda

Multiple studies have demonstrated a knowledge gap among both neurologists and Neurology trainees with regard to palliative care principles [78, 79]. Increasing Neurology trainees and neurologists' exposure to palliative care may improve knowledge and comfort regarding symptom management and end-of-life care [80]. Neuromuscular or EMG fellows in particular should have an opportunity to rotate with Palliative Medicine teams or with hospice agencies to focus on symptom management, difficult conversations, goals of care discussions, and transitioning patients to hospice care. There are opportunities for further integration of palliative medicine into the training environments for Neurology, Medicine, and other specialties that care for patients with ALS.

Research Agenda

There is a significant opportunity to define the unmet needs of patients and caregivers and to determine the most effective and efficient models to address those needs in a standardized fashion. This will need to include studies assessing bereavement support and care for caregivers to better understand how to provide comprehensive care for the family unit that meets their needs as the patient faces this terminal illness. Both quantiative and qualitative research will likely be needed to explore ways to meet specific needs. Randomized controlled trials for pharmacological and nonpharmacological interventions are needed. It is unclear how future emerging therapies in neuromuscular disease may alter the disease course and prognostication, which may impact the delivery of (neuro)-palliative care. Finally, more robust studies are necessary to provide guidelines regarding the role of primary and specialist palliative care providers for ALS patients and caregivers.

Take Home Messages

- Neuromuscular diseases lead to progressive weakness and disability with increasing palliative care needs.
- Amyotrophic Lateral Sclerosis, is a particularly devastating example of neuromuscular diseases that is progressive and terminal.
- The focus of care is on improving quality of life by optimizing functional status and communication methods
- Symptom burden is high and the management often requires a combination of pharmacologic and nonpharmacologic treatments.
- Goals of care discussions should occur throughout the disease course at specific disease- or event-driven milestones ('serious illness conversation triggers')
- Conversations about life-prolonging measures, including artificial nutrition and

mechanical ventilation should be specifically emphasized
- End-of-life care may include hospice services for patients who desire to focus on comfort
- Clinicians caring for patients with neuromuscular disease need to consider support for both patients and caregivers
- More research is necessary to determine the optimal method of delivery of palliative care for patients with motor neuron disease

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Malignant Brain Tumors

9

Akanksha Sharma and Lynne P. Taylor

Case

Eliza is a 54-year-old woman who suddenly develops severe shortness of breath, eventually leading to a diagnosis of malignant pleural effusion. She is diagnosed with metastatic breast cancer and begins treatment. Soon after this, she develops severe headaches and seizures. She is admitted to a hospital, and a lumbar puncture reveals leptomeningeal carcinomatosis.

Eliza wants to spend as much time as she can with her husband, daughters and grandchildren. She has specific goals of celebrating Christmas and making memories with her youngest grandchild. Eliza has an optimistic, cheerful personality, and considers herself to be "someone who is never going to quit!" She is determined to live as long as she can and wants to be offered every treatment possible. She is also clear that being awake, alert, and interactive is very important to her, and she does not wish to be in excessive pain.

Eliza reviews the choices with her medical team and she decides that she wants to proceed with intrathecal chemotherapy. To make it more comfortable, she agrees to an Ommaya reservoir. However, before she can receive any treatment Eliza goes into status epilepticus and becomes obtunded due to increasing intracranial pressure. Eliza's family turns towards you for guidance – "What can we do to save her?"

Neurosurgery is consulted but they feel a ventriculo-peritoneal shunt will not be possible due to the burden of disease in her peritoneum. Eliza can either be transitioned to comfort care, or a more controversial ventriculo-atrial shunt may be placed.

Primary Brain Tumor

Epidemiology

Primary brain tumors have an incidence of 7/100,000 with a prevalence of 222/100,000 individuals. The incidence of primary brain tumors has been increasing over the last 30–40 years, especially in the elderly. Thirty-five thousand new diagnoses will be made each year, and in 2017 alone, brain tumors will lead to almost

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17,000 deaths. In the last few decades there have been significant therapeutic advances, yet the mortality rate remains high with only 35% of patients surviving 5 years following diagnosis. The incidence is higher in men than in women (7.6 versus 5.4 per 100,000 person-years) and the lifetime risk is 0.65% in men and 0.5% in women. Race is also a factor as the incidence is double in white patients compared with black patients [1–4].

One-third of primary brain tumors are malignant. Gliomas account for 80% of this group, and glioblastoma is the most common form of malignant glioma. Glioblastoma multiforme is the most aggressive of the gliomas. The median age of presentation is 64 years of age. Prognostic indicators are age, functional status, resectability of the tumor, and various mutations within the tumor itself. Lower grade gliomas (astrocytomas and oligodendrogliomas) usually afflict younger adults (with a median presenting age of 35). The course and natural history of these tumors can be highly variable, and as a result there is still controversy over the best treatment choice. Age, clinical presentation, tumor size, and genetic/histological features of the tumor all play a role in the prognosis of the patient [5].

Presentation and Diagnosis

Primary brain tumor patients can present with either focal or generalized symptoms. Headaches, nausea, vomiting, fatigue, confusion or altered mental status are more generalized and fairly non-specific symptoms. Focal seizures, weakness and/or sensory loss of a particular limb, language and visuospatial difficulties are more specific, focal symptoms that prompt earlier evaluation. Because tumors infiltrate rather than acutely destroy brain parenchyma (such as with trauma or stroke), symptoms and signs are subtler, which often leads to a delay in diagnosis. A high index of suspicion and awareness of "red flags" are required to accurately diagnose brain tumors early in their course. Headache is a common initial presenting symptom [5, 6]. A new diagnosis of headache or a distinct change in headache pattern in a patient over the age of 50 should be considered a red flag, though the most common brain tumor headache type is indistinct from migraine [7, 8]. Chronic, persistent headache with protracted nausea, vomiting and positional worsening, headaches that wake the patient from sleep, or are provoked by Valsalva, i.e. signs of increased intracranial pressure, typically presage a brain tumor diagnosis [9]. Diagnosis is typically determined by brain imaging (gadolinium enhanced MRI) and treatment is guided by histopathological diagnosis [10].

Treatment

Attempted gross total resection of the tumor remains a first step if it appears to be the best choice for the patient. Factors that are taken into consideration include the patient's age and performance status, initial or recurrent stage of disease, location of tumor, size and number of lesions, and adjacent eloquent cortex. The aim is for maximal safe resection – removing as much of the tumor as possible while minimizing morbidity [11].

As an adjunct therapy to surgery, and when surgery is neither feasible nor appropriate, radiation therapy may be employed. Radiation oncologists have a variety of treatment options including stereotactic radiosurgery (SRS), whole brain (WBRT) or intensity modulated radiation therapy (IMRT) shaped to the tumor contours [12, 13]. Radiation therapy to the brain can result in nausea, hair loss, skin changes and significant fatigue. Late delayed effects include "pseudoprogression" of the tumor where treatment-related factors create local swelling and enhancement that mimics progressive tumor, and cognitive impairment from treatment-related leukoencephalopathy [9, 12, 14].

Chemotherapy is generally offered to all patients diagnosed with a malignant brain tumor. The Stupp protocol in NEJM in March of 2005 showed that concurrent temozolomide (TMZ) and radiation therapy (RT) followed by six

cycles of adjuvant temozolomide at 150–200 mg/m^2 days 1–5/28 days produced a 26.5% 2 year survival with RT plus TMZ and a 10.4% survival with radiation therapy alone [15]. There is very mild toxicity associated with this drug – generally headache, nausea, vomiting and constipation, and these can be addressed with anti-emetics and a bowel regimen [15]. Bevacizumab, a recombinant humanized monoclonal antibody that inhibits vascular endothelial growth factor A and blocks angiogenesis, has been studied with mixed results [16, 17]. Bevacizumab does not prolong overall survival, but can improve progression free survival by acting as a dexamethasone sparing agent, decreasing vasogenic edema and improving neurologic symptoms. It has a role in decreasing peri-tumoral edema and can treat radiation necrosis. Adverse effects of this drug include fatigue, hypertension, poor wound healing, and proteinuria, clotting and bleeding [18–21].

Metastatic Disease and Leptomeningeal Disease

Epidemiology

Up to 10% of systemic cancer patients are affected by symptomatic metastatic brain tumors, which are much more common than primary brain tumors. As patients with systemic cancers live longer, the incidence of metastatic disease to the brain is also increasing. Breast, lung, melanoma, gastrointestinal, and renal carcinomas are the most common (in that order). The majority (80%) of brain metastases occur in the cerebral hemispheres, 15% in the cerebellum and 5% in the brainstem. The mechanism is thought to be hematogenous spread of tumor emboli via the capillary bed to the gray-white junction in the brain [1, 22].

Leptomeningeal metastasis refers to the seeding of the leptomeninges by malignant cells through hematogenous spread and its incidence is reported to be between 5% and 8%. This is termed carcinomatous meningitis, lymphomatous meningitis, or leukemic meningitis depending on the source. This is a serious complication of systemic cancer and one that is very difficult to treat effectively, given the constant flow of CSF through the neuraxis [23, 24].

Presentation and Diagnosis

The signs and symptoms of brain metastases are similar to those of primary brain tumors and determined by their location within the brain. Leptomeningeal disease, as a more global process, can present with severe headaches, mental status changes, seizures, paresthesias, weakness, pain, gait abnormalities, ataxia, and cranial nerve palsies [25, 26]. Elevated intracranial pressure secondary to hydrocephalus can become life limiting without urgent intervention. Metastatic brain lesions and leptomeningeal disease should be high on the differential when a patient with any history of systemic malignancy presents with new neurological signs and symptoms. In the appropriate patient, an MRI with gadolinium, which can be very sensitive, should be obtained promptly as early treatment can improve prognosis [27]. CSF cytology can be very specific [27, 28].

Treatment

The patient's functional status has a significant impact on choice of treatment. The young and well patient is more likely to tolerate and survive aggressive surgery and chemotherapy than the severely disabled.

Primary management of brain metastases is driven by the number of lesions. If there is limited disease (one to three lesions) in a patient with controlled systemic disease, surgery to resect the tumors is preferred. Stereotactic radiosurgery (SRS) is an option both in isolation and with surgery, and has been seen to result in good local control within the brain (75–90% at 1 year and 60–80% at 2 years) [29–31]. If there are multiple (>3) lesions, surgical resection is not considered feasible and whole brain radiation therapy has historically been the recommended treatment,

though has fallen out of favor more recently due to a high rate of neurotoxicity [32–34].

Molecular genetics are playing an increasing role in the choice of treatment, since novel therapies targeting specific gene mutations continue to be introduced.

Treatment for leptomeningeal disease is generally aimed at improving and stabilizing the neurological status of the patient while prolonging survival only minimally. Modalities of treatment include radiation therapy for alleviation of symptoms and treatment of bulky disease. Surgery has a limited role, except in placement of a subcutaneous reservoir for treatment (Ommaya) or an intraventricular catheter. Intrathecal therapy in appropriate cases may extend survival and help maintain a functional quality of life [24].

Prognosis for the Brain Tumor Patient

Prognosticating in the field of neuro-oncology remains complex. There was a time when we could offer only comfort to a patient diagnosed with a malignant brain tumor; this is no longer the case as the field has changed dramatically in the last few decades. Research advances have led to an understanding that differences at a molecular level impact the way these tumors respond to chemotherapy. Overall, the field is moving towards individualized treatment recommendations, rendering generalizations about prognosis less meaningful.

National statistics estimate the 5-year survival following a diagnosis of a primary malignant brain tumor to be 34.7%, but prognosis can vary significantly based on the age of the patient, their functional status and the histology of the tumor. For example, from 1995 to 2013, survival at 5 years was as high as 74% for those aged 0–19, decreasing to 11.2% for those aged 65–74. Glioblastoma remains the most deadly, with a median survival of 14.6 months with standard treatment [15]. Survival from low-grade glioma has a broader range, with the median between 6 and 13 years [35]. The median survival of patients with untreated brain metastases from solid tumors is 1–2 months. Whole brain radiation therapy (WBRT) can improve survival to 4–6 months [12, 36]. Patients with leptomeningeal carcinomatosis have a survival of a few weeks to months without treatment. With treatment, survival can be extended by several months [37].

Presenting Prognosis

When communicating prognosis, it is recommended that terms like “months to years” are used rather than a specific time frame [38], keeping in mind that the median survival statistic is simply part of a distribution, and patients may fall on either side of this curve [39] (See Chap. 12 “Prognostication”). Conversations around prognosis and end of life issues should be tailored to the individual patient and family and their coping abilities. Several visits are typically needed to assess physical, psychological, emotional and spiritual needs. It is valuable to start by ascertaining how much information the patient/family wants and to make this an ongoing, evolving dialogue [38]. A detailed discussion of diagnosis and prognosis is typically not recommended in a high stress inpatient setting unless the situation demands an immediate clinical decision. Because cognitive decline and frontal lobe “neglect” are so common in brain tumor patients, early discussion involving the surrogate and education about difficulties in cognition and language are essential if we are to elicit goals and preferences [40].

It is important to find a balance between conveying information and maintaining hope, even in cases where the prognosis is very poor [41]. Hopelessness can create distance between the physician and patient. One way adults cope and sustain hope is by making plans for the future. Rather than suggesting the future is impossible or unrealistic, providers can help patients and families reframe hope, focusing on more realistic and tangible goals [42]. “Hoping for the best, and preparing for the worst” may be a shared perspective that can strengthen the relationship between patient, family and physician [41] (See Chap. 11 “Communicating Effectively”).

Table 9.1 Serious conversation triggers

Sleeping more than 16 h a day
Extreme agitation or concerning behavioral changes (i.e., severe depression, disinhibition, violence, suicidality, etc.)
Status epilepticus with evidence of tumor progression
Loss of ability to drive due to speed of processing and/or distractibility (not epilepsy alone)
Significant cognitive deficits impacting ability to function in daily life or with dramatic drop in cognitive testing
Dysphagia preventing any oral intake
Worsening speech – dysarthria or aphasia
In metastatic tumors – significant worsening of systemic disease
In primary brain tumors – recurrence of disease
Serious systemic complications requiring hospitalization – pulmonary embolism, strokes, infections and/or sepsis, hemorrhage
Drop in KPS or ECOG by more than one step
Failure of first line chemotherapy
Seizures worsening enough to require addition of a third anti-epileptic drug
Inability to wean off dexamethasone or need to restart dexamethasone

[40, 43–46]

Certain events during the course of the illness may serve as "serious conversation triggers" between the provider and the patient/caregivers. The gravity of the situation or the symptoms may prompt addressing or re-addressing goals of care, and reconsidering treatment options. While these triggers can vary significantly and may be unique to each patient's own course, we list several of the more commonly seen situations in Table 9.1 [43–46].

These triggers also provide an opportunity to have a conversation on advanced care planning with the patient and the caregivers. Advance care planning is important in improving end of life care as it encourages shared decision making, and allows the patient, family and physicians to have honest conversations and establish the patient's own wishes for their end of life. This practice increases the likelihood of the patient dying in their preferred place, increases hospice use, and reduces hospitalizations at the end of life [47, 48]. These conversations are challenging in patients who are rapidly declining cognitively and who may suffer difficulties with language, memory or personality. Up to 40% of brain tumor patients do not have discussions about treatment preferences, health care proxy, hospice or resuscitation [49, 50].

Performance Scores

The Karnofsky Performance Score (KPS) and the Eastern Cooperative Oncology Group (ECOG) system are widely used in the field to assess disease severity and assist with prognosis [51, 52]. The KPS ranges from 0 (death) to 100 (perfect health). The score is often used in clinical trials where independence in all activities of daily living (KPS 70) is a common inclusion criteria. The ECOG is simpler than the Karnofsky score, and provides similar information (Table 9.2).

Symptom Assessment and Management

Cognitive Issues

Neurocognitive problems are extremely common in this patient population. They can be caused by the tumor, seizures, by the treatment itself (surgery, radiation, chemotherapy, steroids and other medications), or by psychological distress [53]. Impairment in executive functioning, memory, and attention are the areas where deficits are most commonly noted [54, 55]. Cognitive performance impacts everyday life and the ability to return to work. Effects on comprehension and memory impact patient's ability to understand prognosis and to plan effectively for the future.

There are few established preventive or therapeutic interventions for cognitive dysfunction in brain tumor patients. In a small recent trial, patients who received memantine within 3 days of initiating radiotherapy had better cognitive function in the areas of memory and executive function after 24 weeks [14]. Donepezil and hyperbaric oxygen therapy have not been shown to improve cognition after radiation therapy [56, 57]. Cognitive rehabilitation involves exercises aimed at improving different cognitive domains and has shown recent promise for brain tumor patients [58].

Table 9.2 Comparing Karnofsky and ECOG performance scales

Karnofsky status	Karnofsky grade	ECOG grade	ECOG status
Normal, no complaints	100	0	Asymptomatic, able to carry all pre-disease performance without restrictions
Able to carry on normal activities. Minor signs or symptoms of disease	90	1	Symptomatic but completely ambulatory (Restricted in physically strenuous activity)
Normal activity with effort	80	1	Symptomatic but completely ambulatory (Restricted in physically strenuous activity)
Cares for self. Unable to carry on normal activity or do active work	70	2	Symptomatic, <50% in bed during the day (Ambulatory and capable of all self-care but unable to carry out any work activities)
Requires occasional assistance but able to care for most needs	60	2	Symptomatic, <50% in bed during the day (Ambulatory and capable of all self-care but unable to carry out any work activities)
Requires considerable assistance and frequent medical care	50	3	Symptomatic, >50% in bed, but not bedbound (Capable of only limited self-care)
Disabled. Requires special care and assistance	40	3	Symptomatic, >50% in bed, but not bedbound (Capable of only limited self-care)
Severely disabled. Hospitalization indicated though death not-imminent	30	4	Bedbound (Completed disabled, cannot carry on any self-care)
Very sick. Hospitalization necessary. Active support treatment necessary	20	4	Bedbound (Completed disabled, cannot carry on any self-care)
Moribund	10	4	Bedbound (Completed disabled, cannot carry on any self-care)
Dead	0	5	Death

Mood Changes

Depression is common in patients with brain tumors, though different studies show a wide variation in prevalence depending on the method of measurement [59–61]. Once identified, depression and anxiety are still undertreated. One studied noted that only 60% of patients with brain tumors diagnosed with depression received antidepressants [62]. There are no case controlled trials exploring side effects of pharmacological treatment for depression in primary brain tumor patients, which may contribute to a reluctance to prescribe [63].

For depression and anxiety, psychotherapy, counseling and cognitive behavioral therapy can be excellent non-pharmacologic options. Participation in support groups can be very helpful for patients and caregivers alike. The newer antidepressants have modest side effects and are well tolerated. These include selective serotonin reuptake inhibitors (fluoxetine, paroxetine, sertraline, citalopram and escitalopram) and serotonin/norepinephrine reuptake inhibitors (duloxetine, venlafaxine) [64]. Bupropion, a dopamine-norepinephrine inhibitor, is generally not recommended as it lowers the seizure threshold in some patients [64, 65].

Other, less common mood changes may be related to tumor location or may be side effects of medications. Frontal lobe tumors can result in obsessive behaviors. Anger, apathy and disinhibition may be seen with frontal or temporal lobe lesions. Steroids may cause agitation or even mania, and the anti-epileptic levetiracetam has been seen to cause nervousness, depression and irritability in some patients [66]. Hospitalization and ICU care can produce delirium, especially in patients with cognitive impairment.

Fatigue

Fatigue can be caused by the disease itself, and may be secondary to treatment side effects, medi-

cations, sleep disturbances and psychological stress [60, 67]. Patients often complain of fatigue more than any other symptom, and it can be what they associate as most affecting their overall well-being and quality of life. Brain irradiation can contribute to fatigue and can cause significant somnolence [68, 69].

The first step in evaluating fatigue is to look for modifiable factors including medications that can be discontinued (anticonvulsants, opioids, anti-emetics), poor diet or appetite, sleep disturbances, anemia or nutritional deficiencies. It is important to offer options to address emotional distress and mood disturbances that can also contribute to fatigue. A recent Cochrane analysis found insufficient evidence for or against specific pharmacological or nonpharmacological treatment for fatigue in patients with primary brain tumor [70].

Existential Suffering

As for patients with other terminal illnesses, brain tumor patients struggle to find meaning in their condition. Patients may worry about the future constantly, and describe "waiting for something to happen" [42]. It is important to be aware of these fears and to address them when possible. While not frequently addressed by providers in routine clinical visits, discussion of these issues or referrals to other professionals such as chaplains or psychologists may be comforting and may be desired by patients and caregivers alike, since it can be a huge source of stress and psychological suffering [71, 72] (See Chap. 18 "Spiritual Care").

Seizures

The frequency of seizures varies by tumor type and can be as high as 90% in gangliogliomas, 50% in high-grade gliomas and 25% in low grade meningiomas [73]. Temporal lobe location and hemorrhage increases the risk for seizures. Brain tumor patients who present with seizures are treated with antiepileptic drugs (AEDs) as the standard of care. No statistically significant benefit has been found for the prophylactic use of AEDs in patients, including those treated with a craniotomy [74, 75]. Anti-epileptics are generally begun when a patient has had a witnessed seizure or provides a compelling history for a brief episode of altered consciousness. The choice of AEDs is based on ease of dosing and tolerance, side effect profile, and interactions with chemotherapy [76].

About one quarter of brain tumor patients on AED therapy experience side effects severe enough to warrant a change or discontinuation of therapy [74]. Some of these side effects can be unique to this population, and may not be well known by most neurologists. For example, after cranial irradiation for glioma, phenytoin or carbamazepine can lead to a severe rash and rarely, even Stevens-Johnson Syndrome [77, 78]. This often is specific to the head and eyes and other irradiated areas. At its most dramatic it can cause functional blindness due to swollen eyelids with limitation of eyelid opening, marked erythema, and scalp tenderness.

Drug interactions are a significant consideration in this population, since polypharmacy, including chemotherapy, is common. Phenytoin is an inducer of hepatic metabolism and can reduce the half-life and bioavailability of the commonly used drug dexamethasone, and dexamethasone can decrease phenytoin levels [79]. AEDs that induce the cytochrome P450 enzyme system can impact the metabolism of various chemotherapy agents potentially decreasing the serum levels by 25%.

Generally, preferred AEDs include levetiracetam, lamotrigine, pregabalin and lacosamide [76, 80]. This is due to the lower side effect and drug interaction profile in this group. Levetiracetam is the most frequently prescribed AED within neuro-oncological practice. It can be initiated at a therapeutic dose, does not have any significant drug-drug interactions, and levels need not be monitored. It can be dosed PO and IV, is effective as monotherapy, and is affordable [81, 82]. However, the mood effects of levetiracetam, which can

include irritability, aggression, hostility and depression, are important to monitor when prescribing this medication [83]. Lacosamide is a newer AED and rapidly gaining favor in the neuro-oncological community. Similar to levetiracetam, it has no known drug-drug interactions, is well tolerated and can be used as monotherapy in both PO and IV formulations [64]. However, it can be expensive and may not be covered by many insurance companies. Pregabalin and gabapentin are other options for brain tumor patients, generally as adjunct therapy [81]. These are both well tolerated and have the added benefit of treating neuropathic pain. Lamotrigine has an excellent side effect profile for this population, but has to be escalated very slowly to minimize risk of skin toxicity; these factors and the lack of an IV formulation lead to less use of this drug.

Newer research suggests that valproic acid may have anti-glioma effects as a radio sensitizer and prolong survival [84, 85]. It may be worth considering using this drug as an AED in the appropriate patient, keeping in mind that it is metabolized by the liver and has side effects of teratogenicity, hyper-ammonemia, hair loss and weight gain.

Surgery is also an important consideration in tumor-related epilepsy and may result in excellent control of seizures, especially in low-grade gliomas which tend to be more epileptogenic and refractory to treatment than higher grade tumors [85–87].

Weakness

As the tumor progresses, especially in high grade gliomas, patients develop generalized weakness due to a combination of fatigue, medication affect, exhaustion and electrolyte derangements, and focal weakness caused by the tumor and/or surgery. Only a small percentage of patients stay fully independent into the late course of their disease [88]. Motor disability can be severe enough to require caregiver assistance for ADLs such as toilet transfers, bathing, dressing, feeding and walking. Focal motor weakness also puts patients at increased risk of thromboembolic complications, a condition that can affect up to a third of brain tumor patients [42].

Edema and Steroid Use

Peri-tumoral vasogenic edema can result in various disabling symptoms, including the worsening of focal neurological deficits, or even obtundation and coma. Steroids can be used to help treat and control this edema and rapidly alleviate focal neurologic symptoms related to the edema, such as breakthrough seizures, nausea, headaches, appetite and mood [64]. In CNS lymphoma, steroids actually have an oncolytic effect and are part of the treatment. They are also used to help alleviate the side effects of radiation therapy.

Due to a longer half-life of almost 36–54 h and lack of mineralocorticoid activity, dexamethasone is the most favored steroid. No clear standard guidelines have been set for steroid use. In acute settings, when a patient presents with acute neurological deterioration due to edema, a 10 mg IV bolus followed by 4 mg every 6 h is a commonly accepted schedule. However, patients may not need as much as 16 mg/day, and lower doses may have equal efficacy. In general, the recommended practice is to start as low as possible and to taper steroids as quickly as possible, given the side effects associated with long-term use [64, 89, 90]. Generally, tapers tend to be over the duration of 6–8 weeks for most patients who have been on steroids for 2 weeks or more, though there is not much data or evidence guiding ideal steroid wean in this population.

Steroid related hyperglycemia, steroid myopathy, weight gain, psychosis and delirium, anxiety, insomnia, irritability and emotional lability are quite common. Peptic ulcer disease and gastritis are other systemic complications that may require the concurrent use of proton pump inhibitors or histamine receptor blockers. Steroids impact bone health, especially when used long term, and can cause avascular necrosis of the hip joints. Calcium and vitamin D supplements usually have to be given in addition to the other medications [64, 80, 89].

Headache

Headache is a frequent symptom of a brain tumor, experienced by up to 50% of patients [91]. It can be a presenting symptom in up to 13% of patients, or present later in the course of the disease as a sign of worsening mass effect and tumor progression [92]. Towards the end of life, headaches may become more frequent or more severe, likely from increased intracranial pressure or inflammation from neoplastic meningitis.

Steroids may be used to alleviate symptoms of edema when it contributes to headaches. Neuropathic headache agents can be tried, weighing the risk versus benefits of side effects. For example, gabapentin may be a good headache prophylaxis agent but can cause sedation and weight gain. Topiramate may be a good option, especially since it can reduce intracranial pressure, but cognitive side effects can limit its use. Opioids and non-steroidal anti-inflammatory drugs (NSAIDs) may also prove to be quite helpful [93]. Opioid use may need to be balanced against the risk of sedation, while NSAID use may be contraindicated in patients who have kidney injury, gastritis, or hemorrhage [44, 94].

Appetite and Weight

Close to 50% of brain tumor patients have changes in appetite and consequently experience dramatic fluctuations in their weight [42]. Chemotherapy can cause nausea, dysphagia, and altered taste. Drugs such as steroids and valproic acid may increase appetite and result in weight gain. Weight fluctuations through the course of the disease are common and have to be addressed differently in different phases. Steroids may need to be weaned if weight gain is excessive or harmful to quality of life. At other times, appetite stimulants such as megestrol or cannabinoids may be used to stimulate appetite [42].

Appearance

Altered appearance can be caused by neurologic deficits, surgeries and treatment side effects. Steroids can result in moon facies, weight gain, and myopathy. Valproic acid can cause weight gain and alopecia. Gabapentin can produce edema and weight gain. Chemotherapy and radiation may impact the skin. Recognition of these insecurities is important, both for medical providers and family members, since these can contribute to depression, anxiety, isolation, and a decrease in quality of life. Validating those concerns by providing support and empathy, and suggesting support groups and counseling is a helpful way to address this, especially in long term survivors coping with the scars of their journey.

Loss of Independence

Cognitive impairment, motor weakness, and seizures all contribute towards the patient becoming increasingly dependent on others over the course of their disease. Patients often have restrictions placed upon their driving, leading to a reliance on caregivers for even simple tasks and errands. Patients may not be able to plan independently, and have to work around the schedules of others. Patients may also be unable to take care of their own finances, and be forced to take a leave from their careers. This can lead to frustration and anger, and have a negative impact on their self-esteem. Patients may also feel like they have become a burden on others.

Supporting the Caregiver

The age and demographics of caregivers of brain tumor patients vary according to tumor type as the average age of presentation and gender varies for each type of tumor. One study of glioblastoma patients noted the median age of the patients to be 63 years and the median age of the caregivers to be 62 years [88]. Since many tumors affect males more than females, it is common that a greater subset of caregivers are females [38, 88]. Generally, most caregivers are partners of the patient, though a smaller percentage are parents, children or siblings [38, 88, 95]. The median time for caring can also vary by tumor type and sever-

ity – from 11 months for a glioblastoma patient to many years for a low grade glioma patient.

Sadness is the most often mentioned symptom reported by 90% of caregivers in the last few months of life followed closely by fear (69%), burnout (60%) and decreased interest in others (54%) [88]. Financial difficulties also dominate this phase. Caregivers often have to either stop working or take a leave of absence in order to fulfill their roles [38].

Many caregivers feel insufficiently informed by the medical staff [88]. Caregivers feel supported when the care teams address their fears and keep them informed about the patient's mental and physical status [96]. Often, caregivers will do their own research, since they find that their providers are not fully up to date on the available experimental treatments or may not have enough time to answer questions [95]. It is also important that when information is given, it is given in appropriate terms; the language used must be understandable by the layperson.

With increasing dependence of the patients as their disease progresses, caregivers may be unwilling or unable to take care of their loved one at home. This is especially true when there is a single caregiver without a strong support system or if there are significant financial difficulties. This often results in the patient dying in the hospital rather than at home. Social workers may be able to find resources for patient and family in the community, volunteer and support groups, and help with the many complex and technical aspects of insurance, home health and hospice.

When our brain tumor patients undergo personality and behavior changes as a result of the disease, it can be a significant challenge for caregivers. They may see the person they love change dramatically and may have to deal with many new, difficult types of behavior (disinhibition, apathy, and aggression). Sherwood et al. [95] described several cases of caregivers receiving no help or advice when it came to neuropsychiatric symptoms of agitation, hallucinations, or violence, leaving them with few options. Cognitive and neuropsychiatric symptoms are the most difficult to manage for the family and caregivers. Healthcare providers may need to prepare caregivers for these problems, and provide options for treatment with antipsychotics, counseling, and psychiatric consultation.

An indirect way to support the caregiver is to encourage the patient to create an advanced directive well in advance. This can be invaluable towards the end of life, when the family may be asked to make important decisions on behalf of the patient who may no longer be cognitively intact or even conscious. Having an existing advanced directive in place can relieve a great deal of stress from loved ones given this very heavy burden of decision-making. It can also allow the patient to share their perspectives on quality of life, and on dying, with their loved ones, developing an understanding that can also ease the pain, sadness and fear of this phase of their disease [95] (See Chap. 20 "Caregiver Assessment and Support").

End of Life Care for Patients with Brain Tumors

How Do Patients with Brain Tumors Die?

Many physicians find this question difficult to answer, and many patients and families have not been properly prepared for this phase. While the steps to the end can vary greatly, certain symptoms may be more prevalent than others. A frank, candid discussion with the patient (if cognitively aware) and the caregivers may be helpful earlier in the course of the disease. The timing of this conversation depends on the course of the patient's illness, their willingness to participate, and the physician's comfort in having this conversation. Triggers that can help the provider recognize situations prompting a 'serious conversation' can be referred to in Table 9.1 above.

Confusion, progressive somnolence and coma are prominent symptoms in patients nearing death and are due to increased intracranial pressure and mass effect, herniation, seizures, sepsis, dehydration or other metabolic derangements [93]. Headache is a frequently reported symptom

in up to 60% of patients; only 13–25% of brain tumor patients reported bodily pain in studies [44, 68, 94, 97], which can be a reassuring statistic to share with our patients. Fever can be commonly noted, even when the source is not identified. Hemiparesis or focal weakness can be a prevalent symptom, and one that furthers the disability of the patient and results in complete dependence [93]. Dysphagia can be present in between 65% and 85% of patients at the end of life, leading to malnutrition, dehydration, and inability to take medication orally [45]. Less prominent symptoms include urinary infections, incontinence, pneumonia, dyspnea, and death rattle [45, 94, 97].

Seizure Management at the End of Life

Most patients with seizures at the end of life have had seizures previously in the course of the illness, though one study found that 14% of the time the seizures were new in the last month of life [95]. It is important to prepare families for seizures in this phase, when alternative routes of drug delivery will need to be considered, because seizure management is complicated by swallowing difficulties from dysphagia and somnolence. There are buccal, rectal, intramuscular/intravenous and subcutaneous formulations of many medications that can be used and are discussed further in Chap. 16 "Hospice and End of Life Care in Neurologic Disease" [98].

Nutrition at the End of Life

Nutritional support for cancer patients has been well studied by the American Society for Parenteral and Enteral Nutrition who published their clinical guidelines in 2009 [99]. This is a group of professionals in the field of medicine, nursing, pharmacy, dietetics and nutrition science using Institute of Medicine recommendations. Most of the published studies have been in pancreatic and GI malignancy patients with malabsorption or bowel obstruction. The guideline is: "The palliative use of nutrition support therapy in terminally ill cancer patients is rarely indicated."

Given the emotionally charged nature of this topic, in those rare cases where they find that parenteral nutrition might lengthen survival and improve quality of life, they have required that patients be physically and emotionally able to participate in their own care with a life expectancy greater than 2 months and with strong support at home. As brain tumor patients develop somnolence at coma at the end of their lives, the criteria above do not suggest that they would benefit from this practice. Therefore, we advise against artificial nutrition or hydration at this stage, and reassure caregivers that our patients do not feel distress from lack of food or water, and in fact may only be able to tolerate ice chips or sips of water if and when awake.

Sedation and Pain Control at the End of Life

Palliative sedation is the intentional lowering of the level of consciousness of a patient in the last phase of life by administering sedatives and analgesics with the goal of providing comfort and reducing physical and psychological suffering that may be otherwise untreatable. It is used in 13–45% of brain tumor patients in this phase with most common indications of intractable seizures, delirium, agitation, restlessness, pain, and air hunger [93, 100]. Between 60% and 90% of brain tumor patients at the end of life receive opioids [45, 101]. The dosage and route varies largely upon the physical location of the patient. Hospitalized patients may have greater access to opioids in various formulations which may be prescribed by physicians and administered by nursing with close monitoring of symptoms. Patients at home may be administered medications by family or by visiting hospice nurses, and these are generally buccal or liquid forms of morphine that can be more easily given to the patient without the need for intravenous access. Drugs administered in this setting include midazolam, diazepam, lorazepam or chlorpromazine. Care at this point is similar to that of

patients with other neurological disorders, and we direct readers to the hospice section for further information. Caregivers should also be made aware that difficulty in clearing upper airways can result in increases in respiratory secretions and the "death rattle" that can be distressing to the family but is *not* distressing to the patient given their level of consciousness. Anticholinergic drugs may be an effective therapy for this symptom [100, 102].

Hospice

Despite the high rate of mortality and morbidity, and the incurable nature of the disease, primary malignant brain tumor patients are referred to palliative care services and hospice quite late. One study noted that 22.5% of the study sample entered hospice within 7 days of death, 35% within 14 days, and 59% within 30 days of death [47]. The same authors also found that male gender, lower socioeconomic status, and lack of a primary care provider were risk factors for late hospice referral.

Hospice services are highly regarded by families and described as invaluable [95]. They provide physical assistance, guidance with decision-making, and help allowing patients to die in their own homes. Notably, there may be practical obstacles to hospice care – often caregivers can have difficulty findings the services or meeting the criteria for services [95] (See Chap. 16 "Hospice and End of Life Care in Neurologic Disease").

Education Agenda

There remains a need for education within the neuro-oncology community on palliative care and how it can be integrated into the overall management of malignant brain tumor patients. Despite a high symptom burden, these patients receive fewer palliative care services than other cancer populations, including advance directive and end of life planning [103–105]. The perception of palliative care as "giving up" and confusion with hospice and end of life care is common and makes it harder to address with patients and families. We need to educate providers involved in any aspect of the journey of the brain tumor patient, from the surgeon to the radiation oncologist, to bring up the "goals of care" discussion as often as possible. Practical aspects of care, such as how and when to refer to hospice and how to guide families through advance directives, remain areas where education is also needed.

Research Agenda

The impact of palliative care access on the quality of life and survival of primary brain tumor patients is still being explored and is not as clearly defined in the field of neuro-oncology as it is for systemic cancers. There is an urgent need for early intervention with palliative care because, when utilized, it has been helpful in setting goals of care and advanced directives, and helping manage symptoms of dehydration, urinary retention, edema, and seizures, among others. There is also a need to validate or develop appropriate outcome measures for this population, including quality of life, as brain tumor patients may differ in important ways from other cancer or neurologic conditions. Once we have a better measurement, we will need to find pharmacological and non-pharmacological ways to improve quality of life. Early integration of palliative care into neuro-oncology practice is still a work in progress and we need additional studies to demonstrate how the timing of this intervention affects survival and quality of life in the brain tumor population. We need to have a better understanding of what support and education caregivers need and find ways to fulfill these needs. Finally, we must continue to explore how we help our patients and their families have a meaningful life review and transition to hospice with a peaceful death.

Case Concludes

Eliza's doctors are aware that while quality of life is very important to her, she also wants to use every tool available for her to extend her life and time with her family. This is why a ventriculo-atrial shunt is offered, and the family asks that the medical providers proceed with this. Placement of this shunt in a terminally ill cancer patient is controversial and is seen by many as inappropriately aggressive. It is, however, consistent with the patient's own goals of care.

She wakes up from surgery alert and at her baseline, grateful to be alive. She proceeds to receive systemic methotrexate followed by whole brain radiation. Despite the side effects of the treatments, she continues to enjoy every day with her family. She sets and fulfills many goals – celebrating each milestone and holiday. Eliza is able to celebrate Christmas, her favorite holiday, with her whole family. Spring comes and she is able to take a trip down to her favorite city with her children and grandchildren. She celebrates her birthday with great enthusiasm, and visits the local tulip festival with her best friend.

A month after her birthday she is admitted to the hospital for dyspnea. After failing thoracentesis for malignant pleural effusions, she finds that her right lung is thick with cancer. Drastic surgery can be done, but Eliza decides she does not want such surgical intervention. Consistent with her wishes, she is discharged home on hospice.

A few days after discharge, she passes away peacefully at home, surrounded by her family and friends. It has been 14 months from her diagnosis, and she has lived 6 months past the "expected prognosis" given to her.

Take Home Messages

- Patients diagnosed with malignant brain tumors continue to have high morbidity and mortality, despite advances made in brain tumor therapies in the last several decades.
- Because tumors infiltrate rather than acutely destroy brain parenchyma (such as with trauma or stroke), symptoms and signs are subtler, which often leads to a delay in diagnosis.
- A new diagnosis of headache or a distinct change in headache pattern in a patient over the age of 50 should be considered a red flag, though the most common brain tumor headache type is indistinct from migraine
- For brain metastases patients, if there are multiple (>3) lesions, surgical resection is not considered feasible and whole brain radiation therapy has historically been the recommended treatment, though has fallen out of favor more recently due to an unexpected high rate of neurotoxicity.
- Because cognitive decline and frontal lobe "neglect" are so common in brain tumor patients, early discussion involving the surrogate and education about difficulties in cognition and language are essential if we are to elicit goals and preferences.
- Goals of care conversations are challenging in patients who are rapidly declining cognitively and who may suffer difficulties with language, memory or personality. Up to 40% of brain tumor patients do not have discussions about treatment preferences, health care proxy, hospice or resuscitation during their illness.
- No statistically significant benefit has been found for the prophylactic use of AEDs in patients, including those treated with a craniotomy.
- Phenytoin is an inducer of hepatic metabolism and can reduce the half-life and bioavailability of the commonly used drug dexamethasone, and dexamethasone can decrease phenytoin levels. AEDs that induce the cytochrome P450

enzyme system can impact the metabolism of various chemotherapy agents potentially decreasing the serum levels by 25%.

- Steroid management. In general, the recommended practice is to start as low as possible and to taper steroids as quickly as possible, given the side effects associated with long-term use.
- Confusion, progressive somnolence and coma are prominent symptoms in patients nearing death and are due to increased intracranial pressure and mass effect, herniation, seizures, sepsis, dehydration or other metabolic derangements. We advise against artificial nutrition or hydration at this stage, and reassure caregivers that our patients do not feel distress from lack of food or water, and in fact may only be able to tolerate ice chips or sips of water if and when awake.

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Child Neurology

10

Monica E. Lemmon and Renee D. Boss

Case

Gail and Taylor just had a new baby, a daughter. After a normal pregnancy, Gail suffered a uterine rupture, such that their daughter's brain lost oxygen and blood flow for about 30 min. When she was born, she did not have a heartbeat and was not breathing, but the neonatal team initiated cardiopulmonary resuscitation and brought her to the neonatal intensive care unit. There, she received therapeutic hypothermia for 3 days. During that time, she developed seizures and required multiple anticonvulsants. At 4 days old, she remains critically ill and intubated, and is not breathing over the ventilator. A brain MRI on day of life 5 revealed bilateral basal ganglia injury and extensive cortical injury, consistent with severe hypoxic ischemic injury.

Questions for discussion:

1. *How will you discuss predicted neurologic prognosis?*
2. *How can you facilitate shared decision making with this family?*
3. *Should Gail and Taylor choose to take an approach focusing on comfort over longevity, what added supports should be made available?*

Children with neurologic disease and their families have a diverse set of palliative care needs. Diseases impacting pediatric neurology patients range from congenital conditions diagnosed in the fetal period to acute brain injury in otherwise healthy teenagers. Child neurologic conditions not only span fetal, neonatal, and child life (Table 10.1), but also different stages of family life. Having a neurologic condition at birth or as a young person presents unique considerations regarding autonomy, personhood, and how to balance child and family needs. In addition, the burden of making treatment decisions typically falls to parents, who may be suffering and/or grieving amidst a recent or worsening diagnosis.

While this chapter attempts to cover a wide range of conditions and age groups, it is not exhaustive. Here, we will focus on those

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Table 10.1 Scope of pediatric neurologic conditions across pregnancy, infancy, childhood, and adolescence

	Representative conditions
Prenatal	Congenital brain malformations (i.e. anencephaly, schizencephaly)
	Neuromuscular conditions (spinal muscular atrophy, fetal akinesia)
	Destructive brain conditions (hydranencephaly, perinatal infection)
Infant	Complications of prematurity (intraventricular hemorrhage, periventricular leukomalacia)
	Neonatal encephalopathy
	Neuromuscular conditions (spinal muscular atrophy, fetal akinesia)
	Neurologic complications of congenital heart disease (stroke, hemorrhage)
Childhood and adolescence	Neuro-oncologic conditions
	Neuromuscular conditions (Duchenne muscular dystrophy)
	Traumatic brain injury
	Epilepsy (refractory epilepsy, epileptic encephalopathy)
	Neurodegenerative disease
	Neurovascular conditions (stroke, venous sinus thrombosis, arteriovenous malformations)
	Neurologic complications of chronic illness

A number of representative conditions can present throughout the life of a child; this table is meant to highlight common entities encountered at each life stage

conditions that may not have an adult correlate, and give an overview of the elements of palliative care specific to children with neurologic disease and their families. These include (1) prognosis, (2) symptom management, (3) family support, and (4) end of life care.

Estimating and Communicating Prognosis

Neurologic prognosis may have a profound impact on parents' decisions to initiate, forgo, or withdraw life-sustaining therapies. Accurate estimation and effective communication of prognosis are among the most important and complex jobs a pediatric neurologist performs.

While prognostic tools exist for a number of pediatric neurologic conditions, prognostic uncertainty is a reality of care for the vast majority of children with neurologic disease and their families. Here, we will outline a framework to optimize prognostication and manage prognostic uncertainty in pediatric neurologic conditions.

Prognostic Tools

There is tremendous interest in defining blood, urine, and Cerebrospinal fluid (CSF) biomarkers in pediatric neurologic conditions; to date, definitive biomarkers of brain injury severity remain elusive [1]. Similar to adult neurology, Magnetic Resonance Imaging (MRI) is a popular diagnostic and prognostic tool for a variety of conditions. Advanced neuroimaging techniques can add prognostic value in certain conditions. For example, MR spectroscopy has been suggested to enhance prognostic yield in neonatal encephalopathy [2, 3]. Continuous Electroencephalogram (EEG) is an important tool for neurophysiologic monitoring in children with neurologic diagnoses. In neonates and infants, quantitative and amplitude integrated EEG offers bedside monitoring to aid in seizure detection and monitoring of encephalopathy. Continuous or amplitude integrated EEG background may add prognostic value in certain conditions, including neonatal encephalopathy [4, 5]. Near infrared spectroscopy (NIRS) offers real-time information about cerebral blood flow and is currently used—primarily in children with cardiovascular conditions and infants in the neonatal intensive care unit—to screen for emerging pathology. However, the value of NIRS in prognostication is mixed [6, 7].

Genetic testing, including next generation sequencing, has become increasingly available with improving turnaround times. For children with neurologic disease of unclear etiology, ranging from congenital malformations in newborns to older children with neurodegenerative disease, next generation sequencing may represent the most efficient way to arrive at a diagnosis. As technology improves, and cost becomes more manageable, use of genetic testing in pediatric

neurology will likely increase. Currently, the diagnostic yield of whole exome sequencing approaches 40% in carefully selected populations [8]. While this improved yield has treatment implications for many children, the likelihood of cure following diagnosis is typically low. Nonetheless, next generation sequencing frequently has important implications on treatment decisions for individual children. For some, decisions may be delayed while awaiting genetic confirmation of disease. For others, a confirmed genetic diagnosis may prompt decisions about continuation vs. withdrawal of life-sustaining treatment. Many families face ongoing prognostic uncertainty due to genetic variants of unknown significance or limited certainty of how a known genetic diagnosis with a heterogeneous natural history will manifest in an individual child.

Limitations of Prognostication

Prognostication in pediatric neurology is complex, and outcomes are mediated by neuronal plasticity, home environment, and early intervention. For many pediatric neurology conditions, limitations in available data complicates prognostication. First, prognostic studies can be limited by self-fulfilling prophecies, especially for conditions in which the primary mechanism of death is withdrawal of life-sustaining treatment, for example in the neonatal period (see also Chap. 12 "Prognostication") [9]. Second, pediatric outcome data are limited by the prevalent use of composite outcomes. For example, because the clinical conditions are relatively rare, many studies in pediatric neurology use a primary composite outcome that includes some combination of moderate neurodevelopmental disability, severe neurodevelopmental disability, and death. Neurodevelopmental disability itself is a composite outcome and typically includes patients with cerebral palsy, developmental delay, blindness, or deafness [10–12]. That is to say, in a trial that uses a composite outcome of death or major neurodevelopmental disability as its primary endpoint, death is valued equivalently to deafness. It is unlikely that parents or clinicians value these outcomes as equal. While many trials offer subgroup analyses and secondary endpoints that attempt to further parse the groups, their ability to do so has been limited by inadequate power.

Communicating Prognostic Uncertainty

A fundamental skill within pediatric neurology is communicating prognostic uncertainty. Prognostic uncertainty can be extremely distressing for families, regardless of condition [13, 14]. Helpful ways to frame uncertainty, and other communication strategies, can be found in Chap. 11 "Communicating Effectively", and Chap. 12 "Prognostication". Outcomes should be described with limited use of jargon, or veiled terminology. For example, discussion of therapy needs or the need for children to be seen in "developmental clinic" should not be a substitute for direct discussion of cerebral palsy or blindness [15]. Instead, discussion of expected infant and potential family outcome should include concrete examples of expected function, tailored to outcomes that matter most to individual families. Most conversations should start with an exploration of what the family or patient understands about their specific condition, prognosis, or treatment options, as well as prior relevant experiences.

For Gail and Taylor in the case above, conversations regarding their infant's prognosis could begin by exploring their prior experience with disability, specifically asking about their experience with people in wheelchairs, with feeding tubes, or with cognitive disability. Many parents of young children are young themselves and may have limited life exposure to illness or disability. In addition, new parents are expecting to bring home an infant who is totally dependent on them and may not understand what lifelong dependence would mean. Clinicians should tailor their discussion of prognosis with concrete examples of expected child function, including feeding, walking, and interacting; and the potential impact on family life. For Gail and Taylor, that might

begin with a description of expected motor outcome, given their daughter's pattern of basal ganglia injuries, discussed in the context of best case, worst case, and most likely outcome, and inclusive of several time horizons (e.g. 6 months, 5 years, or 10 years) [16, 17]. The clinician might then guide a discussion of how expected disability might be particularly relevant to their family, for example, whether their child could attend regular daycare or would require an around-the-clock health provider. The impact on siblings should also be discussed. For many families, these topics may be covered in a series of discussions, as clinical information evolves.

Symptom Detection and Management

Pain

A number of non-pharmacologic and pharmacologic treatments exist to address pain in pediatric neurology patients (Table 10.2). Children with neurologic disease are at risk for under-recognized (and thus, untreated) pain and discomfort because they may have minimal or no verbal or sign language and may have developmentally discordant expressions of pain [18]. Clinicians at all levels of training perceive that infants and children with neurologic impairment experience less pain than those without neurologic impairment [19]. A number of scales that assess pain rely heavily on behavioral components such as crying, body movements, and facial expressions [20–23]. These components may not be useful in neurologically impaired children or those who are on sedating medications including anticonvulsants [24]. Assessment is further complicated in pediatric neurology patients who experience symptoms of withdrawal in the setting of a prolonged ICU course or neonatal abstinence syndrome. Finally, there are ongoing concerns that both pain and analgesics may negatively impact the developing brain, a concern particularly relevant to the infant or young child with neurologic disease [25, 26]. Often the best judges of whether an individual child with neurologic disease has discomfort or pain are their daily caretakers, usually their parents. Even for non-verbal patients, caretakers can assess whether the child's behavior deviates from baseline or is consistent with increased agitation or lethargy. When possible, clinicians should partner with parents to identify distressing symptoms and institute non-pharmacologic strategies that may offer benefit without adverse effects.

Non-pain Physical Symptoms

Unexplained irritability can occur in neurologically compromised infants and may require a combination of pharmacologic and non-pharmacologic therapies. For example, infants with brain injury may benefit from frequent swaddling or low-stimulation environments, in addition to pharmacologic treatment of irritability with, for example, gabapentin [27].

Difficulty managing secretions is common in children with neurologic disease; glycopyrrolate and, when available, botulinum toxin injection to the salivary gland can be effective treatment strategies [28].

Seizures can be much more difficult to detect in children, especially neonates, and represent an important source of parental and patient distress. In patients with seizures, anticonvulsants can both minimize seizure burden and optimize comfort. A trade-off can exist between anticonvulsant use and level of alertness and medication burden; for these patients, parents and clinicians must decide together how seizure freedom figures into the child's quality of life.

Infants being treated with therapeutic hypothermia experience *shivering*. While the level of discomfort associated with shivering is not known in infants, data from adult patients shows that shivering and sensations of cold are uncomfortable and should be avoided [29]. There are additional concerns that shivering may add to metabolic demand [30, 31]. Morphine or clonidine are often used to control shivering, with the consideration that during therapeutic hypothermia, morphine clearance may be decreased [32, 33].

Table 10.2 Pharmacologic strategies to minimize discomfort and manage symptoms

Site of care	Route	Symptom	Medication
Delivery room	Oral	Pain or distress	Acetaminophen (also rectal)
			Midazolam (also IN or SL)
			Lorazepam (also SL)
			Morphine (also SL)
			Oral sucrose[a]
Intensive care unit	Oral	Pain or distress	Acetaminophen (also rectal)
			Oral sucrose[a]
			Midazolam (also IN or SL)
			Lorazepam (also SL)
		Irritability	Morphine (also SL)
		Irritability	Gabapentin
		Spasticity	Clonidine
		Increased secretions	Baclofen
			Glycopyrrolate[a]
	IV	Pain or distress	Midazolam
			Lorazepam
			Morphine
			Fentanyl
	IV continuous infusion	Pain or distress	Midazolam
			Morphine
			Fentanyl
	Topical	Pain	Fentanyl patch
			Clonidine patch
Home	Oral	Pain or distress	Acetaminophen (also rectal)
			Sucrose
			Midazolam (also IN or SL)
			Lorazepam (also SL)
		Irritability	Morphine (also SL)
		Irritability	Gabapentin
		Spasticity	Clonidine
		Increased secretions	Baclofen[a]
			Glycopyrrolate[a]
	Topical	Pain	Fentanyl patch
			Clonidine patch

IV intravenous *IN* intranasal, *SL* sublingual
[a]Most relevant in infancy; oral sucrose may be most useful to treat acute mild pain

Psychological, Social, and Spiritual Distress

The presentation and incidence of psychological, social, and spiritual distress is best described in older children; relevant data in young children and those with profound neurologic impairment are limited.

Children with neurologic disease, including epilepsy and migraine, are at risk of co-morbid depression or anxiety [34–36]. Psychological distress is likely compounded amidst hospitalization. Pediatric patients with complex medical needs risk social and school isolation. Children with epilepsy have described feelings of vulnerability and discrimination, stemming in part from life disruption, limits on social freedom, and social stigma [37]. Instances of prolonged hospitalization may worsen these outcomes, and many children may be separated from their family unit for long periods of time [38, 39].

Supporting the Family

In pediatric neurology, parents and caregivers face unique challenges in caring for their child with neurologic disease. Many of these children are born with their conditions, and families experience the grief of losing a "normal" child. The daily care burdens for these children may require parents to quit their jobs indefinitely. In many cases, children have lifelong needs. Insurance and rehabilitation benefits can be quickly exhausted, causing significant financial strain. For children with profound neurodevelopmental impairment, children may outlive parents' ability to care for them, prompting consideration of long-term care. Here, we will outline how clinicians caring for pediatric neurology patients can provide added support around communication, shared decision making, and family needs.

Communication

Conditions or situations that may prompt a serious conversation are outlined in Table 10.3. Many neurologic diseases that occur in childhood require ongoing, longitudinal conversations about advance care planning, choices about life-sustaining treatment, and the potential for lifelong disability. For most neurologic conditions that occur in childhood, these should occur at diagnosis and then iteratively at periods of significant clinical worsening. Consideration of life-sustaining therapies, including gastrostomy tube or tracheostomy placement, should be accompanied by a multidisciplinary conversation between parents and clinicians; neurologist presence in these conversations is critical as families consider how to make choices about treatment in the face of potential disability. Specific symptoms that should prompt clinicians to start or revisit a serious conversation about life-sustaining therapy might include new swallowing difficulties or failure to thrive, both of which may suggest the requirement of new feeding support. Loss of developmental milestones, such as losing the ability to talk, walk, or see, should prompt clinicians to revisit conversations about quality of life and goals of care. Major transitions in care—team changes in the acute setting, or transition from pediatric to adult health care providers in the outpatient setting—serve as additional opportunities to share meaningful conversations with patients and families.

Table 10.3 Triggers for serious conversations in pediatric neurologic disease

Diagnosis
Congenital brain malformations
Severe perinatal asphyxia
Neurodegenerative conditions
Predicted need for lifelong care
Predicted visual or hearing impairment
Periods of clinical worsening
Loss of developmental milestones
Failure to thrive
Swallowing difficulties
Requirement for multiple anticonvulsants
Anticipated requirement of life-sustaining therapies
Prolonged mechanical ventilation
Prolonged inability to feed orally

Families caring for children with neurologic disease often interact with multiple clinicians at varied sites of care, including local, regional, and specialized medical centers, as well as various inpatient and outpatient clinicians. This fragmentation of care can lead to incomplete and inconsistent communication, and parents may lack a single provider or provider team with whom they can build a trusting relationship. A large proportion of patients with neurologic disease receive a significant amount of their care in the critical care setting—a chaotic environment that focuses on saving lives and demands added attention to the delivery of consistent and comprehensive communication to families. Families of patients with prolonged hospital admissions, who experience multiple team and care transitions, are at risk of feeling increasingly less informed over time [40]. A model in which complex patients are assigned a primary physician and/or nurse may improve continuity and has been adopted by approximately 25% of neonatal and 40% of pediatric ICUs [41]. Given the complexity of care for pediatric neurology patients,

detailed communication about complex therapies risks undermining parent capacity to see the "big picture" [14].

Parents of neonatal intensive care unit graduates have provided simple guidelines for effective communication between clinicians and parents. These guidelines are equally relevant for families in pediatric neurology and include referring to children by their given names, providing a consistent treatment approach, acknowledging the family's role on the medical team, and tailoring language to each family's needs [15]. Family-centered rounds are another opportunity for neurologists and families to have joint discussions. One randomized controlled trial suggests that parental presence during rounds is acceptable to parents and clinicians, and parents report increased knowledge about their infant's care, improved communication, and increased collaboration [42]. Dedicated and regular family conferences between family members and the health care team can be used to ensure families have access to the "big picture" of their child's medical course and reduce the risk of inconsistent information. Data from adults show that family meetings within the first 72 h of ICU admission results in decreased length of stay, reduced mortality, and increased consensus between clinicians and families [43–45].

Shared Decision Making

Parents and clinicians caring for children with neurologic diagnoses must make challenging decisions about care; these decisions frequently occur in the absence of clear information about the child's experience of quality of life or child assent. *Should we consider tracheostomy tube placement in a child with profound traumatic brain injury? Would a gastrostomy tube improve quality of life for a child with spinal muscular atrophy?* Such fundamental treatment decisions require clinicians to communicate effectively with families about their role in determining what is best for their child. It also requires frank discussion about parents' perception of what a life worth living looks like for their child.

Traditional shared decision making frameworks are modeled for adult patient or surrogate decision makers. Surrogate decision making for adults, however, differs in several important ways from parent decision making. Family members of critically ill adults often base decisions on their loved one's prior statements, presumed preferences, or quality of life before the illness; these concepts are not as straightforward in the pediatric setting. Parents are far from objective surrogates, and it can be unclear how, or whether, to disentangle the parents' interests from those of their child. In some cases, clinicians may perceive that parents are not acting in their child's best interests, making it difficult to determine the child's best advocate. It is important to note that the values that guide parents' decisions about life-sustaining therapies for their children may differ from those of clinicians. In a multicenter qualitative study of bereaved parents, parents of infants who died prioritized their religious and spiritual beliefs, and their hope, as the main drivers of decision making, and clinician predictions of morbidity and death were less important [46]. Poor alignment between parent perception of future outcomes and clinician understanding of prognosis can result in significant moral distress among staff [47, 48].

Young parents rarely have prior experience making serious medical decisions for a loved one, may have no prior experience with serious illness, and may have ill-defined values relevant to health and disability. This creates unique challenges for clinicians who wish to share values-sensitive decisions with these families. For Gail and Taylor, in our case above, clinicians may wish to begin conversations about decisions with a discussion of prior experience with medical decision making and values related to health and disability. A variety of decision tools may help young parents prepare for serious discussions about their child. The Seattle Decision-Making Tool, for example, is designed to help families articulate and prioritize their health-related goals and values [49]. Question prompt lists, or other communication interventions, may be a particularly useful way to help young families find words for questions that matter to them [50–54].

In certain situations, it may be appropriate for clinicians to make a recommendation about treatment intensity that is in accordance with parent values and preferences, recognizing that patients and surrogates likely value physician recommendations heavily [55].

Family Needs

Pediatric neurologic disease impacts a patient's entire family. Parents may have difficulty disentangling the needs of their ill child from those of other children and their personal needs [13]. Logistical concerns—time off work, lost income, medical bills—may cause added distress.

Parents are at risk of poor health outcomes of their own; for example, up to one-quarter of parents caring for critically ill infants experience post-traumatic stress symptoms [56–58]. Tailored parent support can reduce parental anxiety, depression, and stress [59, 60]. Feelings of guilt and regret may be present for many parents, especially those for whom neurologic injury arose at birth or is related to a congenital condition [13]. Parents are additionally at risk of spiritual distress; multiple studies have shown that parents' religious and spiritual beliefs are central to their coping with their child's illness. Pastoral care can offer spiritual support and help families make sense of how to consider their spiritual beliefs when making decisions for their child. Further, because many pediatric medical services are regionalized to large cities, parents often have to travel long distances to bring their child for medical care. Parents may benefit from logistical resources such as assistance with transportation, finances, and local housing.

Parents may be unsure of if and how to discuss their ill child's course with healthy siblings. This is a longitudinal task, as the siblings' understanding and worries will evolve as they enter different developmental stages. Sibling support, frequently offered through child life services and specialty palliative care programs, can help parents and children cope together as a family.

End of Life Care

While many aspects of end of life care are discussed elsewhere, here we will focus on those aspects particular to caring for dying children and their families.

Making Memories

Parents of children with pediatric neurologic conditions may have had little time to make memories with their child. For parents of neonates, a lifetime of meeting and loving their child may be condensed into days. For parents of older children with chronic neurologic conditions, typical family rituals or child milestones may not have occurred. Many parents value the opportunity to make memories with their child at the end of life [61, 62]. Examples of memory-making might include the creation of photographs, videos, molds, and scrapbooks. Memory boxes, which include mementos from a child's life, can offer additional tangible reminders of a family's time with their child. For families prenatally diagnosed with neurologic disease, prenatal memory-making might include 3D ultrasounds, ultrasounds that incorporate additional family members, and the creation of a birth plan that allows families the opportunity to spend time with their infant. In the midst of critical illness, clinicians can provide opportunities for parents to interact with their child, including touching and holding, reading books, bathing, and rituals of naming, dedication, or baptism.

Care of the Family

Most parents of children who die are relatively young themselves and rarely have participated in end of life care or decision making. Some have not even experienced the death of a loved one. These parents may require added preparation and support as death approaches.

Clinicians caring for parents of dying children should learn how much parents would like to know about the specifics of what may occur as

death approaches. Child life specialists, who are professionals with training and expertise in helping children cope with illness and hospitalization, are an important family resource. Child life clinicians can help prepare siblings for what they may see if they visit and can help parents find words to discuss illness with other children. Child life specialists may also be helpful to young parents themselves. Clinicians must ascertain whether specific cultural or religious actions, such as baptism, are desired before death. Parents and families should be provided with a private space, without limits on time, to grieve following death; this can require exceptions to hospital policies which may require patient bodies to be transported to the morgue shortly after death. Guidance from social workers and/or palliative care clinicians on how to make arrangements for a funeral may be appreciated; often local funeral homes will provide discounted services for children. If relevant, options for autopsy or organ donation should be presented to the family. Autopsy and/or perimortem genetic testing may be particularly relevant to children with neurologic conditions, as it may provide diagnostic clarity that could have implications for future childbearing.

Bereavement

Support around a dying child must continue beyond death; follow up with families is critical [63]. Physicians may do this via telephone, a condolence letter, or attending the child's funeral [64]. Physicians can also offer to meet with families to discuss results of the child's autopsy or tests pending at time of death [65]. Parents are likely to face sustained challenges as they transition back into their community. Society is often less comfortable with the death of children, and parents may be isolated in their grief. Mothers grieving a pregnancy loss may require enhanced support, as their body recovers from childbirth and serves as a physical reminder of recent pregnancy. Clinicians can offer counseling to parents around how to share information about their child's death with children and family members, as well as colleagues or friends. Grief is often retriggered by milestones – a new pregnancy, siblings reaching the age of the deceased child, a new school year without their child. Formal bereavement programs may offer support groups, hospital memorial services, or anniversary acknowledgements. In the follow-up period, clinicians should review the events surrounding the child's death, and autopsy findings if relevant.

Palliative Care Consultation

Regardless of prognostic certainty, children at risk of serious neurologic impairment all face the possibility that cure is not possible. Families attempting to understand and weigh information received by clinicians may require an added layer of support, best facilitated by the involvement of the palliative care team. Chronic care teams, which are often led or staffed by palliative care clinicians, are additionally available at a growing number of institutions [66]. Early introduction of enhanced support for all high-risk children ensures that those patients at risk of a devastating outcome receive timely services, including transition to outpatient or home hospice services where relevant. Given that prognostic uncertainty is often an ongoing challenge for families, palliative care providers can facilitate coordination between the medical home, hospice, and specialists, and provide continuity during readmissions and clinic visits [67].

Palliative care clinicians can additionally provide added support for both acute and chronic pain management, including pain management for cognitively impaired and nonverbal patients who may have recalcitrant pain. Bereavement support is best performed by clinicians with experience caring for families following a child's death; palliative care clinicians are well-suited to this task.

Research Agenda

As highlighted in this chapter, there is a critical need for rigorous research in palliative care within pediatric neurology. To effectively study

these topics will require the effective use of complementary methodologies, including qualitative and mixed methods studies, interdisciplinary teams, and multicenter collaboration.

First, the majority of pediatric neurology conditions lack accurate prognostic models. Prognostic studies should be adequately powered to detect the range of the most severe outcomes experienced by patients and families, and ideally study outcomes identified by families as most important. Registering prognostic studies, as has been suggested by others [68], would allow meta-analyses access to primary data and strengthen study conclusions. In primary efficacy studies, composite outcomes must be avoided when feasible and should include detailed information about the nature of death and treatment decisions.

Second, despite the frequency with which neurologists must discuss neurologic prognosis with families, there is little data on how to do this well, and its impact on parent decision making or psychological outcome. Next steps include defining how discussion of neurologic prognosis occurs in current clinical practice, followed by the development of frameworks to discuss neurologic prognosis. Communication and decision making interventions, including the use of question prompt lists and decision support tools, should be adapted to suit the needs of pediatric neurology patients.

Third, research around symptom detection and management needs to start with the development of pain detection scales or biomarkers suitable for children with an abnormal neurologic exam [69]. Next steps include defining the current use of sedatives and analgesia in children with neurologic conditions, and their impact on injury repair and brain development.

Finally, we must work to define and study models of palliative care delivery. We propose an integrated, multidisciplinary palliative care approach to address the specific needs of pediatric neurology patients and their families. While many pediatric neurology patients will require specialized palliative care support, all patients can benefit from a baseline level of enhanced support, with formal palliative care team involvement reserved for the most challenging cases. In other words, pediatric neurology training needs more formal palliative care and communication training, as well as screening tools for early identification of palliative care needs. We would additionally advocate for an increased number of palliative care clinicians with dedicated training in neurology, to help guide the development of symptom management order sets, clinical pathways, and communication tools.

The growing presence of palliative care within pediatric neurology is encouraging. As we consider ways to improve our care of children with neurologic disease, we should leverage the complementary expertise of both fields to enhance the care of our patients and families.

Take Home Messages

- Life-limiting and life-altering pediatric neurology conditions span fetal life, infancy, childhood and adolescence.
- Both estimating and communicating prognosis for children with neurologic prognosis is complex, and prognostic uncertainty can cause significant parent distress. Clinicians need skills to provide families with accurate, clear, and decision-relevant information about outcomes.
- Parents caring for children with neurologic disease have unique palliative care needs that require targeted support.
- More education and formal training is needed for pediatric neurologists in prognostication and prognosis communication, symptom management, communication skills, and shared decision making.
- Research priorities to enhance care for families of pediatric neurology patients include (1) symptom identification and management, (2) neuroprognostication, (3) enhancing shared decision making, and (4) communication interventions.

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Part II

Improving Communication and Treatment Decisions

Communicating Effectively

11

Jessica M. McFarlin and Joshua S. Barclay

For patients with a serious illness, palliative care starts at the time of diagnosis. High quality communication with patients and families is a key tenant of providing palliative care to patients with neurologic illness. Core communication skills include delivering serious news regarding diagnosis, effectively estimating prognosis, navigating treatment choices with shared decision making and, finally, preparing families to make choices near the end of life [1]. Neurologists must consider both the biomedical and the psychosocial effects of the illness on the patients and their families. Learning to engage in thoughtful, empathic conversations leads to ensuring that treatment plans match the patient's goals and values. Excellent communication improves a patient's adjustment to illness, lessens physical symptoms, increases treatment adherence and results in higher satisfaction with care [2].

Excellent communication in the setting of serious illness is hard, and patients with neurological disease have reported unmet informational and emotional needs during encounters with neurologists [3]. Surrogate decision makers are often displeased with the frequency of communication, the limited availability of attending physicians, and report feeling excluded from discussions [4]. When family meetings do occur, surrogate decision makers report inadequate understanding of diagnosis, prognosis, and treatment plans. The effects of poor communication can be deleterious to patients and their family members including prolonged ICU care and increased psychological distress, and interventions to improve communication can improve the quality of care [5, 6].

Although multiple professional societies such as the American Academy of Neurology and the Accreditation Council for Graduate Medical Education emphasize communication with patients and families as a key component of high quality care, few neurologists receive formal training during residency about communication [7, 8]. Doctors who routinely deliver difficult news admit that they are unsure of their ability to properly perform this task [9]. Critical care fellows report not feeling adequately trained to conduct family meetings [10]. Intensivists worry that high quality family meetings are time consuming and difficult to do in a busy ICU [11].

Good communication includes understanding the patient's perspective and identifying and responding to their emotions. Good communication can be taught. Teaching tools and standardized strategies have increased communication skills amongst oncology fellows [12]. Skill

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workshops can improve the ability of residents and oncologists to recognize emotional cues when delivering bad news [12]. Importantly, clinicians who feel comfortable with their communication skills report less job distress and had less emotional stress and burnout [13]. This chapter outlines key principles of good communication that are fundamental to providing high quality palliative care. Using clinical cases, we will highlight tools that can be used to ensure empathic communication throughout a multitude of encounters with patients facing serious illnesses.

General Communication Skills

In the setting of serious illness, the critical communication task of a neurologist is to integrate medical facts with the emotional, psychological and social realities of their patients and families [14]. High quality communication considers both the agendas of the physician and the patient. Neurologists must share information: explaining the diagnosis, treatment options and prognosis. The patient may have a more personal focus: what it means to be ill, the effect on family, their need for information or the degree to which they want to participate in the treatment plan [15]. The communication task is to address both agendas and create treatments plans that match the goals and values of the patient, resolving conflicts that might occur [16].

Several general skills improve communication between patients and neurologists. These patient centered behaviors help ensure correct information exchange, build trusting partnerships with patients, decrease utilization of health care resources and may facilitate recovery from illness [17]. Both verbal and nonverbal behaviors are important. The following clinician behaviors both aid in information transfer and are linked to increased patient satisfaction [18]:

- Prepare in advance to understand prognosis, treatment options
- Provide a private, quiet, comfortable space
- Sit down during the interview
- Maintain eye contact
- Minimize medical jargon
- Ask the patients about their thoughts and feelings
- Ask open ended questions
- Check for patient understanding
- Use empathy to acknowledge patients concerns
- Involve the patient in decision making based on the needs of the patient

Communication Tasks in the Setting of Serious Illness

Task One: Delivering Serious News and Attending to Emotions with Empathy

Mr. H is a 66 years old, retired truck driver who has a 5-month history of weakness. His primary care physician is concerned he may have a serious neuromuscular illness. On his first visit with you the history, physical and EMG are consistent with a diagnosis of Amyotrophic Lateral Sclerosis. Following the study, you meet with him to discuss that his illness and workup are consistent with ALS. Mr. H is accompanied by his wife of 30 years.

Delivering serious news is a complex communication task and the delivery has a lasting effect on patients and families. It requires neurologists to balance expert delivery of cognitive data with careful attention to emotional responses. Delivering bad news is a psychologically difficult task for physicians [19]. Thoughtful discussions can be beneficial for both the patient and clinicians [13]. Patients and families benefit from the support of this caring relationship, have improved understanding of diagnosis, [20] and may avoid interventions that would not advance their goals [21].

Discussing serious news requires the transmission of a large amount of medical data. Patient satisfaction increases when the information is

given at the patient's pace and the level of detail that they are comfortable with receiving [22]. Families want bad news to be conveyed in a truthful and direct manner, but report that bluntness may take away hope [23]. Finally, they value time to ask questions and check for comprehension.

One specific communication strategy, Ask-Tell-Ask (Table 11.1) allows for the information to be calibrated to what patients and their loved ones know, what kind or amount of information they may be ready or willing to know, and how they may feel or think about their health.

Table 11.1 Ask-Tell-Ask strategy for serious news

	Neurologist	Patient
Ask	"Mr. H, I know you had conversations with your primary care provider about your weakness before we met to do the study. Please tell me, what did you and she discuss about?"	"She told me the weakness could be a lot of things. That is why she got the MRI and sent me to you for the nerve test. She mentioned that she was a little worried about Lou Gehrig's disease but that you were expert at knowing that"
Tell This is the headline	"You have a good understanding of why she wanted me to see you. I'd like to tell you the results of the study. Unfortunately, your weakness is caused by ALS, also known as Lou Gehrig's disease	"Are you sure? We thought there was very little chance that would be the diagnosis" (*Patients are likely to have an emotional response to serious news. The next section discusses how to respond with empathy*)
Ask	"I know this is a lot of new information. And when it is serious I like to make sure I did a good job of explaining it. Can you tell me in your words what I told you so I can make sure I was clear?"	I guess there's no doubt now that I have ALS, which *is* Lou Gehrig's disease. I have heard that there's no cure for it and that's pretty much all I can take right now

The first ASK is a question that allows a patient to explain, in their own words, their understanding of the current condition in order to determine what information will be most helpful to the patient. It allows them to tell the story and not hear the doctor's reiteration of medical findings they already know. If family is also present it may be appropriate to gather their perspective as well. By actively listening to the patients and family perspective, a neurologist can better understand the level of health literacy, begin to gauge their emotional state and coping strategies, and with this understanding calibrate the news they are about to give at an appropriate level. After providing enough time to gather the perspectives, TELL the information that needs to be communicated. Families find too much detail overwhelming; it is therefore important to focus on *the headline* (Arnold RM, 2015, personal communication): the one to two key points that the family should take away from the conversation. The key points may include the results of a test, progression of disease or disclosing a poor prognosis. Once families have heard the news they will react with emotion that will need to be attended to (see next communication skill NURSE). The final "ask" in ASK-TELL-ASK is to check for understanding. If a family understands they can "teach back" the information. This final ask provides opportunity to clarify any misconceptions and gives insight into the emotional responses of the patient.

Hearing a worrisome diagnosis naturally leads to an emotional reaction. The news is accompanied by significant stress and naturally the emotional response may impede an individual's ability to process cognitive information and make it hard to make good decisions about what should be done next [24]. Continuing to give more information, rather than pausing to respond to emotions that accompany the news, may result in the patients hearing "nothing" after bad news. Patients can more fully process information when their emotional responses have been attended to.

Empathy is the process of recognizing an emotion and imagining what this must be like. The neurologist's ability to notice these emotional cues and respond empathically is a key

communication skill [25]. Data shows that physicians don't always recognize opportunities to respond to emotional cues [26]. Failure to recognize emotional cues and respond with empathy may result in misunderstanding of the diagnosis [20], an overly optimistic approach to prognosis, feelings of hopelessness, or a breakdown in trust between the clinician and patient. Empathic responses improve the family-clinician relationship and help build trust and rapport [27]. Well-placed empathic statements may help patients disclose concerns that help the physician better understand the goals and values of the patient. They can also help reduce feelings of isolation, express solidarity and normalize the thoughts and feeling of patients.

Neurologists can develop the capacity to recognize and respond to the emotional cues family members are delivering. These cues are the "data" that helps lead to an empathic response. Cues that are easy to identify may include crying or the use of emotional words such as "*shocked*" or "*sad*". But sometimes the emotional responses are more difficult to recognize. A patient may respond with extended silence. Patient's may continue to ask for specific cognitive information after hearing bad news such as "*How reliable is the test*?" or "*What could have caused this?*" It is natural to start answering these questions with more facts. However, if the questions come after bad news, they may be expressions of frustration or sadness rather than a request for more information. Resist the temptation to deliver more cognitive data and first acknowledge the emotion in the room by using an empathic statement.

The NURSE mnemonic illustrates effective empathic statements [14]. These five types of empathic responses can be used in any communication setting where an emotional response is noticed: name, understand, respect, support and explore. Table 11.2 provides guidance on using NURSE statements and offers specific examples. Emotions may not be cleared with one empathic statement. Providing silence can be a powerful way to allow patients space to process the news. Using "I wish" statements can help acknowledge sadness and show solidarity, for example "I wish the tests results had been better too." Or "I wish

Table 11.2 The NURSE Mnemonic for responding to emotions

Name	Naming the emotion that a patient appears to be having shows you are trying to be attuned to what is being experienced. Naming statements should be suggestive not declarative to avoid "telling" people how they feel	*This news must be very overwhelming*
Understand	We can only try to understand the emotions patients are feeling. Acknowledging this helps family feel heard and shows that you are trying to understand what they are going through	*I can't imagine how hard it is to hear this news*
Respect	Respecting their emotional response can communicate that their emotions are important. Praise is a way to show respect for someone's ability to cope with the illness or care for a loved one	*You all have done a wonderful job of researching this illness and asking questions*
Support	Statements of support can be varied depending on the trajectory of the illness. Support may be offered while waiting for test results, throughout the progression of an illness or when transitioning to end of life care	*We will be here to support you and your wife step by step*
Explore	Sometimes conversations may go off track or reveal information that is surprising to the physician or family. "Tell me more" statements allow the clinician to further explore what the patient or family may be attempting to understand. They also allow patients to further reflect on their emotions and think about what other pieces of information they may need from the clinician	*Tell me more about what is worrying you*

we had more treatments available." If the emotion does not dissipate the patient or family may need more time before moving on to discussing more facts about their illness. This is normal and the conversation can wait for another day. Reassuring the patient that they have your support to work through this news at their own pace is another way of expressing empathy.

Having a standardized approach to addressing the distress that follows serious news can increase physician confidence and improve patient participation in planning treatments [28]. One proposed strategy to deliver serious news is represented in the mnemonic SPIKES [29]. SPIKES is a six-step approach that allows for learning and teaching the skill of breaking bad news similar to learning and teaching other medical procedures such as a lumbar puncture. Use of such a protocol can help meet patient expectations regarding setting, the information given, and the emotional support throughout the conversation [30] (Table 11.3).

Table 11.3 SPIKES protocol

Overview	Behaviors	Statements
Setting	Ensure a private space	
	Have tissues available	
	Have seats for everyone involved (patient, family, clinicians)	
	Have uninterrupted time	
	Ensure the patient has opportunity to invite others to the meeting if desired	
Perception	Use open ended questions to determine the patients understanding of the medical situation	"What have your other physicians told you about your medical illness?"
	Notice the patients level of comprehension and medical vocabulary	or
	Actively listen to their perception to assess for misinformation, coping skills and involvement of other family members. The information you hear will be helpful as you discuss the serious news	"I want to make sure we are all on the same page, can you tell me in your words where things are right now with your illness?"
Invitation	Obtain permission to give the serious news	"Is now an OK time to talk about what the tests have told us?"
	Discuss information preferences with patient	or
		"Some people like all of the details and others prefer a big picture at first. Which do you prefer?"
Knowledge	Give the knowledge and information to the patient	"The tests revealed you have ALS, you may know it as Lou Gehrig's disease"
	Deliver information in small chunks, focus on the "headline" not the details	
	Avoid jargon	
	Stop after delivering the news and attend to the patient's response, which will likely be an emotional reaction	
Emotion	Address the patient's emotions with empathy	Use NURSE statements
Summary and strategy	Use "teach back" methods to ensure good understanding	"What questions do you have about this illness?"
	Ask open ended questions, not "Do you have any questions"	or
	Negotiate next steps with the patient in regards to when they may be ready to talk about treatments or prognosis. They may still be processing the emotion of the news and unable to move to developing a strategy	"I know this is a lot of new information. Can you explain it back to me so I can make sure I told you the information correctly?"

Task Two: Discussing Prognosis and Understanding the Information Needs of the Patient

Ms. W is a 46 year old with primary progressive multiple sclerosis. She has had increasing disability over the past 3 years and is no longer able to work as a teacher. The patient's mother has moved into her home to help care for her two children ages 8 and 12. It is becoming harder for her to walk independently and Ms. W notes she worries about how her illness may affect her ability to interact with her children.

Discussions about prognosis include communicating about life expectancy and survival but also planning for loss of independence, change in abilities and social roles, needs of the family and maybe even the end of life (see Chap. 12 "Prognostication"). One of the issues that patients may be least comfortable raising with their healthcare team is prognosis, but studies show that they want to discuss this with their physicians [31]. Discussing prognosis is a complex communication task, as it requires the language to help patients understand the biomedical information, the ability to evaluate what type and how much information a patient needs or desires, and the skills to respond empathically to emotions that may be detected in the discussion. In addition, clinicians often shy away from discussing prognosis when there is uncertainty. Instead of adding further tests in the futile hope for more certainty, it is important that clinicians address the inherent and inevitable uncertainty by acknowledging and normalizing it, by describing a best case, worst case and a most likely case and by attending to the emotions that accompany of uncertain future [32, 33].

There is much variation in the type of information patient's want about prognosis. First, most patients want as much information as possible, especially early in the course of their illness, while others desire less information. Further, patients may also change their desires for information as their illness progresses. Patients value truth telling that leaves room for hopefulness [34]. However, patients' report that overly optimistic information may lead to distrust when they later understand the information is not entirely true, and clinicians need to find the delicate balance between hope and realism [35]. Finally, cultural differences impact how much patient's want to know and some patient's may defer to family members entirely. Given all of these differences, it is not surprising that clinicians often avoid prognostic discussions unless the patient brings it up. Instead, we encourage clinicians to learn and engage in a patient centered approach to discussing prognosis that allows patients to help moderate the timing, type and amount of information they hear at different points in their illness.

Drawing on the skills used in delivering serious news allows for discussions about prognosis that are calibrated to the type of information a patient wants to know. By explicitly asking a patient or family member what type of prognostic information they want, the neurologist can determine what will be the most helpful (Table 11.4). Exploring the patient's information preferences helps build trust and creates an opportunity for the patient to lead the discussion. Being responsive to a patients' information needs can help support hope, even in the setting of a poor prognosis [36].

Task Three: Exploring Goals of Care by Mapping Patient's Values

Mr. W is a 77 year old who was diagnosed with Parkinson's disease 12 years ago. He has had two hospitalizations with ICU care this year due to pneumonia likely related to aspiration. The hospitalizations were followed by post-acute care in a rehabilitation facility for 2 weeks. In a clinic visit he notes that "The rehab doesn't really help, I can't walk anymore and I have lost more weight." You are worried that he may have increasing frequency of hospitalizations.

Table 11.4 Ask-Tell-Ask strategy for discussing prognosis

	Neurologist	Patient
Ask	"You mention you are not sure what to prepare you children for. It sounds like you are asking about prognosis. I wonder if it might be a good time to talk a little about prognosis and what you might expect in the future. How comfortable do you feel talking about that today?"	"I have already done some reading on the internet about it. But I do want to start talking to you about what might happen as my disease gets worse. My mom is not here with me today but she wants to know more too"
	"We can certainly talk about what might happen. Some patients really want to know a lot of details about what to expect. Others would rather have information given a little more carefully. What way do you prefer?"	"I know I don't want to talk about time lines yet or how quickly you think this might progress. But I do want to know about what disability I might continue to see so I can think about how to take care of my daughters"
Tell	"Thanks for helping me understand what is important for you to know. We can talk about how to prepare for what you might need in the future. This includes discussing how your walking, communication and eating may change"	Be prepared for emotion and respond to it with NURSE statements
Ask	"Since your mom wasn't able to be here today how are you going to summarize what we talked about"	"I am going to update her on the changes we might see in how I get around the house and about the possibility of having trouble swallowing. She will probably want to know more information about timeline of this disease. She is a planner!"

Routine discussions about disease progression provide opportunities for conversations regarding care preferences as patients move through the continuum of disease [37]. These conversations are commonly called "goals of care" discussions and involve complex medical decisions. The practice of shared decision making is further described in Chap. 13 "Improving Medical Decisions". Ideally, these conversations occur at deliberate time points and in a pro-active manner rather than when the patient is already nearing the end of life or in a crisis situation [38]. This book has developed a set of disease-specific triggers that create opportunities for clinicians and patients as well as their families to have timely, honest and iterative conversations to explore the patient's broader goals of treatment and to recognize situations that may require a reassessment (see Chap. 1 "Neuropalliative Care: Introduction", Table 1.1). Determining goals of care requires discussing prognosis, exploring values, attending to emotion and using this information to develop a plan or recommendation [39]. One teachable model for exploring values in order to best make a recommendation for care is the REMAP framework [40]. This framework can be used to explore most complex medical decision including broader treatment goals as well as more specific treatment preferences (Table 11.5).

Exploring Goals of Care with Surrogates

Patients with aphasias, dementias or significant brain injuries may rely on surrogates to represent their voice and values. The role of the surrogate as an ethical idea is to provide substituted judgment of an incapacitated patient's treatment preferences. In reality, patients may designate proxies to do "what they think is best" rather than simply what they think the patient would want [41]. Surrogates need assistance in applying the thoughts and values of their loved ones to the medical situation. Neurologists can use the communication skills from this chapter to break bad news, respond to emotion and explore goals of care with the surrogate decision makers. One way to help families focus on the values of the patient is to "highlight the patient's voice." Questions a neurologist can use to highlight the patient's voice are listed in Table 11.6.

Table 11.5 REMAP framework

Reframe	Highlight that current medical therapies are no longer working	*"Mr. W. I noticed you have had more frequent hospitalizations. I am worried we may be in a different place now"*
	May require breaking bad news if the patient does not recognize changes in the clinical status	
Emotion	Use NURSE statements to express empathy around the news that the disease has progressed	*"I can tell that this information is really sad"*
Map values and the future	Intentionally explore values before presenting options for care	*"Given this situation, what is most important to you?"*
	These values will allow the neurologist to develop a patient centered treatment plan	*"When you think about the future, what are things you want to do?"*
		"What worries you the most about the future?"
Align	Reflect back what the patient has said	*"It sounds like you no longer want to continue to going to the ICU for care as it is becoming too uncomfortable and keeping you away from home for long periods of time without improving your illness"*
	Clarify or expand statements to ensure you understand what is most important	
Plan	The plan should be linked to their values	*"From what you told me it sounds like aggressive care in an ICU is no longer helpful. I recommend we put a Do-Not-Resuscitate status into your medical record and make a plan to avoid ICU care in the future. What do you think?"*
	Consider making a recommendation or discussing possible next steps	

Table 11.6 Questions that highlight the patient's voice

If your dad was sitting here and could hear what we have been saying, what would he think?
What would your dad say is most important to him?
What would your mom think about her quality of life if it turned out that she was permanently dependent on a mechanical ventilator?
How would your dad balance quality and length of life?
Has anyone in your family ever been through a situation like this? What did you mom think about that?

Modified from Schumann et al. [42]

There is no one-size-fits all tool that ensures high-quality communication with seriously ill patients. Disease specific research is needed to understand the unmet communication needs of patients with neurologic illness including addressing the communication needs of caregivers. Communication skills that meet patient's needs are a component of the neurology residency milestones and trainees will benefit from a formalized communication skills education that is not part of the "hidden curriculum". Future education steps include identifying the key skills to be acquired, developing metrics to assess success and ensuring access to this curricula across programs [43].

There will always be communication challenges that may benefit from a referral to a palliative care specialist. Consider a consultation with a palliative care specialist in the setting of worrisome coping skills such as denial or ambivalence, conflict between clinicians and patient or the patient and family members, signs of existential distress or suffering, or when families need extended periods of time to explore goals and values.

Take Home Messages

- Patients view a clinician's communication skills as important as their medical skills
- High quality communication aims to elicit that patient and family's perspectives, acknowledge emotional impact of illness and work to build a collaborative relationship that ensures medical treatments match the patients' goals and values.
- Practicing a standardized approach to serious illness communication helps internalize the key elements of serious illness communication and may increase clinician skill during difficult conversations

- Useful communication strategies include Ask-Tell-Ask, NURSE, SPIKES, REMAP
- Neurology residency programs must ensure high quality communication is taught and skills are evaluated as trainees progress though their careers

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Prognostication

12

Brian Mac Grory and David Y. Hwang

A core component of information shared in the field of neurology is estimating and communicating prognosis. Uncertainty is the rule in most neurologic illnesses, and wide variation exists in the approach to prognosis. Illness severity scores and outcome data attempt to aid the clinician in deciding an individual patient's prognosis but are limited in their applicability, as they may not be tailored to an individual patient's clinical characteristics and circumstances. In addition to determining prognosis, communicating it effectively is also essential in a patient's care. In many cases, the neurologist must ask a family member to act as a surrogate decision-maker owing to the patient's incapacity. A sensitive approach is needed to ensure that there is clear, honest presentation of relevant information tailored to each individual's need, and that the surrogate decision-maker is comfortable in his or her shared decision-making role. Prognostic information should be presented in a way that is understandable to the layperson and that does not inadvertently bias his or her decision-making. By recognizing and embracing prognostic uncertainty, patients and families can be empowered to plan for the future.

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The Importance of Prognosis in Neurology

The prognosis of a patient with neurologic disease is important for several reasons: First, prognosis is important to assist patients and families develop goals and plans of care. If possible, clinicians should offer to discuss the likely course of the illness early in the course of the disease in order to allow patients and families to psychologically manage this information and to develop prognostic awareness ("a patient's capacity to understand his or her prognosis and the likely illness trajectory") [1]. The cultivation of prognostic awareness can help patients and their families make medical decisions that are based on realistic goals, and incorporate what matters most to the patient. A theme highlighted in the disease-specific chapters of this book is that certain events (e.g. falls) or symptoms (e.g. dysphagia) associated with severe or advancing neurologic disease may act as "triggers" for the clinician to have a 'serious conversation', including the possibility of involving a palliative care specialist and/or to initiate hospice care (see Chap. 1 "Neuropalliative Care: Introduction", Table 1.1).

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Second, prognosis is important because patients and families have a right (and, most of the time, a desire) to know it. In a study of older adults who were told that they had a lifespan of less than 5 years, 65% wished to discuss their prognosis in detail. In the same study, among older adults who were given a projected lifespan of less than 1 year, 75% wished to discuss their prognosis in detail [2]. Similarly, most patients with cancer rate prognostic information as the most important part of communication, even when the prognosis is poor; studies have also identified that patients feel ambivalent about this information: wanting to be told about their prognosis but also not wanting to know [3–5]. It should be noted that preferences among patients and families for receiving prognostic estimates can vary based on individual preferences, cultural and ethnic background [2].

Finally, prognosis is powerful because it can directly affect life-or-death treatment decisions. A patient (or his/her surrogate decision maker) may not be inclined to pursue life-sustaining ("aggressive") treatment if this treatment is not expected to meet the patient's individual values of longevity, quality of life, independence or other, specific goals. Conversely, a patient may be inclined to pursue aggressive interventions if the treatment is expected to meet the patient's goals. When the prognosis is uncertain, premature decisions to limit life-sustaining treatment may deprive patients of the chance of a reasonable outcome. This dilemma has been described especially in the acute inpatient setting [6–10]. For example, for adults with moderate-to-severe traumatic brain injury, withdrawal of life-sustaining treatment (which is typically based on prognostication) is the most important predictor of in-hospital mortality, independent of key patient characteristics [11]. For chronic conditions, this link is much less well established and sometimes, aggressive care can even be associated with worse outcome and shorter survival. For example in patients with advanced neurodegenerative diseases including dementia and parkinsonian conditions, gastrostomy placement does not increase, and may actually worsen, survival [12]. Similarly, higher numbers of hospital admissions for elderly patients receiving home care were associated with increased mortality, suggesting that hospital stays were a marker for poor health status rather than an effective intervention for improving survival [13]. All of these observations emphasize the importance of accurate prognostication especially as it guides fundamental treatment decisions that need to be carefully considered along with the values of the patient.

The Determination of Prognosis in Neurology

Formulating prognosis in neurology (i.e., "prognostication") should be considered as essential as formulating diagnosis and treatment plans [14], especially so that quality of life for patients and their families can be appropriately addressed [15]. Accurate prognostication is the bedrock for maintaining patient autonomy and patient-centered decision-making in all of neurology, but particularly in advanced disease [14]. Most neurologic illnesses diminish patient autonomy early on due to cognitive or communication deficits, often requiring early prognostication and timely conversations when possible. Determining accurate prognosis in neurology is often a difficult task given that it is often "bad news" with considerable uncertainty. That said, when presented with skill and compassion, an honest prognosis can be empowering for patients and family and gives them an opportunity to prepare for the future and make the most of the present Chap. 11 "Communicating Effectively".

Prognosis is usually based on (A) evidence, i.e. the use of observational data and severity scales and (B) neurologist expertise, both of which can be inaccurate and variable, especially for individual patient outcomes as reviewed below.

In addition, as the neurologist explores the expected course of a patient's illness, it is important to consider the goals of the prognostic information provided. For example, when considering time (how long?), the conversation may focus on what might happen over the course of the next

several days, months or years, including not only survival but also physical function, symptoms, patient and caregiver needs and quality of life ('how well?'). Considerations also depend on the patient's disease and their trajectory: In patients with severe acute brain injury, the focus of early prognostication may be on the potential degree of a patient's recovery; shortly after a diagnosis of glioblastoma, the focus may be on how much time the patient has left to live; a patient with dementia may want to know how long they are expected to remain independent. Finally, the inaccuracy of prognostic models can lead to either an optimistic or a pessimistic bias—in a patient with severe acute brain injury, an overly pessimistic prognosis can risk a decision to withdraw life sustaining treatment in someone who could have recovered well; in a patient with glioblastoma or amyotrophic lateral sclerosis (ALS), an overly optimistic prognosis may lead to unnecessary suffering, unpreparedness, or delayed referral to palliative care or hospice.

Disease-Specific Observational Data and Severity Scores

The use of outcomes data derived from disease-specific studies and associated with severity grading scales can be very attractive for clinicians desiring to "scientifically" prognosticate an outcome for a neurologic patient. However, before utilizing an outcomes study for prognostication, the clinician must decide on (1) the quality of the evidence and whether or not it is sufficiently powered to provide meaningful data [16]; (2) whether the population that was studied is relevant to the individual patient being treated; (3) whether the standards of care that were applied to the study population are relevant to the standards applied at the present time, particularly with reference to up-to-date medical and surgical therapy [17]; and (4) whether the study has itself been compromised by a self-fulfilling prophecy bias [18]. Regarding the last point, many observational studies in neurology have not taken in to account that early treatment decisions are a major confounding variable [18].

Severity scales developed from population studies attempt to capitalize on easily obtainable clinical data and relatively crude diagnostic measures, in part to aid predictions about clinical outcomes. While their results may be relevant on a population level, such scoring systems are challenging to apply to individual patients. Understanding the limitations of such scales is critical for their proper use.

As an example, Yourman et al. [19] conducted a meta-analysis in 2012 of published indices that are utilized to predict mortality in older adults (>60 years of age) in a range of circumstances ranging from healthy adults in the community to those in nursing home care. They found that, of all the indices included in their meta-analysis, none were free from potential bias. Sources of bias included an inadequate description of the population included in the study, poorly-reproducible prognostic variables, incomplete data collection, and non-blinded measurement of prognostic and outcome (e.g., mortality) variables. Only a small proportion (12.5%) were validated by investigators that were not directly involved in the development of the index.

Limitations with severity scales specific to neurologic disease have been described in detail. As an inpatient example, Rosen and Macdonald [20] explored subarachnoid hemorrhage grading scales and concluded that commonly used scales (such as the Hunt and Hess scale, Fisher scale, World Federation of Neurological Surgeons Scale, and Glasgow Coma Score) have a high degree of inter and intra-observer variability and in practice are only useful in particularly mild or particularly severe cases of the disease when predicting long-term outcome early on during patients' hospitalizations. In the outpatient setting, four of the most widely used Parkinson Disease severity scores (Hoehn and Yahr scale, Clinical Global Impression of Severity Scale, Clinical Impression of Severity Index and Patient Global Impression of Severity Index) were assigned to 433 patients with Parkinson's disease. The authors found substantial discordance between the severity score assigned to patients among the different scoring systems [21].

Outcomes such as quality of life, cognitive, and emotional outcomes that are of critical importance to patients and families are rarely addressed by outcome measures examined by population-level studies and predicted by severity scales [22, 23]. For example, a recently developed prognostic model for patients with a new diagnosis of Parkinson's disease suggested that the following factors predicted an "unfavorable" outcome: (1) increased patient age, (2) higher Unified Parkinson Disease Rating Scale (UPDRS) motor examination score and (3) lower verbal fluency score [24]. However, "unfavorable outcome" was defined in this model as the presence of axial instability or dementia at 5 years from symptom onset. This model is only one of a multitude of predictive scoring systems that highlight the general problem in neurology of ascribing a binary outcome (i.e., favorable versus unfavorable) to a person suffering with a chronic disease affecting multiple cognitive and functional domains.

To assist an earlier and more appropriate referral to hospice in neurologic diseases, criteria exist to assist in making eligibility determinations for patients with ALS, stroke, dementia and Parkinson's disease (see Chap. 16 "Hospice and End of Life Care in Neurologic Disease"). Attempts to identify predictors for 6-month mortality, however, have been modest for these diseases and the available data to assist with prognostication are discussed in more detail in the respective chapters.

The Palliative Performance Scale [25] is a prognostic scale widely used in palliative care that is not disease-specific but instead takes advantage of the fact that most patients who are terminally ill, regardless of the diagnosis, have a convergence of symptoms at the time their death nears. Based from the Karnofsky Performance Scale (see Chap. 9 "Malignant Brain Tumors", Table 9.2), the PPS rates performance across the following domains: ambulation, activity and evidence of disease, self-care, nutritional intake and level of consciousness. While it has been shown to correlate with survival in advanced cancer, there is less data available for patients with neurologic disease. A recent study in England found the PPS helpful in identifying disease progression in patients with cancer, but not in those with dementia [26].

Neurologists' Subjective Assessment of Prognosis

Some prognostic scales have been compared with clinician's subjective clinical predictions of outcomes. For example, Hwang et al. prospectively enrolled 121 patients with intracerebral hemorrhage (ICH) at 5 tertiary referral centers in the United States. They asked the clinicians taking care of enrolled patients to predict the functional outcome of each patient at 3 months, within 24 h of patient admission, as measured by the modified Rankin Scale (mRS). The attending physicians' predicted outcomes correlated better with the patient's actual 3-month outcomes than the outcomes predicted by the prognostic scale (ICH score) completed at admission, even after controlling for early decisions to withdraw life-sustaining therapy [27]. Another study used hypothetical patient cases of acute ICH and varied individual factors such as age and Glasgow Coma Score on presentation to generate a total of four separate cases. Using a written survey, they asked 742 neurologists and neurosurgeons to estimate the prognosis in each case. They found a wide variation in the predictions of mortality; in two of the four cases, the predicted mortality ranged from 0% to 100%. This result was particularly striking given that the outcome metric chosen (mortality) is not open to variable interpretation among survey respondents.

For neurodegenerative diseases, clinicians tasked with outcome prognostication must face the additional challenge of a longer and highly variable speed of cognitive and functional decline. An example is the prediction of future decline for patients with mild cognitive impairment (MCI); although 60% of MCI patients develop dementia within 10 years, many MCI patients remain cognitively stable, making accurate prognostication for individual patients difficult, even by specialists [28]. Even among patients with Alzheimer's

disease, the progression of illness is rarely linear and is often marked by periods of relative stability punctuated by abrupt or subacute decline [29]. To explore the prognostic accuracy of multiple sclerosis (MS) specialists, an international panel of 17 MS specialists was presented with 40 real-life vignettes of MS patients and asked to predict the time points at which the patients would develop various degrees of functional disability on the 10-point Extended Disability Status Scale (EDSS). The study found not only a high degree of inter-rater variability among the vignettes but even found a high degree of *intra*-rater variability when individual experts on the panel were presented the same vignette more than once over the course of the exercise [30].

The "surprise" question—"Would you be surprised if this patient died in the next 6 (or 12) months?"—is a subjective assessment by the physician and has emerged as an attractive, simple solution for identifying patients who might benefit from palliative care [31, 32]. While the accuracy of this question was high in patients with advanced cancer [33], a study among primary care providers with a more heterogeneous group of patients showed the surprise question to be less accurate and unable to predict most deaths at 1 year (i.e., lower sensitivity).

In summary, each of these studies demonstrate that prognostic inaccuracy pervades both objective and subjective assessments, and caution is advised when assessing each individual.

Communicating Prognosis in Neurology

As difficult as formulating prognosis in neurology can be, communicating prognostic estimates with patients and families can present an even greater challenge. This section reviews initiating conversations about prognosis with patients and families, presenting risk data, discussing inherent prognostic uncertainty, and addressing prognostic discordance between patient/families and clinicians. Further communication skills and strategies can also be found in Chap. 11 "Communicating Effectively".

Cultivating Prognostic Awareness

Early conversations about a patient's prognosis can foster patient autonomy by encouraging informed decision-making and to help deliberate about preferences. In the ambulatory setting, early conversations about goals of care improve quality of life and reduce depression [34]. However, physicians tend to be reluctant about discussing prognosis because of prognostic uncertainty, because of a concern that it can eliminate hope, and/or because of a show of respect for a perceived cultural background [35].

We recommend a structured approach to any prognosis conversation, including anticipating the type of prognostic information most likely needed during the discussion, anchoring the disease course on the most likely disease trajectory and adapting the information to the patient's preferences for discussing prognosis [2]. Keeping this point in mind, prognosis communication should start as soon as possible following diagnosis of serious neurologic illness [36] so as not to begin at the time of clinical deterioration, or after a patient has become cognitively impaired and unable to understand the information provided. In chronic, life-limiting neurologic disorders, it is important to talk about the possibility of future disability and death in the outpatient setting, in order to facilitate timely incorporation of palliative care before crisis strikes [1, 37–39].

Methods of Expressing Risk

The exact way in which prognostic information is conveyed affects how patients and their surrogates perceive prognosis [40]. Using quantitative risk language evoking individual cases like "1 in 50 deaths" leads to more pessimistic impressions than using percentages (e.g., "2% risk of death") which is equivalent mathematically but may be more abstract to most people [41]. Also, framing prognosis presented as median survival time may lead to a more pessimistic impression than framing prognosis as a survival probability over a specified time frame [40]. For example, a surrogate may interpret the statement, "Your family member has a 40% chance to survive up to one year, a 20% chance to

survive up to 3 years, and a 10% chance of survival up to 5 years" as more favorable than the statement, "The median survival time for a patient like your family member is about 6 months."

Fagerlin et al. [42] suggest ten recommendations for presenting prognostic language in a way that communicates risks of health outcomes in a manner that is readily understandable and avoids prejudicing the listener. Their guidelines pertain specifically to making decisions relating to cancer treatment but are readily generalizable to neurologic illness (Table 12.1).

Table 12.1 'Methods of risk communication to patients

1. Use plain language to make written and verbal material more understandable
2. Present data using absolute risks (i.e., instead of, "there is a 50% reduction in the risk of death", use "there is a reduction of risk of death from 10% to 5%")
3. Present information in pictographs if you are going to include graphs
4. Present data using frequencies (i.e., as opposed to using percentages: 1 in 100 versus 1%)
5. Use an incremental risk format to highlight how treatment changes risks from preexisting baseline levels (e.g., when offering a hemispheric stroke patient a craniectomy, the risks of poor outcome both with the procedure and without the procedures should be communicated to the family)
6. Be aware that the order in which risks and benefits are presented can affect risk perceptions (i.e., presenting risks after benefits can give risks more prominence in a person's mind, compared with risks being presented first [43])
7. Consider using summary tables that include all of the risks and benefits for each treatment option (particularly for major treatment decisions, such as the decision to place a percutaneous endoscopic gastrostomy (PEG) tube in dementia)
8. Recognize that comparative risk information (e.g. what the average person's risk is) is persuasive and not just informative
9. Consider presenting only the information that is most critical to the patients' decision making, even at the expense of completeness (i.e., when discussing PEG placement in a person with dementia, steer the conversation away from minutiae of the PEG placement procedure itself and focus more on the overall goals of care)
10. Repeatedly draw patients' attention to the time interval over which a risk occurs

Adapted from Fagerlin et al. [42] by permission of Oxford University Press

Dealing with Uncertainty in Neurologic Prognosis

Uncertainty is a defining factor in almost every communication with patients and families regarding prognosis. This uncertainty about what the future holds can deprive patients and families of a sense of control and substantially contributes to stress and emotional turmoil [44]. However, most patients and families understand that prognosis cannot be certain and want to engage with the clinical team in a productive manner despite these realities [45, 46]. One way to present prognostic uncertainty is to frame the anticipated trajectory as best case, worst case and most likely case scenarios. This is congruent with the palliative care model of offering patients and families the ability to simultaneously hope for the best and prepare for the worst [47] and should always include an assurance from the clinician of a meaningful engagement and non-abandonment during the course of the patient's illness. Acknowledging uncertainty also requires that clinicians give patients and/or their families signposts that they can use to understand if things are getting better or worse. Anticipatory guidance helps patients and family prepare for anticipated developments, expect complications and plan for potential future decisions and includes reviewing common issues that could affect living well (for example falls, need for assistance or cognitive impairment) as well as anticipated events that my trigger another conversation about goals of care and needs.

If framed in the correct manner, uncertainty can act as a positive factor in the patient's journey by allowing optimism in the face of tragedy [48]. Understanding and recognizing uncertainty in prognostication can be the first step to empowering a person to develop an informed perspective on their care and to determine their vision for their remaining time. Similarly, sharing prognostic information in a non-biased [49] way allows for joint decision-making and promotes autonomy and a sense of control.

Finally, the use of time-limited trials can be an effective way to manage uncertainty. Time-limited trials are an agreement between patient/

family and clinicians to use certain medical therapies over a defined period to assess the patient's response according to agreed upon clinical outcomes that define relative successes or failures in view of the patient's goals [50]. A time-limited trial allows opportunity to (1) evaluate trends and progress; (2) allow the patient to reflect; (3) engage the family; (4) re-address goals; (5) adapt to a "new normal; (6) address symptoms and suffering; (7) build trust; (8) recruit community resources; and (9) allow for rehabilitation and functional improvement.

Prognostic Discordance

Sometimes, the clinician and patient/surrogates differ in their perspective of prognosis [51]. In the critical care literature, rates of prognostic discordance between physicians and surrogate decision makers range from 53% [52] to 64% [51], with a strong tendency towards higher optimism among surrogates. Prognostic discordance may be due to a misunderstanding of the medical facts by the surrogate, a difference in the surrogate's view or belief of the patient's prognosis despite a common understanding, or a combination of both [52]. Discordance due to misunderstanding may be addressed through more effective communication, while discordance in belief may not be modifiable. Reasons for a difference in belief between the surrogate and the physician include a perceived need to maintain hope for the patient's sake, a belief in the patient's underlying strength, and religious conviction.

Education and Research Agenda

Neurologic conditions are the second most common reason for initiating a palliative care consultation in tertiary referral centers [53], and one of the key elements in these consultations is prognosis [54]. It is therefore crucial that neurology trainees receive adequate training in prognostic formulation and communication, and that there is a high level of cooperation between different disciplines in dealing with neuroprognostication, particularly at the end of life [55]. Opportunities in education in the field of neurological prognosis in palliative care include establishing formal collaboration between palliative care and neurology training programs in order to promote a reciprocal understanding of the two fields; developing a consistent didactic curriculum within neurology residencies in order to improve neurologists' skills in prognostic formulation and communication; and formalized follow-up of patients who are discharged from inpatient neurology and neurocritical care services so that clinicians can gain a sense of their prognostic accuracy.

The need for further research around neuroprognostication is tremendous. The development and validation of predictors of survival and other types of outcome for individual neurologic illnesses should be a priority, including finding predictors relevant at different stages of progressive diseases and specific predictors for survival and hospice eligibility. This will require additional research on outcomes after severe neurologic injury to understand the interaction between currently used metrics of severity, functional impairment, disability, and ultimate quality of life. In addition, we need to assess in more detail the factors underlying differences in prognostic impressions between physicians and patients/surrogate decision makers and develop strategies to address them. To improve prognosis communication, we need to explore ways to help both clinicians and patients/surrogates manage prognostic uncertainty and biases that may affect decision-making.

Take-Home Messages

- Prognostication can influence a patient's care both positively and negatively. An excessively optimistic prognosis can lead to potentially inappropriate care while an excessively pessimistic prognosis can lead to premature withdrawal of life-sustaining therapy.
- Widely used prognostic scores (such as those used for predicting mortality in subarachnoid hemorrhage) should be applied with caution to the individual patient, as they may contain

within their construction an inherent early withdrawal bias.

- Neurologists exhibit a great degree of variability in their approach to prognostication, and need to be aware of both inaccuracies and inconsistencies in objective and subjective methods of prognostication.
- The communication of prognosis in the practice of neurology is as important as arriving at the correct prognosis.
- Sharing prognostic information in a non-biased way allows for joint decision-making and promotes autonomy and a sense of control in the patient's care.
- Uncertainty is one of the biggest challenges in prognosticating and communicating prognosis in neurologic disorders. By acknowledging and understanding this uncertainty, patients and surrogates are empowered to actively plan for the future.
- Neurology trainees need to receive adequate training in prognostic formulation and communication; a high level of cooperation between different disciplines is necessary in dealing with neuroprognostication, particularly at the end of life [55].
- Future research in the area of prognostication in palliative care should focus on how best to reconcile historical, population-level data with individual patients with individual needs and values.

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Improving Medical Decisions

13

Jorge Risco and Adam Kelly

Introduction

Physicians can make over one hundred decisions in a workday. For neurologists, this can range from increasing the dose of an antiepileptic medication, to more high-stakes decisions such as administering tissue plasminogen activator for acute stroke or initiating tube feeds in a patient with Amyotrophic Lateral Sclerosis (ALS). These decisions vary in risk, benefit and complexity. Caring for patients nearing the end of their life is a common yet special medical scenario. End of life decisions have important consequences on patients and their families. These decisions can be complex, require deep thought and careful balance with patient values. In these situations, what constitutes a good or bad decision? Can we say that one decision is better than another?

A medical decision is slowly molded by multiple factors. Developing a framework of the decision making process can be helpful. The process can be conceptualized in three main steps: (1) diagnosis, (2) option assessment and (3) shared decision making. Diagnosis is a step that involves gathering information surrounding the problem. Option assessment is a step where the risks and benefits of potential solutions are weighed against each other. Finally, once the problem and potential solutions have been studied, one engages with patients or surrogate decision makers in shared decision making. The potential solutions are shared with patients. They are taken in the context of patient values to arrive at a medical decision. These steps are often intertwined and do not occur in perfect sequence, but all three are required for an optimal decision-making process.

In this chapter, key concepts in the decision-making process will be further explored. These can be applied to most medical scenarios though areas of particular relevance to neuropalliative care will be highlighted.

Variations in Clinical Practice

Anecdotal experience and observational studies show significant variation in clinical practice across neurologic disorders, including palliative care aspects of these disorders. The underlying reasons are diverse. Variation can arise from different interpretation of available evidence; paucity of evidence; strong patient or family preferences; systematic over or under treatment of certain populations (racial groups, women); or financial incentives. Less patient-centered factors should be minimized to whatever degree possible.

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Diagnosis

The foundation of good decision making relies on understanding the problem. A physician must diagnose (a) the medical problem, (b) the problem from the patient's perspective and (c) the patient's preferences and values. Failing to understand the patient's perspective can lead to overuse or underuse of therapy [1]. An assessment of (d) patient capacity and (e) skilled doctor-patient communication are intrinsic to the process.

Medical Problem

The medical problem should be framed as clearly as possible. Misdiagnosis leads to unnecessary and harmful risks. One series assessing misdiagnosis in multiple sclerosis found that one third of patients had experienced unnecessary morbidity [2].

Understanding the medical problem leads to an understanding of the prognosis (see Chap. 12 "Prognostication"). There are two types of prognostic questions: how long? And how well? [3]. The medical options that we will offer our patients will be framed within this foundation. If "how long" and "how well" are not clear, we risk decisions for unrealistic or potentially harmful options. Failing to grasp the problem at hand or relying on incorrect information leads to poor decision making.

Patient Understanding

As we prepare to guide patients through a complex decision, a physician needs to understand the problem from the patient's perspective [4]. This insight allows us to anticipate and understand the choices they will make.

A starting point is asking what a patient knows about their medical problem. Numerous studies have demonstrated that patients recall and comprehend very little of what they are told by their physicians [5–7]. This communication gap between physicians and patients can have several reasons including poor patient health literacy; poor physician communication skills; a patient's emotional state; a patient's cognitive or communication impairment; or different belief systems [8]. A national assessment of health literacy found that one third of US adults had a basic or below basic level. These individuals were unable to use a prescription drug label to correctly take medications [9]. On the other hand, physicians often fail to disclose key information and rarely verify patient understanding [10–12]. The communication gap between physicians and their patients often goes undetected [13, 14]. Prior to embarking on important decision making, a patient must have a clear understanding of their disease and prognosis, and the clinician needs to have a clear understanding of the patient's perception. Disease misconceptions should be clarified.

Recognizing limited health literacy allows physicians to adjust their communication strategy. In some cases, limited health literacy may only become apparent after a lengthy interaction between a provider and a patient or surrogate. However, there are two questions that can more rapidly screen for lower literacy. They have sensitivities ranging from 54% to 83%, depending on the clinical setting [15]:

- How often do you need to have someone help you when you read instructions, pamphlets, or other written material from your doctor or pharmacy?"
- How confident are you filling out medical forms by yourself?

While ensuring that patient or surrogate understanding has occurred is important in any medical scenario, it is of utmost importance in a palliative care setting. Not only are many of these decisions "high stakes" in nature (for example, goals of care decisions), but there are considerable knowledge gaps on the part of the public on the roles of palliative care specialists and hospice approaches [16, 17].

Values and Preferences

A patient's *values* are the aspects of life which they find important. They remain relatively stable over time, rarely changing with medical scenarios. They sit at the core of a patient's decision making process.

A *preference* is a choice that pertains to a specific medical scenario. It is the end result of a

patient's decision making process. A preference is constructed from an individual's core values and is influenced by multiple factors: their understanding of disease, their understanding of medical options, physicians, the opinion of friends and family and the media (Fig. 13.1) [18]. A preference-sensitive condition has more than one clinically acceptable solution (for example medical vs. surgical management) and may therefore be guided by what matters most to the patient. A preference-sensitive treatment decision or recommendation aims to find the solution that is most in line with a patient's values and preferences.

Poorly constructed preferences do not reflect patient values. Consider the case of an 82 year old man with terminal cancer including brain metastases. He may value the ability to engage with friends and family over the duration of his life. He may elect to maintain a full code status not knowing that there is a low chance of subsequently achieving a successful resuscitation and an even lower chance that he will return to his prior functional state. In this case, the patient's preferences are not aligned with his values due to a poor understanding of his medical problem.

Because preferences are susceptible to undue influence, the more important question is: What does my patient value?

We *value* aspects of life differently. Some find accomplishment through work; others through connections with family and friends; others through creativity and art. The paths towards well-being are as diverse as we are.

Similarly, as health declines, we experience illness in many of ways. The predominant concerns of patients with Parkinson disease can vary from falls to unemployment. Understanding what a patient values about their health and illness is crucial.

As the complexity of medical problems increase, they demand a greater understanding of a patient's values. When selecting first-line therapy for episodic tension type headaches, a superficial expression of preference may suffice. On

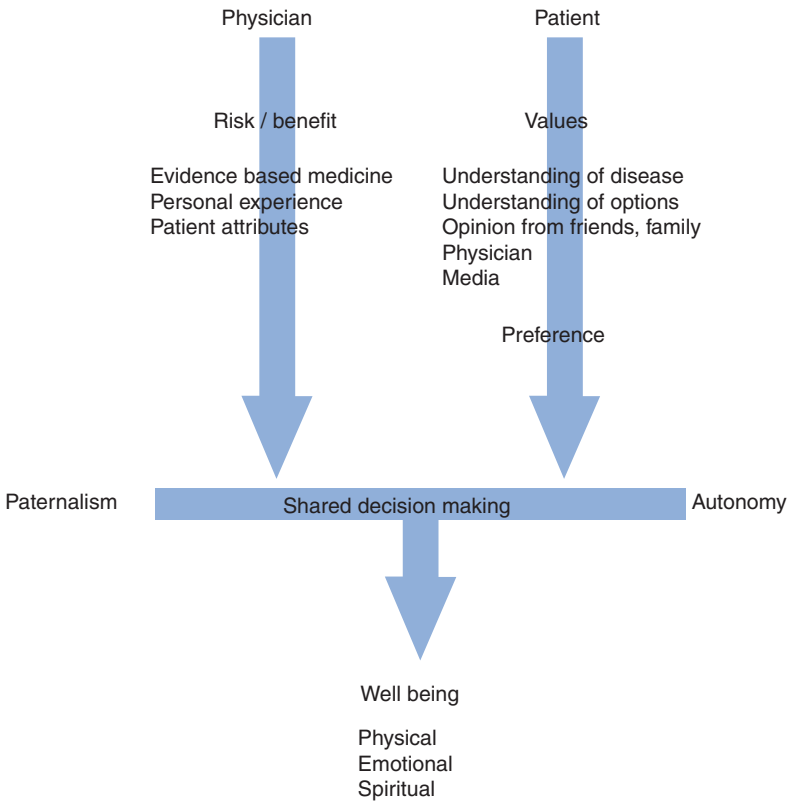

Fig. 13.1 Medical decision making overview. Physicians bring their expertise and patients bring their values. Participating in shared decisions is engaging in dialogue, where both perspectives are expressed. The overall objective of a medical decision is to promote patient well-being

the other extreme, physician assisted death or terminal extubation require a full understanding.

Impaired patient capacity is common in neurological illnesses and adds a layer of difficulty to medical decision making. This is particularly true in many disorders where neuropalliative care plays a key role, including severe stroke, neurodegenerative conditions, and brain tumors or metastases. Often, there are no written advanced directives to guide management. Even so, patients cannot anticipate an infinite number of medical scenarios and therefore judgement is required. We turn to the surrogate decision maker and ask "What would (the patient) have done?". The underlying question is "What does (the patient) value?". We construct a preference that pertains to the specific medical scenario from the patient's core values.

Eliciting patient values is not an easy task. The goal is determining: what elevates this individual's well-being? In other words, what brings him or her: relief, comfort, joy, meaning and purpose? It requires a great deal of introspection on the patient's behalf. This is triggered through interviewing with open ended questions. In more difficult cases, when capacity or introspection are limited, answers may be inferred from a patient's behaviors over the course of life.

The following questions can serve as starting points (Table 13.1). A follow up open question such as "why?" or "tell me more" allows for further exploration:

Table 13.1 Eliciting patient values

Health
What aspect of your health can we focus on maintaining?
What aspect of your current health is most important to you?
What is the most distressing symptom/deficit/barrier?
What do you think about the risks involved with therapy X?
What is important to you about therapy X?
What would be unacceptable?
Emotional/spiritual
What do you enjoy in life?
What are you proud of?
What makes you laugh?
What gives you peace of mind?
What makes you sad/angry?
What are you hoping for?
What do you fear?

Capacity

An assessment of the patient's ability to make decisions is an intrinsic aspect of medical decision making. Does a patient have capacity? This should be an early consideration, as it determines the need for surrogate decision making.

Patients with neurologic illness are at high risk of having impaired decision making capacity [19–21]. Neurologic diseases are often characterized by cognitive impairment, the main determinant of impaired capacity [22]. Capacity is impaired in over half of people with mild-to-moderate dementia and nearly all people with severe dementia [23]. Even mild cognitive impairment is associated with decreased performance in capacity evaluations [19, 24]. Similarly, capacity is acutely impaired in patients with severe acute brain injury and even among stroke survivors with excellent functional recovery, cognitive impairment is seen in over one half [20, 25].

Impaired capacity is also common near the end of life. In a US nationally representative cohort of subjects that required end of life decisions, 70% lacked capacity [26]. This proportion is likely higher for people with neurological illness.

There are four components that constitute capacity: understanding, expressing choice, appreciation and reasoning [27]. Expressing a choice is a patient's ability to clearly indicate a preferred treatment option. Understanding is the patient's ability to grasp the meaning of the information communicated by the physician. Appreciation is the patient's ability to acknowledge their medical condition and the consequences of treatment options. Reasoning is the patient's ability to engage in a rational thought process of manipulating the relevant information.

Capacity is implicitly assumed in healthy adults. The presence of cognitive impairment should raise concern for impaired capacity and prompt a more formal assessment. These components are generally assessed in a semi-structured interview with the use of open ended questions (Table 13.2). While standardized cognitive tests

Table 13.2 Assessing capacity

	Patient objective	Physician questions
Communicate choice	Indicate a choice	What is your decision?
Understand information	Repeat the information regarding their:	What have you been told regarding:
	Medical problem	Your medical problem?
	Treatment options	The treatment options?
		The risks and benefits of the treatment options?
Appreciate the situation and its consequences	Acknowledge the:	What do you believe:
	Medical problem	Is wrong with your health?
	Consequence of the treatment options	The treatment effects will be?
		Will happen if you are not treated?
Reason about treatment options	Compare the different treatment options	Why did you choose X over Y?

Adapted from Appelbaum [27]
The table reviews the four components of capacity, each component's objective and assessment questions

cannot substitute a capacity evaluation, low scores correlate well with impairment. In one study of Alzheimer's dementia, MMSE scores below 19 or above 23 were helpful in discriminating capacity [28].

Communication

The word doctor is derived from the latin word "*docēre"*, which translates "to teach". Educating patients on their disease and therapeutic options is one of a physician's main responsibilities. Patients cannot make good decisions if they have incomplete or incorrect information. It becomes increasingly relevant when barriers exist, such as poor health care literacy or cognitive impairment from neurologic disease.

Effective communication can be considered as an intervention. When assessing capacity in patients with mild cognitive impairment, "understanding" is the most deficient consent ability [19, 29]. Understanding complex medical facts relies heavily on short term verbal memory, which is prominently affected in MCI and dementia. In elderly populations, promoting clear communication through educational interventions and disclosure forms improved decision making abilities [30, 31]. However, studies involving people with moderate to severe dementia are equivocal in the effect of the interventions [23].

While cognitive impairment is the main determinant of impaired capacity, aphasia is also a barrier to decision making [32]. Patients with aphasia may have capacity, yet their ability to fully participate in a dialogue regarding a proposed medical intervention is impaired [33]. Language pathologists can sometimes facilitate communication, allowing aphasic individuals to reveal their capacity, often in complex scenarios. Modified consent forms with simplified writing and pictographic representations can be used. Every exchange of information is followed by a series of questions to verify comprehension [34].

Several strategies have been recommended to improve communication with patients [15] and more are discussed in Chap. 11 "Communicating Effectively" and Chap. 12 "Prognostication".

- Slow Down. Communication can improve by slowing the rate of information. New information requires time to be processed and comprehended. If one component of the message is not understood, subsequent pieces of information may also be lost. Use pauses. Listen instead of speaking. Take additional time to deliver an important message.
- Use non-medical language. Use plain conversational language instead of complex medical terminology. Explain things as you would to a family member without a medical background. This creates the opportunity for dialogue with patients.

- Show or draw pictures. Images are remembered better than words or letters. Simple images, devoid of distracting details, are more effective forms of communication. They can support the written and spoken message.
- Limit the amount of information at each encounter. There is a limited amount of new information a patient can remember and process. If there is a complex message, this can be broken up into smaller pieces. Each encounter should have a set goal. Start by laying out the "big picture". Subsequent encounters can be used to fill in the details.
- Use planned redundancy. Repetition of information helps consolidate memory. Repetition can also occur after the patient visit, through the use of handouts. In follow up encounters, summarize prior information.
- Proactively plan meetings. In the ICU setting, the implementation of a communication strategy with the relatives of dying patients reduced the burden of bereavement [35]. The strategy included a proactive end of life conference and a brochure. It resulted in decreased post-traumatic related symptoms and symptoms of anxiety and depression three months after the patient's death.
- Use the "teach back" technique [36]. Teaching back is an effective method of verifying patient comprehension, and involves asking the patient to explain what they have learned. For example, you can say "When you get home, your spouse will ask you what the doctor said. What will you tell your spouse?". In doing so, a physician takes responsibility for adequate teaching. If a patient is unable to complete the task, we assume that our explanation was not adequate. This method should replace the common practice of asking patients: "Do you understand?". Despite poor comprehension, patients frequently answer "yes" to such questions. They may be embarrassed to admit the contrary.

Option Assessment

After diagnosing and communicating the problem, we need to find potential solutions. This includes (a) assessing benefits and risks of each option including a consideration of costs; (b) understanding and managing uncertainty including the use of time limited trials and default options; and (c) considering the biases associated with option assessment and ways to debias.

Assessing Benefits and Risks

Our actions will affect patients in good and bad ways. We generate viable therapeutic options with potential benefits in mind. Almost all therapy carries the risk of adverse events and these need to be considered as well.

Benefits and risks each have two attributes: impact and probability. The impact is the clinical importance of the effect. The probability is the chance of the effect occurring. For example, natalizumab is a disease modifying therapy used in the treatment of aggressive relapsing-remitting multiple sclerosis. It is highly effective and viewed as superior to first-line drugs. However, its use has been limited by the occurrence of progressive multifocal leukoencephalopathy (PML), an opportunistic encephalitis caused by the ubiquitous JC virus [37]. With therapy, the risk of developing this disease is less than 1:1000 in patients treated for 2 years or more. In this scenario, the impact of the therapy's risk is large, as PML is a devastating and potentially fatal neurologic disease. The probability of this occurring is low.

The impact and probability of both risks and benefits are determined in three different ways: Scientific evidence, clinical experience, and patient attributes.

The first is derived from evidence based medicine. Published articles report the probability that an effect will occur for a given study population. It can be expressed as a percentage, relative risk, relative risk reduction, absolute risk reduction, etc. The exact probability can never be known. The true probability lies somewhere in the neighborhood of a point estimate. This neighborhood is expressed as a confidence interval [38]. Research provides a probability for a large yet not necessarily diverse population; this raises questions about its applicability to a specific patient.

The second is derived from anecdotal, personal experience. Compared to other disciplines,

neuropalliative care has a relative lack of evidence from large clinical trials. Providers may need to draw more from personal experience (themselves or others) for guidance. Estimating probability can also be derived from a physician's personal experience. This is particularly relevant for some procedural based therapies. For example, a physician may recognize that, at their institution, the rate of gastrointestinal hemorrhage from gastrostomy tube placements is higher among gastroenterologists than interventional radiologists (or the other way around).

The third are the attributes of the patient. A physician uses published articles and personal experience to make an estimate that applies to an average patient. The estimate, is then refined upwards or downwards depending on the attributes of the patient. Considerations such as age, sex, comorbidities and life expectancy are taken into account. We may think of these as being physician cognitive exercises, but patients and their surrogates also adjust their perception of treatment effects. Their estimate is influenced by media, personal experiences, stories, beliefs, culture and understanding of disease.

Considering Cost Historically, treatment-related costs were disregarded in the context of a specific medical decision. Health-care costs were evaluated by economists and policymakers from a societal perspective, but an individual physician preferred to remain agnostic. As insurance plans have increasing out-of-pocket expenses, a physician's acknowledgment of cost is important. Choosing a slightly less effective agent, which the patient can afford, is preferable over the option that is unaffordable (or one that is paid for at the expense of food or housing) [39]. However, overemphasizing cost in a physician's decision making process runs the risk of increasing health care inequalities between the rich and poor.

This analysis leads to an overall appreciation of a therapy's benefits and risks. There may be multiple viable therapeutic alternatives that need to be compared against each other. It is helpful to place these options in one of four quadrants (Fig. 13.2). Ideally, a therapy should provide high benefits with low risk, located in the bottom right quadrant. Mentally placing all options in this space can help summarize complex medical information.

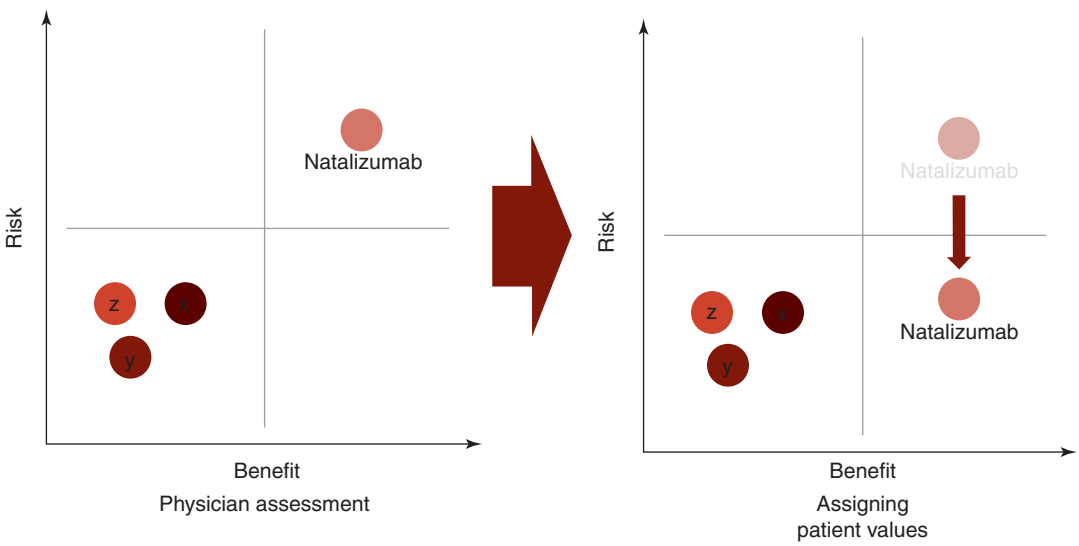

Fig. 13.2 Assigning patient values. In this example, therapies for multiple sclerosis are compared against each other. Ideally, a therapy should provide high benefits with low risk, located in the bottom right quadrant. In a physician's assessment, Natalizumab carries high benefits and high risk, with a 68% annualized relapse rate reduction and a 1:1000 risk of developing PML, respectively. In this case, a patient values disease remission over the risk of PML. Given the benefits, the patient's perception of PML risk is lower

Uncertainty

Uncertainty is an overarching component of clinical medicine though perhaps no specialty epitomizes this more than neurology. Examples include diagnostic uncertainty with atypical patient presentations or rare disorders, prognostic uncertainty in many settings (such as acute brain injuries like stroke or hypoxic-ischemic encephalopathy), and therapeutic uncertainty in scenarios without the support of high quality evidence [40]. Neurologists must develop skills to make decisions in the setting of uncertainty and to clearly communicate this concept in a productive fashion [3]. Some of the following strategies may be helpful in dealing with various types of uncertainty:

Diagnostic uncertainty Find out what diagnoses are most distressing to the patient and reassure that these are unlikely (if possible). "Although I can't tell you exactly what happened, I know you said you we're worried about a brain tumor – I think that is extremely unlikely based on your normal MRI scan."

Therapeutic uncertainty At present, many neurologic disorders lack clear evidence-based management strategies. Participating in a shared decision making process is critical in these settings, in order to review possible benefits and risks of various options. This should include a timeline of when therapeutic benefit will be reassessed.

Prognostic uncertainty Define a prognostic range, from the best to the worst case scenario. Frame this in the context of outcomes that are most important to the patient. "Some recovery of her language and right-sided weakness is possible, however I doubt that this is going to be to an extent where she can return to her prior state of independence." Take additional time to increase the prognostic precision if reasonable. If managed well, prognostic uncertainty can still lead to high quality decision making.

Time limited trials Acute brain injuries such as stroke, intracranial hemorrhage, and hypoxic-ischemic encephalopathy are distinct among neurologic disorders in that they can require life support (mechanical ventilation, artificial nutrition) while maintaining a highly variable prognosis in the short term (see Chap. 2 "Severe Acute Brain Injury"). In these settings, a time-limited trial of supportive measures can be helpful. A time-limited trial is an agreement between the patient and/or family and their clinicians to use certain medical therapies over a defined period to assess the patient's response according to agreed upon clinical outcomes that define relative successes or failures in view of the patient's goals [41]. First, although prognosis will not always be clarified over the course of a several day-long trial of interventions after acute brain injury, one can potentially begin to see some early signs of improvement that may predict a more optimistic prognosis. Conversely, progression of the initial injury or development of additional complications (venous thromboembolism, aspiration pneumonia, etc.) may lead the provider to downgrade a prognosis in a less favorable direction. Second, a time-limited trial often serves to give family members or other surrogate decision makers additional time to process the diagnosis, extent of injury, and expected impact on function (e.g., psychosocial time-limited trial). Disorders with a more slowly progressive course (e.g., dementia, ALS) allow for patients and families to prepare themselves for decisions on life-sustaining interventions; this lag time is not present in acute brain injuries. As a result, extra time may be necessary to reach a decision that is felt to be consistent with a patient's wishes.

While there is no one-size-fits-all approach to initiating a time-limited trial, some common elements can be identified. An initial meeting with key members of the decision making process should be considered, during which the nature of the disorder and active medical issues can be reviewed. Specifically, the key decisions that are anticipated (such as placement of a feeding tube or tracheostomy) should be explicitly stated. At that time, it is often helpful to place limits on further escalations of intensity of care, such as placing a DNR order or discussing withholding mechanical ventilation if it becomes necessary.

Finally, a timeframe to reconvene for another meeting, discuss prognosis, and make key decisions should be established; this time should be appropriate to the patient's overall clinical state as opposed to being an arbitrary duration.

Default options/smart defaults As described first in psychology and decision making research, a default option is the option that a decision maker will be provided if he/she chooses nothing [42]. Default options are used implicitly or explicitly in a number of different clinical settings; while often purported to be a way to increase workflow and efficiency, there are some unintended consequences of this form of decision making. Obtaining daily blood draws on patients who have been hospitalized for long periods of times, with resultant over-phlebotomy and both a burden on the patient (discomfort) and the healthcare system (cost), is one example [43].

From a palliative care standpoint, a common scenario involving this type of decision making is the choice of cardiopulmonary resuscitation (CPR) versus do-not-resuscitate (DNR) status. In almost all clinical settings, the default option is to proceed with CPR if a patient's (or their surrogate's) wishes are not queried. Yet prior research has shown that older adults are much more likely to proceed with DNR status if this is provided as a default option when resuscitation status is discussed [44]. Some authors' recommendations have gone so far as not offering CPR in situations where CPR might be considered inappropriate or futile [45]; at the very least, changing DNR to the default option in the case of patients with advanced neurologic dysfunction is likely to result in fewer unsuccessful resuscitation efforts with their resultant emotional burden.

Bias

Recognition of biases are vital to optimize medical decisions [46]. They can occur in both patients and physicians, at any stage of interaction. Some biases are personality traits, which reflect a person's confidence or natural response towards ambiguity and risk. The first step to overcome biases is becoming aware of their existence [47]. Among over forty types of clinical biases have been described, the following are examples that arise when assessing therapeutic options, particularly ones that are relevant to neuropalliative care. For readers wanting a more in-depth review of cognitive biases in medical decision-making, we refer them to several recent reviews [46, 48, 49].

Regret bias is the perception that harm by commission is worse than by omission. If a bad outcome occurs, the regret is greater if it resulted from treatment than from adopting a "watchful waiting approach". Physicians may experience an anticipated sense of regret, which may influence the decision towards inaction.

Framing bias is a tendency to draw different conclusions, depending on how information is presented. Physicians can transfer their preferences to patients. This occurs by using different connotations when communicating: presenting a favored option first, highlighting benefits, minimizing risk or using a different tone of voice. Physicians are also susceptible to this bias when interpreting medical information.

Alternative bias is the decisional conflict generated by increasing the number of options. This manifests as a tendency to change preference when also presented with an additional option that is asymmetrically dominated. In one scenario involving a patient with osteoarthritis, family physicians were less likely to prescribe a medication when deciding between two medications than when deciding about only one medication [50].

Ambiguity aversion is the tendency to avoid options for which missing information makes the probability seem "unknown". In a study of primary care physicians, overutilization of prostate cancer screening among healthy individuals was associated with aversion to ambiguity [51].

Risk tolerance is a measure of uncertainty that someone is willing to accept with respect to negative outcome. As expressed earlier in this segment, patient and physicians may have different set points.

De-Biasing. Cognitive psychologists have postulated a dual system of decision making. System 1 refers to a fast, automatic and unconscious process of decision making. System 2 is a

slow, non-programmed and conscious process of decision making [52].

Clinical work involves repetitive activity, which can resort to system 1 thought. Overuse of this system likely causes cognitive biases [46]. Conversely, techniques that enhance system 2 could counteract these biases, thereby improving medical decisions. Reflective reasoning, checklists and decision analytics are strategies which induce physicians to pause and adopt more analytical thought [53, 54]. Advice can be drawn from these strategies, which pertain to variable medical scenarios:

- Decrease your reliance on memory. Review medical literature to confirm or broaden your diagnostic and therapeutic possibilities.
- Think about your thinking. Step back from the immediate problem to examine your thought process. Ask yourself: Was I comprehensive? Was my judgment affected by bias? Can this problem be seen from a different perspective?
- Assign weight. Complex medical problems have multiple variables and not all are relevant. Ask yourself: which variables are more important?
- Check your emotions. Recognize that altered mood states influence your thought process. If fatigue, hunger, sleep deprivation, anxiety are present, take steps to reduce their presence.
- Know your set point. Our form of practicing medicine can reflect personality traits. We have different set points of tolerance to risk and ambiguity. Ask yourself, where is *my* set point? Reflect on your overall practice as a physician. Compared to your peers, where do you stand? If you do stand towards one extreme, realizing this may help you adjust your practice towards more balanced decision making.

Shared Decision Making

We have diagnosed and 'understood' the problem. Through evidence based medicine, we have generated viable therapeutic options. The next step is engaging with patients to arrive at a decision.

Decision making roles between physicians and patients occur along a continuum [55, 56]. At the physician end of the continuum lies the paternalistic model. In this model, physicians assume what is in the patient's interest and the patient has a passive role, with limited participation in decision making [57]. At the other end of the continuum is a fully autonomous patient. Over the past few decades, there has been a shift from paternalism towards an emphasis on patient autonomy.

In 1988, the Picker Institute coined the term "Patient Centered Care". It is defined as health care that meets and responds to patients' wants, needs and preferences and where patients are autonomous and able to decide for themselves [58]. The model has become prevalent in modern medicine. No approach within medicine embodies this more than the palliative care approach, where goals revolve around maximizing quality of life and relieving suffering. Shared decision making is the core process of this model [59]. Shared decision making is often viewed as the middle ground along the decision making continuum. Both parties have different but equally valuable perspectives and roles. Physicians bring their expertise and patients bring their values. Participating in shared decisions is engaging in dialogue, where both perspectives are expressed [55]. Successful communication is critical to this process. The need to engage in shared decision making is greatest when a treatment plan has a high risk to benefit ratio; when the plan could conflict with patient values; and/or when there is no single best solution.

Two factors influence the balance between autonomy and paternalism: prognosis and the certainty of prognosis, and patient's decision making role preference [56]. For example, if the prognosis seems certain and one option promotes well-being over another, it is our duty to promote it. In doing so, the decision making balance may temporarily tilt towards paternalism. Similarly, if a family is making a decision about life sustaining treatment in an incapacitated patient, whose poor prognosis seems certain, the physician may ease the burden of a tragic choice by recommending limitation of life-sustaining treatment.

Most patients and families prefer a shared relationship with their physician. A sizable minority wish to retain full autonomy or contrarily, have a passive role [60, 61]. Despite its importance, physicians infrequently engage with patients in their preferred way. In one study assessing 1000 office visits, less than 10% of all decisions met the minimum standard for informed decision making [62]. Lack of time, resources and expertise may limit the incorporation of patient preferences [63].

Assigning Patient Value

Earlier in this chapter, the process of placing different medical options along a graph of benefits and risks was reviewed. These options should be further adjusted along this space by the patient's values (Fig. 13.2). For example, one multiple sclerosis study compared neurologist and patient perceptions of natalizumab therapy. Given the risk of PML, 49% of neurologists would stop treatment, while only 17% of patients would do so [64]. Certainly, a patient's values will not affect the probability of achieving a benefit or risk. With natalizumab, the risk of acquiring PML will remain 1:1000 and the annualized relapse rate reduction will remain 68% [65]. Conversely, the perceived impact of risks and benefits will change with patient values. In this case, patients were willing to accept higher risks in exchange for therapeutic benefits, valuing disease remission over the risk of PML.

Decision Aids

Decision aids are tools that enhance patient and family participation in the decision making process. They come in a variety of media (print material, video, interactive computer interfaces, etc.) and are developed with the goal of conveying complex medical information in an easily understandable and standardized way. Decision aids improve patient knowledge, decrease decisional conflict, improve risk perceptions and result in a more engaged role for patients [66]. Disease-specific decision aids present prognosis or treatment risks and benefits. Other decision aids, such as the Ottawa Personal Decision Guide, can be used to probe patient goals, concerns, and values [67].

Decision aid benefits have been shown in a variety of clinical settings and certain states in the US as well as the Center for Medicare and Medicaid services are increasingly requiring clinicians to use decision-aids in an attempt to enhance discussion about treatment options [68]. However, research in the neuro-palliative care setting is limited. Within this domain, a study of advanced dementia patients' surrogates found improved knowledge and decreased decisional conflict when deciding on artificial nutrition [69]. The neurological intensive care unit, where many decisions involve a trade-off between high-intensity interventions that can prolong survival in a disabled state versus a palliative approach, seems ripe for decision aid research.

Challenges

Shared decision making research has focused on cognitive and behavioral patient outcomes (satisfaction, decisional conflict, knowledge and adherence). However, research on health outcomes is limited, with most studies using patient-reported and un-validated instruments [70]. Furthermore, shared decision making has not improved physiological measures (e.g. hemoglobin A1c, blood pressure, lipid levels) [71, 72].

Studying shared decision making is inherently challenging. Engaging with patients is the final step of a complex process. Errors can occur at any preceding step: assessing diagnosis, prognosis, therapy risks/benefits, patient values, etc. Thus, a high quality shared decision between physicians and patients does not guarantee a high quality medical decision.

Despite the need for more research, there is an ethical imperative to advocate for shared decision making. It strengthens patient autonomy, a fundamental right.

The Objective

What constitutes a good decision? What constitutes a bad decision? Can we say that one decision is better than another?

In order to address these questions, we must reaffirm our purpose as health care providers. Medicine begins and ends with patients. Our purpose is to promote their well-being. This is meant in the broadest sense possible: physical, emotional and spiritual. Therefore, the success of our medical decisions should be measured in a patient's well-being.

Physical well-being is more than just the absence of disease. It includes lifestyle choices to ensure health, such as diet, exercise and sleep. Emotional well-being is what enables an individual to be able to function in society and meet the demands of everyday life. People with good emotional well-being can recover effectively from illness, change or misfortune. Spiritual well-being is what enables us to experience and integrate meaning and purpose in life. It is achieved through a person's connectedness with self, others, art, music, literature, nature, or a power greater than oneself. This focus on multiple domains of well-being is at the heart of palliative and neuropalliative care.

The concept of an ideal state of well-being is evolving and is open for continued debate. There may be many ideal states and many paths to these states. In addition, most aspects of well-being are difficult to quantify. As physicians with scientific training, emphasis is placed on objective quantitative outcomes: blood pressure, tumor size, seizure frequency, survival time, etc. We often fail to value subjectivity. The human experience is entirely subjective and therefore so is much of well-being: disease symptoms, mood and our sense of purpose in life. Subjectivity does not preclude differentiating better states of well-being from worse states of well-being.

How can we elevate well-being in the face of certain death? Imagine the following scenario: A 30 year-old man presents to the hospital with severe headache and nausea, and is found to have an acute intraparenchymal hemorrhage from metastatic melanoma. Clearly, symptomatic treatments for his headache and nausea should improve his well-being. Likewise, facilitating his wife's visit and playing his favorite Pink Floyd album while in the ICU, bring comfort and enhance his well-being. Unfortunately, his status suddenly decompensates, he becomes unconscious and he is intubated. He had expressed wishes for aggressive medical care, with the goal of surviving one week, until his child's birth. How long is it reasonable to continue life sustaining measures? While the most appropriate answer will be difficult to ascertain and will vary from patient to patient, it should always be framed with the goal of improving well-being.

Well-being should not be conflated with satisfaction. Satisfaction is seeking positive emotions while avoiding negative emotions. What would life be devoid of pain, anxiety or sadness? In many cases, we have to endure temporary displeasure to achieve higher states of well-being. An Olympic athlete cannot achieve a high state of physical prowess without enduring pain or forgoing sleep. A Buddhist monk cannot achieve a high level of spirituality without sacrificing hours of meditation and experiencing hunger. A child cannot develop immunity without coughing and sneezing from a cold.

Physicians should be cautious about overly emphasizing patient satisfaction. Patients typically bring expectations to medical encounters, often making specific requests. Satisfaction correlates with the extent to which physicians fulfill patient expectations [73–75]. In a US nationally representative sample, higher patient satisfaction was associated with higher health care expenditures and increased mortality [76]. When practicing patient centered care, we must recognize that a patient's requests are not always conducive to well-being. What they want may not be what they need.

Conclusion

On a broad scale, what can be done to improve medical decisions? First, there is a need to emphasize patient well being. Medical specialization leads to focused clinical problem solving. Conversely, complex medical problems demand that we maintain a broad appreciation

of the factors that enhance a patient's physical, emotional and spiritual well being. Second, there is a need for metrics to describe decision making quality in advanced neurologic illness. Third, there is a need to study implementation strategies. High quality decision making requires time. The additional time and the added value of applying shared decision making should be reflected in compensation strategies. These considerations are relevant in an era where physician burnout is prevalent, particularly among neurologists. Finally, there is a need to incorporate the teaching of shared decision making skills into the medical curricula for all providers, particularly neurology residents, fellows, and others that are highly engaged in the care of patients with neurologic disorders.

Take Home Messages

- Educating patients on their disease and therapeutic options is one of a physician's main responsibilities. Strategies to improve communication with patients include: slowing down, using non-medical language, using pictures, limiting information at each encounter, repeating information, proactively planning meetings and using the teach back technique.
- A patient's *values* are the aspects of life which they find important. A *preference* is a choice that pertains to a specific medical scenario. A preference is constructed from an individual's core values, is influenced by multiple factors.
- Therapeutic risks and benefits are determined in three different ways: Scientific evidence, clinical experience, and patient attributes. Therapeutic options should be further adjusted by incorporating patient values.
- Bias can occur in both patients and physicians, at any stage of interaction. The first step to overcome biases is becoming aware of their existence.
- Shared decision making is often viewed as the middle ground along the decision making continuum. Both parties have different but equally valuable perspectives and roles. Physicians bring their expertise and patients bring their values.
- The need to engage in shared decision making is greatest when a treatment plan has a high risk to benefit ratio; when the plan could conflict with patient values; and/or when there is no single best solution.
- The success of a medical decision should be measured in a patient's well-being: physical, emotional, and spiritual.

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Addressing and Managing Requests to Hasten Death

14

Neal Weisbrod and Timothy E. Quill

Case in a Box

AA was a 56 year old man who led an active life riding motorcycles and working in building construction. Five years ago he began dropping his tools and very gradually became weaker over the ensuing 6 months. A neurologist determined that he had both upper and lower motor neuron findings, and he was diagnosed with amyotrophic lateral sclerosis. No specific treatment was offered. He gradually became weaker such that he had to stop working, and over the next 4 years he became progressively dependent on the care of others. One year ago he had a palliative care consultation and asked specifically about ways that he could end his life in the future if his situation became unbearable. He was not depressed, but he could not make sense out of his life that was now dependent on constantly having a health aide present in his home as he needed assistance with all of his ADLs. He expressed interest in physician assisted death, but he lived in New York State where the practice is illegal. Even if he lived in a state where physician assisted death was legal, it remained uncertain whether would qualify based on prognosis. He felt trapped and wondered if he had any other options.

The field of neurology holds particular challenges in the management of the end of life. In this chapter we will delve into special considerations regarding requests to hasten death by neurology patients. For the purposes of this discussion we will use several neurological conditions as prototypes because of unique obstacles each poses. Amyotrophic lateral sclerosis (ALS) will be our model disease for a gradually progressive neurologic condition which, in one of its extremes, results in a locked-in condition with preserved cognition. Advanced Alzheimer's dementia will model the state of gradual but ultimately severe cognitive dysfunction with relatively preserved physical attributes. This sets these two diseases as opposite ends of a spectrum in which advanced Parkinson disease lies

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somewhere in the middle with its variable impairment in both cognition and physical function. In our discussion of stroke we will explore the impact of an acute condition with possible recovery on requests to hasten death. Glioblastoma will model a condition which can cause rapid loss of capacity to make decisions, and Huntington's disease will illustrate the situation of psychiatric illness complicating neurologic deterioration.

Oncology has dominated the clinical discussion around requests to hasten death. While prognostication is nebulous in any field of medicine, the prognoses of many of the aforementioned neurologic diagnoses are especially difficult to predict. Consequently, hastening death is delicate territory, particularly when combined with a patient's fear of their disease stripping them of the ability to live an autonomous life, to make their own decisions, or to simply bring an elixir to their mouth and swallow.

> For those suffering unbearably and coming to the end of their lives, merely knowing that an assisted death is open to them can provide immeasurable comfort.
> —Desmond Tutu

Definitions

Through this chapter we will use the term "physician assisted death" (PAD) to refer to the act of a physician prescribing lethal medication for a patient with a terminal diagnosis and full mental capacity to subsequently self-administer at a time of her own choosing. Physicians are needed for clinical assessment and prescribing, though the act often (but not necessarily) occurs in the absence of the physician. Different terms are used to refer to this practice. Most notably, those in opposition nearly universally use some variation of "physician assisted *suicide*," conflating PAD with mental illness.

The term "voluntary active euthanasia" (VAE) refers to the act of a physician directly administering lethal medication to a terminally ill patient at his explicit request. Etymologically the word "euthanasia" means "a good death." To date euthanasia has not been a major part of the debate in the United States, although it is a well-accepted practice in the Netherlands and has been recently legalized in Canada. We will explore differences between PAD and euthanasia and distinguish them from other "last resort" options later in this chapter.

Evaluating Requests

The first response to any patient request to hasten death should be exploration. Start by asking open ended questions about what they are asking: "Tell me more." During discussions about dying it is helpful to mirror the patient's language while ensuring everyone understands the meaning of whatever terms the patient is using. For example, if a patient asks what to expect when "my number is up" clarify initially that the euphemism is intended to mean "dead" and then use the patient's preferred language in subsequent conversation. It is important to determine whether patients are having suicidal ideation from unrecognized depression, or are they rationally investigating whether you will hasten their death now or at a future point of deterioration. When patients ask about a hypothetical future death they want to learn more about what to expect in the future. This is a chance to have a deep and potentially therapeutic conversation. While we acknowledge the potentially protracted nature of these conversations, each ignored comment about wishing for death is an enormous missed opportunity. A 1999 survey of neurologists with 645 respondents indicated that 5–7% of patients engaged them in a discussion of physician assisted death or euthanasia [1]. Every neurologist would benefit from being prepared for this discussion. Remember, having this conversation is not condoning PAD or agreeing to assist, but rather shows empathy and enhances understanding of your patient's fears. These are often emotional conversations but they can be tremendously rewarding if done well – solidifying a deep connection and reinforcing your patient's humanity (See Chap. 11 "Communicating Effectively").

On the other hand, patients who are adamant that they want to die *now* usually have unrelieved

suffering. Suffering comes in many forms – physical, psychological, social and existential. By existential suffering we are referring to a threat to identity and loss of aspects of one's self which are felt by that individual to be self-defining [2]. Part of the initial conversation should be to determine whether the patient has symptoms that are incompletely treated. Intensification of symptom management can allay many requests to hasten death. The question "Why now?" is a helpful tool for the physician to bring forth the concerns that are foremost in the patient's mind. Regardless of your personal values regarding PAD, talk with the patient about how you approach his circumstance, and assure him he will not be abandoned.

Exploration of symptoms of anhedonia, guilt, and worthlessness can indicate depression. Many of the other symptoms of depression (fatigue, sleep disturbance, weight loss) are non-specific and often present in patients with serious illness in the absence of a depressive disorder. While depressed patients may ask for a hastened death, there are distinctions between the suicidal patient and the patient who is ready to die and wishes for suffering to end. Clinically depressed patients may distort their clinical situation or future progression, and their actions may be inconsistent with their personal values and past behavior. They may have a prior history of clinical depression or other major psychiatric illness. If concern remains about clinical depression the patient should be referred to a psychiatrist or psychologist who has experience treating seriously ill patients [3]. A psychiatrist can also be helpful in situations where the decisional capacity of the patient is uncertain. We encourage a low threshold for referral especially if you are considering providing any "last resort" intervention.

If the patient is not depressed and symptom management is felt to be maximized but the patient still would like to investigate options to hasten death this should trigger a palliative medicine consult if not already initiated. This is important for several reasons. One, it will ensure that your patient is receiving optimized palliative care. Additionally, a second opinion serves as an important safeguard for both physicians and patients that all participants fully understand one another. Third, a palliative care consultation will yield another clinician with whom you can voice any stress or uncertainty about the process being contemplated. Most patients who have a persistent desire for assisted death have either severe physical symptoms other than pain or existential suffering which cannot be addressed by medications [4, 5]. An honest discussion about what end-of-life will likely entail given their diagnosis may relieve their concerns, but involvement by members of an interdisciplinary palliative care team can be helpful regardless. A chaplain, for example, may be able to explore existential or spiritual suffering from a different angle than a physician, and a social worker is often essential to ensure support services are maximized.

The most likely outcome of this conversation is that care will be improved and the patient's desire for a hastened death may be alleviated or at least postponed. While questions about death are frequent in patients with serious illness, very few ultimately follow through with physician assisted death. In a study of decedents in Oregon after the Death with Dignity Act 17% decedents considered PAD with their families, only 2% talked with their doctor about obtaining a lethal prescription and the process accounted for only 0.33% of deaths [6]. Of note, an estimated 3.4–6.7% of patients with ALS seek PAD in Oregon and Washington, representing the disease with the highest percentage of patients seeking PAD [7]. This highlights the importance of neurologists developing a strong foundation of basic palliative care skills to engage patients in these discussions.

Ethics

The ethical debate regarding physician-assisted death has been active for two decades in the United States, and experts and scholars tend to be steadfastly aligned on either side. Ultimately, one's belief about whether PAD is an acceptable practice often comes down to an individual's reaction to the questions eloquently posed by the Task Force on Physician-assisted Suicide of the

Society for Health and Human Values in 1995: *"What are we to make of individuals so beset with suffering and loss of function that they declare further life extension to be personally meaningless? Do we sympathize with them for the extremes to which disease and disability have brought them? Or do we exhort them to more strenuous efforts to find meaning in their present plight, citing instances of others who have successfully withstood terrible suffering, yet have affirmed life throughout?"* [8].

We will now provide an overview of some of the major arguments for ([2]) and against ([9]) PAD.

We begin with the arguments in opposition to PAD. One central tenant of critics is based on the wrongness of killing. This facet of the opposition is straightforward – prescribing or administering lethal medications to a patient is intended to kill them, and killing is wrong. By extension, critics have expressed great concern that engaging in PAD will undermine patient trust in medicine as a profession. Many are concerned about the so-called slippery slope – that if we assist terminally ill patients in dying we will not be able to continue to limit this service only to the terminally ill. By this logic, eventually anyone who wants to die will have a right to PAD and, even worse, physicians will begin to kill patients who do not request or even necessarily want to die [9]. A particular concern is that PAD will be applied as a means of killing underprivileged and burdensome patients, with particular attention to minority and disabled populations. Opponents turn to the Netherlands as an example of the progression of legalizing PAD to euthanasia. They also use the Netherlands to make an argument that PAD runs counter to the development of hospice and palliative medicine [9].

In contrast, the fundamental principle guiding proponents of PAD is respect for patient autonomy. The principle of autonomy holds that the burden of proof rests with those who wish to restrict patient choice. While autonomy alone does not indicate that PAD should be morally acceptable, it shifts responsibility to opponents to provide a clear reason to limit patients' ability to be the author of their own life stories. Of course, the physician's autonomy also needs to be respected – physicians should have the option of non-participation if it violates fundamental personal values even if the practice is legally permitted. The principles of non-abandonment and mercy round out the central arguments in support of PAD. Non-abandonment makes it imperative that physicians be willing to engage in the discussion and search for common ground with the patient without either party violating their own fundamental values. The principle of mercy is well described by Marcia Angell: "If tomorrow will be worse than today, one day after another until the end, why not die today? Why continue to disintegrate, to lose bodily functions, to grow ever more helpless and dependent" [2]. Suffering has many forms that mercy can target, and when palliative care is optimized and creative solutions are explored the remaining cases where PAD is sought by terminally ill patients to mercifully relieve suffering should be few. Proponents also point out that in Oregon and the Netherlands where PAD is legal, a study did not find evidence to support critics' concerns about PAD being used selectively in vulnerable populations [10].

If one agrees that in certain situations it is acceptable for a physician to prescribe lethal medication for a patient to end her own life, what does one do when she is unable to self-administer the medication? This hypothetical is more frequently encountered in neurology than in other fields of medicine. Does a patient with advanced ALS who is nearly locked-in have the same right as a cancer patient who can potentially self-administer the lethal medication to avoid unbearable suffering? Ethically, we believe physical disability should not be a barrier to rights. Consequently, if one accepts the arguments in favor of PAD then euthanasia should potentially be permitted in select circumstances when a patient who would otherwise qualify is not physically capable of participating in PAD. However, from a pragmatic standpoint there are clear differences. PAD has a built in safeguard that the patient must finally take the medication on her own, while in euthanasia the physician not only evaluates and prescribes, but also administers the lethal medications. Data

from the Netherlands suggests that euthanasia may be more difficult to regulate, though there may also be cultural differences about how regulations are viewed and adhered to in different countries [11, 12]. Regardless of concerns about abuse, it is essential that physicians participating in PAD or euthanasia obtain second opinions ideally from someone with expertise in palliative care to ensure that all alternatives have been explored and criteria met.

Options for Responding to Reasonable Requests for Hastened Death

The next section will address what to do in the infrequent circumstance where palliative care is maximized, but a patient continues to request a hastened death. Table 14.1 summarizes the different methods to approach requests to hasten death in order of societal consensus about

Table 14.1 Summary of different methods of a hastened death in order of societal consensus about acceptability

Process	Factors promoting applicability in neurology	Factors hindering applicability in neurology
Withdrawing/withholding life-sustaining treatment	Legal, consensus on ethical acceptance	Only addresses suffering in the context of life support
	May be enacted via health care proxy	Narrow scope within neurology outside of artificial feeding and the common final pathway of respiratory failure
	Frequently does not require additional consultants	
Palliative sedation	General consensus on legal and ethical acceptance	Addresses mainly physical suffering, but also may be used to address terminal delirium
	May be enacted via health care proxy for incapacitated patients	Largely limited to imminently dying patients with severe physical suffering
	May be rapidly enacted	
Voluntarily stopping eating and drinking (VSED)	Minimal legal risk to physician	Duration often 1–2 weeks, longer if not strictly limiting fluids
	Highly patient-driven, lower risk of coercion	Thirst and dry mouth can be difficult to manage
	May address all forms of suffering	Loss of connection of sharing meals at the end of life may be inconsistent with patient values
		Not appropriate for addressing acute and severe suffering (too slow)
Physician assisted death (PAD)	May address all forms of suffering	Illegal in most US jurisdictions
	Median time from ingestion to death of 30 min, but can take considerably longer	Requires cognitive capacity and ability to self-administer
	Avoids physical symptoms associated with VSED	Lack of consensus on ethical acceptance
	May provide patient with peace of mind as an "insurance option"	Limited where legal to life expectancy <6 months
	Built in safeguard of patient self-administration	Complications may be difficult to manage in the absence of a physician
		Medications fluctuate in availability and many accepted preparations are expensive
Voluntary active euthanasia (VAE)	May address all forms of suffering	Illegal in all but a few Western European countries and Canada
	Rapid effect within minutes	High risk of prosecution if discovered in countries where prohibited
	Physician may immediately respond to complications	
	Potentially accessible to all patients regardless of physical limitations	Lack of consensus on ethical acceptance
		Requires additional safeguards due to highest theoretic risk of abuse

acceptability. Withdrawal of life sustaining treatment and proportionate palliative sedation are both legal and generally ethically accepted. As always, we encourage physicians to seek a second opinion from someone with palliative care expertise regarding strategies to minimize the patient's suffering.

Withdrawal of Life Sustaining Treatment

Since the case of Karen Ann Quinlan formalized the legality of withdrawal of life support there has been a great deal of medical literature on the subject. All physicians who care for seriously ill patients would benefit from developing comfort navigating decisions regarding withholding or withdrawing life-sustaining treatment (see Chap. 15 "Withholding and Withdrawing Life-Sustaining Treatments"). Outside of the field of neurology there are many examples of life-sustaining treatment such as left ventricular assist devices (LVADs) for heart failure and dialysis for end-stage renal disease. Within neurology this discussion is primarily centered on mechanical ventilation and artificial nutrition/hydration. As medical technology has grown more complex we have discovered new ways to maintain life, but as a result the distinction between keeping people alive and bodies warm has become less clear. Brain death is at one end of the spectrum and legally, at least in theory, does not require consent by the family for withdrawal of cardiopulmonary support. However for moral and legal reasons physicians should be sensitive to the religious beliefs of the family and in the case of disagreement with the family involve ethics and legal teams to ensure compliance with state precedents and accepted medical practice [13]. Physicians can also reference the guidelines published by the American Academy of Neurology (AAN) on the diagnosis of brain death [14]. The opposite end of the spectrum from brain death is a patient who has suffered high cervical spinal cord injury and is cognitively intact but ventilator dependent. Such patients clearly have the legal authority to forego life sustaining therapy, but it might be a greater burden on the participating physician which requires an assessment similar to what would be performed with a case of PAD (involvement of a multidisciplinary team and a second opinion from a palliative medicine consultant).

In addition to potentially withholding or withdrawing ventilators, a neurologist might consider withholding or withdrawing glucocorticoids in a patient with widespread cerebral edema due to an underlying neoplasm. Patients declining artificial feeding in the setting of stroke-related dysphagia would also fit into this framework. The conversation follows similar principles to any request for a hastened death, though in these situations the patient is often incapacitated requiring the decision to be between clinicians and family or health care proxy. When the patient is incapacitated it is helpful to repeatedly frame the conversation as *what the patient would want*, not what the health care proxy wants for the patient. During exploration the question "If your mother was sitting at this table with us, what would she say?" clarifies to family that you are looking for them to imagine their mother's voice – not render their decision ***for*** her. Of all of the options we will discuss, withdrawing or withholding treatment is one case where we do not always necessarily recommend an independent palliative medicine consultation. These conversations fall under the purview of "primary palliative care" – the set of skills we hope all physicians who treat seriously ill patients will develop [15]. However in complex cases or where there is uncertainty about how to proceed, a palliative medicine consult can often be helpful. Patients who are going to be removed from mechanical ventilation as part of a withdrawal of life-sustaining therapy may also benefit from a palliative medicine consult for recommendations on symptom management during and after terminal extubation, and for further support if respiratory failure does not ensue quickly.

In stroke patients for whom artificial feeding is being withheld or withdrawn, any oral nutrition the patient desires and receives pleasure from should be permitted. Remind family and friends that forcing the patient to eat more than they desire will not make them more comfortable. Typically when artificial feeding is declined

and comfort measures are being pursued, withholding intravenous fluids is also recommended. Artificial hydration is akin ethically and legally to artificial feeding.

When mechanical ventilation is being withdrawn and death is anticipated, planning and anticipation of how to manage dyspnea are key (see Chap. 16 "Hospice and End of Life Care in Neurologic Disease"). A time for the actual withdrawal should be agreed upon with family and adhered to. Prior to palliative extubation, we recommend initiation of opioid and benzodiazepine infusions at dosages similar to those that would be expected in the situation of palliative sedation. Respiratory rate should be closely monitored and tachypnea should be treated as an indication of dyspnea in the unresponsive patient in addition to grimacing or other physical indications of distress. Special attention and preparation is needed to manage extubation in the alert patient, which can be emotionally challenging [16]. Of course, for a patient being extubated where there is a meaningful chance that the patient can breathe independently off the ventilator, but is also not going to be re-intubated (a "sink or swim" extubation), sedation should be minimized at first to give the best chance of surviving. However, if the patient goes into respiratory failure and is not going to be re-intubated, transition to more aggressive terminal sedation should be initiated.

Palliative Sedation Potentially to Unconsciousness

Moving from de-escalating/withholding treatment to escalating treatments for acute, otherwise unrelenting suffering we will discuss palliative sedation. As long as the intent is not to hasten death, there is consensus that palliative sedation is ethically acceptable even to the point of unconsciousness if necessary to control otherwise unrelenting, severe symptoms [17]. A physician who is administering palliative sedation should clearly document the symptoms being managed and escalate palliative treatments incrementally to ensure clarity about the medical necessity. With this evidence, palliative sedation, potentially to unconsciousness, is a tool already available in the arsenal of combating extreme suffering. An important tenant of palliative sedation is that the degree of sedation is proportional to the symptoms – in other words that the dosage is reasonably expected to lead to symptom relief and not necessarily death [18]. Death if it comes quickly is an unintended side effect and not the means to relieve the suffering (as distinct from PAD or VAE). Additionally, the suffering individual may lack capacity for self-directing medical decisions and still be a candidate for relief by palliative sedation.

Most pain and dyspnea can be relieved without the use of sedating doses of opioids, though occasionally at the very terminal phase proportionately sedating doses are required. Agitation is common in the final days and weeks of patients dying with many conditions including dementia or stroke, and is another symptom frequently targeted by palliative sedation. Seizures could also be classified as a symptom which can be targeted by palliative sedation. In rare cases frequent or intractable seizures may complicate end-of-life. Single doses of benzodiazepines should be used (subcutaneous or IV) for seizures initially, and less sedating anti-epileptics should be considered in most situations. Regardless of the symptom being targeted the general procedure of palliative sedation is similar: a short-active sedative such as midazolam or propofol is administered to achieve the desired reduction in symptoms, with consciousness maintained if lesser degrees of sedation can alleviate symptoms.

Palliative sedation is usually targeted at hard to control physical symptoms. It is much more controversial and infrequently practiced to administer palliative sedation for primarily existential or psychiatric suffering. Most often, total suffering includes aspects of many dimensions, but the practice of palliative sedation without a strong and compelling physical component is rare and should require input from specialists in palliative care and psychiatry. Furthermore, some patients may be agreeable to the final paragraph of their life narrative being aggressive sedation for symptom control, while others may be appalled by the idea of lying in a drug-induced

stupor for days to weeks. While palliative sedation is widely accepted in the management of imminently dying patients there are many terminal neurodegenerative diseases characterized by slowly progressive deterioration with symptoms present for months if not years before they are imminently dying. Clearly in these circumstances palliative sedation is not an ideal tool.

Voluntarily Stopping Eating and Drinking (VSED)

The next method of hastening death that we will explore is voluntarily stopping eating and drinking (VSED). VSED has a few theoretical advantages over PAD or euthanasia. The process is largely patient-driven and does not necessarily require physician involvement. A consequence of the patient-driven nature is that VSED has a lesser risk of coercion. A more pragmatic advantage is that there is unlikely to be any legal risk to the physician assisting in VSED [19]. However, the ability of VSED to occur outside of the confines of medicine also means it could theoretically be done without the patient being fully evaluated. VSED should have similar safeguards in place to PAD including informed decision-making and maximal palliative care [20]. Note should also be made that VSED is relatively poorly studied compared to other modes of hastening death, which limits detailed examination of the process [21].

To assist in informed decision making data are required, and few studies describe the course of VSED. One retrospective survey regarding 96 patients in the Netherlands demonstrated that the majority of patients who underwent VSED died within 2 weeks, but the tail of the survival curve extended out to 35 days. From clinical experience we can presume that the patients who are outliers on extended duration of survival were receiving small amounts of fluids, as dry mouth and thirst can be difficult to palliate without drinking. The most common symptoms at the end-of-life with VSED in this study, in order of frequency were: pain, fatigue, impaired cognitive functioning, thirst or dry throat, delirium, dyspnea, reduced consciousness, agitation, and impaired communication. While these symptoms were reported with a low percentage (4–14%) the methodology of a retrospective survey of physicians is likely not an accurate way of determining the prevalence of symptoms, and almost certainly the degree of thirst was underreported [22].

We have several concerns about the use of VSED as an end-of-life intervention even in well-managed circumstances. For some patients who are suffering and wish to hasten their death they may see this as starving/dehydrating themselves to death in an inhumane manner. Deterioration can become drawn out if strict avoidance of fluids is not maintained. For others, the descent into unconsciousness threatens a loss of dignity not compatible with their sense of self and is exactly the circumstance they are trying to avoid their disease imposing upon them. Finally, it is a slower process than other measures we will discuss and consequently may be less appropriate to address acute suffering.

The main utility of VSED is that it is almost entirely under the patient's control, and therefore does not require "permission" from physicians or society. It is also an option that can respond to less severe forms of suffering where a patient might not qualify for other last resort options – there might be no life sustaining treatments to stop, their prognosis may be too long and uncertain, and they may have no severe physical symptoms to palliate. Due to the risk of severe physical symptoms developing during VSED, we recommend discussion of palliative sedation as a tool to respond to these symptoms prior to initiating VSED. This may allow prompt intervention if the worst comes to pass, particularly if terminal agitated delirium develops late in the process and other palliative options have been exhausted.

PAD

Physician assisted death (PAD) marks our transition into more ethically controversial and legally restricted territory. It is important to acknowledge that PAD has long been practiced covertly in the US and Western Europe regardless of legalization. A 1996 national survey of physicians found that 3.3% reported they had written a prescription for

medication for a patient to use with the primary intention of ending their life [23]. PAD practiced without fully informed consent, second opinions, and documentation is fraught with danger. In this environment discussion with the patient may be circumstantial to avoid legal responsibility. This could lead to misunderstandings about the intentions of the patient as well as nebulous instructions and expectations. In an illegal environment, documentation is typically lacking and second opinions are strongly discouraged. This leads to a physician and a patient acting alone in secret, possibly unable to confirm that palliative care has been maximized and most likely not having an outlet to discuss this emotionally burdensome request or outside support for this action.

Since Oregon initially passed the Death with Dignity Act in 1994 six additional jurisdictions (Washington State, Vermont, Montana, California, Colorado, and the District of Columbia) have legalized physician assisted death as of 2017. A few of the remaining states have explicit laws against PAD, but even in the majority where it is not specifically addressed there is a significant risk of conviction and/or loss of license if a case goes to trial. Canada recently legalized both PAD and voluntary active euthanasia (VAE) on a national level in June 2016. The past two decades have seen a gradually growing acceptance of PAD as potentially ethical, and in some places legal end-of-life intervention. This makes it all the more important for physicians to be knowledgeable and open to the discussion regardless of personal beliefs. In the US, three mechanisms exist to legalize PAD: referendums, legislation, and case law. The process of initiatives or referendums varies from state to state but involves a ballot measure which can amend the state constitution or accept/reject legislation [24]. Legislation is written and voted on by state government. Case law goes through the judicial system and can set new precedents or interpretations of the law based on a judicial ruling.

Regarding the logistics of PAD, the most commonly used medications are barbiturates. The exact combination of medications varies based on availability and cost. Standardization of the cocktail with a stable production supply and cost would be beneficial to improving the science evaluating outcomes. Patients are often instructed to take an antiemetic prior to ingestion of the barbiturate [25]. Loss of consciousness is rapid after taking the barbiturate, but time to death can be significantly longer. Using 5 years of data from Oregon's experience with PAD, the median time from ingestion to unconsciousness was 5 min and the median time from ingestion to death was 30 min with a range of time to death from 4 min to 37 h. Three percent of patients vomited during PAD in this sample [26]. This illustrates that while PAD using barbiturates has a low rate of complications they do occur and, in the absence of a physician, family are left to wait out the uncertainty. This argues strongly for physician availability if not presence when this option is being acted upon.

Euthanasia

Euthanasia, also referred to as voluntary active euthanasia (VAE), is more controversial than any other "last resort" interventions – largely because of the direct and central role the physician plays in the process. In discussing euthanasia it is necessary to separate pragmatic concerns from ethical dilemmas. Many clinicians and ethicists do not see a fundamental ethical distinction between giving lethal medication to a patient for them to take at home to hasten their own death and directly administering lethal medication to hasten death at the request of the patient. In both circumstances the two parties intend the action to cause death, and in both circumstances the physician is providing the means for doing so. The key difference is the final hand that administers the medication. Pragmatically, however, the two practices are profoundly distinct. The more independent the patient is in their actions to hasten death the less risk of coercion there is. In PAD the patient raising the barbiturate to their own mouth is a final safeguard that it is a voluntary action. Removal of this safeguard does not make the action immoral, but it does necessitate greater care is taken to ensure death is desired by the patient absent external influences. Psychologically, VAE is likely to

be much more difficult on physicians than PAD as there is no escaping the physician's direct contribution to the timing and actuality of the patient's death.

Euthanasia is illegal in all US states, and physicians will almost certainly be prosecuted if the action is discovered. Jack Kevorkian, for example, provided PAD for over 100 patients. He was tried and acquitted of "assisting in suicide" three times before escalating to appearing with a video of himself directly injecting lethal medication to end the life of Thomas Youk, who had ALS. This led to his ultimate conviction for second degree murder [27]. In other words, Kevorkian openly assisted in the death of over 100 patients by PAD and was not convicted, but he directly administered lethal medication in *one* patient (VAE) and was convicted of murder and imprisoned.

One cannot have a thorough conversation of euthanasia without acknowledging data from the Netherlands where VAE is legal. One major criticism of the Dutch practice is data about Life-ending Acts Without Explicit Request by the patient (LAWER). The percentage of deaths studied due to LAWER varied between 0.4% and 0.8%, with the highest percentage in data from 1990 and the lowest percentage in data from 2005 (the last year included in the study). Opponents point to this as evidence of the slippery slope of legalizing euthanasia – stating that it indicates when euthanasia is legalized it will inevitably lead to *non-voluntary* mercy killing. However, data do not support this interpretation. Van der Heide investigated LAWER in six European countries: Belgium, Denmark, Italy, Sweden, Switzerland, and the Netherlands. At the time of the study PAD and euthanasia were both illegal in Denmark, Italy, and Sweden, and euthanasia was illegal in Switzerland and Belgium. That study demonstrated that legalization of PAD and euthanasia did not predict higher levels of LAWER. LAWER represented 0.67% of studied deaths in Denmark and 1.5% in Belgium; both countries where euthanasia was illegal while it was 0.6% of deaths in the Netherlands where euthanasia was legal. Our interpretation is that the differences between LAWER rates are more based on the cultural differences than legal status of PAD or euthanasia. Data also suggests that the majority of cases of LAWER involved incapacitated patients who had either previous discussion with the physician about circumstances in which they would desire euthanasia, or are the result of a physician-family discussion. Taken together, our current evidence indicates that cases of euthanasia without prior discussion with the patient and without discussion with the family are rare, but their existence at any level is extremely concerning [28, 29]. Transparency about end-of-life is likely to provide the best defense against such circumstances. Mandatory reporting of all instances of PAD or euthanasia is beneficial to science and society as a whole to allow retrospective review of how and why the practice is being pursued.

Application to Neurology

At this point we have discussed the most relevant mechanisms for hastening death: withdrawal/withholding of treatment, palliative sedation, VSED, PAD, and euthanasia. Now we turn to incorporating these interventions into our understanding of the specific challenges in neurology. We will start with the obstacles specific to amyotrophic lateral sclerosis (ALS).

ALS

End-of-life decisions in ALS are complicated by the fact that patients typically retain cognitive functioning while being subjected to a gradual deterioration of their physical functioning over the course of months to years (see Chap. 8 "Neuromuscular Diseases"). In fact, there is no relationship between depression, cognitive impairment, or behavioral impairment and wish to die in this population [30]. Proficiency in navigating end-of-life discussions and describing options is essential to physicians caring for patients with ALS. Although few patients with ALS end up engaging PAD, many consider the option in their exploration of the effect the disease will have on them (like our initial case

study). In a study of 100 ALS patients in Oregon and Washington 56% reported they would consider PAD [31]. In a Netherlands study, 17% of patients with ALS died by VAE and 3% died by PAD [32]. In the terminal stages of ALS patients may approach a state similar to being locked-in and with maximal intervention typically become ventilator dependent. PEG placement is also a frequent occurrence and artificial nutrition becomes necessary to sustain survival. When such life prolonging treatments are chosen, the option of withdrawing them at a later time as disease progresses may lead to a quick death. However, not all patients are willing to subject themselves to this level of intervention. Patients who decline ventilation and/or artificial nutrition will potentially be candidates for palliative sedation as they develop dyspnea or symptoms from dehydration/starvation. The main circumstance that makes hastened death unique in ALS is that a fully capacitated patient may be physically unable to engage in PAD independently. Such a patient may go through the legal process in a state such as Oregon and demonstrate a consistent wish for hastened death despite maximal palliative care, lack of major depression, and receive a lethal prescription for barbiturates only to be unable to self-administer the medication. A caretaker would be required to deliver the medication in this scenario who could then be legally prosecuted for assisting suicide. Aside from legal concerns, family may be extremely uncomfortable with directly administering lethal medication to their loved one despite respecting his wishes. Should this particular disability preclude such a patient from practicing his legal right to self-determination in end-of-life? It is precisely this situation that argues for ethical parity between PAD and VAE.

Dementia

Dementia, on the other hand, involves a nearly opposite pattern of functional impairment (see Chap. 6 "Dementia"). Patients experience gradually progressive cognitive decline with a relative preservation of physical function. Perhaps the greatest barriers to consideration of end-of-life options in dementia are prognostic uncertainty and loss of capacity prior to this discussion. Patients with frontotemporal dementia may have a more rapid and to some extent predictable decline but particularly in Alzheimer's dementia the decline is insidious with median survival of about 6 years after diagnosis [33, 34]. While the natural history is generally understood, death in patients with Alzheimer's dementia typically comes at the hands of secondary events such as infections (namely, pneumonia). The onset of these secondary events is unpredictable. Aside from the uncertainty about prognosis, end-of-life decisions in dementia are also complicated by the fact that an intrinsic part of the natural history is loss of the capacity to make complex decisions such as pursuit of a hastened death. For those who believe the deterioration of dementia runs contrary to what they see as a dignified life there is fear of waiting too long and losing the ability to make the decision [35]. The case of Sandra Bem illustrates this clearly. Sandra was a psychology professor at Cornell for whom independence and cognition were fundamental to her self-image and sense of self-worth. Early in her disease it was clear to Sandra that her only way to protect her sense of self was to end her life before the disease degraded everything about her that she valued. Her family initially convinced her to put off hastening her death, but as she became more and more a shadow of her former self they too realized the mercy of avoiding further cognitive decline outweighed the loss of time together. Ultimately, Sandra ordered pentobarbital from Mexico and about 7 months later, when she was barely able to hold a conversation she self-administered the medication and died with her husband at her side, in her own home [36]. Ultimately, all of the philosophical and ethical arguments are unlikely to change one's perspective on PAD and euthanasia, but understanding an individual's choice can persuade more than any debate.

If one accepts the potential merits of PAD or euthanasia in dementia, there remain questions about what degree of cognitive decline would preclude these life and death decisions, and also

whether a patient with early dementia would qualify in terms of prognosis even where the processes are legal. No easy answers to these questions exist. In Sandra Bem's case she was able to balance on a knife's edge the risk of losing the capacity to end her own life with spending as much time with her family as possible, but this decision can be haunting for people like her. For some, the solution may be to access a hastened death after they have lost the capacity to make the decision on their own, but this option would require acceptance of euthanasia by advance directive and corroborating discussion with family. The practical issues of allowing such options are undeniably multifaceted, but the complexity of the problem should not bar an attempt at a solution. Even in places where PAD is legal, most patients with dementia would not qualify in terms of a terminal prognosis. The "catch 22" is that by the time they are terminal most would no longer have decision-making capacity. The last resort option currently available to patients with dementia who retain decision making capacity would be voluntarily stopping eating and drinking.

Parkinson Disease

Parkinson disease involves a combination between the complexities of physical and cognitive deterioration (see Chap. 5 "Parkinson's Disease and Related Disorders"). Additionally, Parkinson disease has a high prevalence of comorbid depression (around 23%) [37]. Early on in the course of Parkinson disease impairment is typically pure motor, but dementia becomes more prevalent (up to 60–80%) as the disease progresses and related diseases such as Lewy Body Dementia involve a more even pace of functional and cognitive decline [38, 39]. These diseases can be seen on a spectrum with ALS at one end representing (nearly) pure physical impairment and Alzheimer's dementia at the other representing (nearly) pure cognitive impairment. The loss of independence, sense of identity, and dignity caused by these neurodegenerative conditions demands empathy and attention to patients' wishes at the end of life. Care will be improved by individualized, creative solutions including the full range of last resort options. Involving family members, the neurological subspecialist, and primary care physician or general neurologist in the decision-making should be considered if possible, with the addition of a palliative medicine specialist for complex cases.

Glioblastoma

Brittany Maynard's publicity and passion for broadening the conversation about requests to hasten death undoubtedly went a long way toward legalization of PAD in California. She was suffering from glioblastoma and moved from California (where PAD was not yet legal) to Oregon to access PAD. Brittany was an activist for patients' right to PAD before ultimately using PAD to end her own life as symptoms from her brain tumor progressed and became intolerable [40]. Glioblastoma is a particularly frequent diagnosis where options for hastening death are considered due to the grim prognosis and incurability of the disease (See Chap. 9 "Malignant Brain Tumors"). The median survival remains <15 months and sudden loss of capacity can be caused by progression of the tumor itself or common complications such as hemorrhage, seizure, and venous thromboembolism [41, 42]. Consequently, glioblastoma presents several specific challenges. Perhaps the most important for our discussion is that advance care directives and end-of-life discussions must occur earlier in the therapeutic relationship with the patient than with many other diseases which have a much longer time course and less potential for losing decision making capacity from presentation to death.

Status epilepticus and pulmonary embolism are common in patients with glioblastoma, and either may potentiate the need for mechanical ventilation. These events often produce reversible respiratory failure and this is important to note when discussing advance directives. A patient who desires a hastened death may opt to forego treatment of the complications that arise in place of other measures of hastening death. While it remains appropriate to withhold intubation if the patient does not desire any means to

prolong his or her life, these are often ideal circumstances to discuss time-limited trials of life support with the patient and family [43]. Glucocorticoids such as dexamethasone are commonly used for symptomatic relief in patients with glioblastoma. If patients have a clinical response, glucocorticoids can be continued up to the time of PAD or euthanasia with the goal of providing the maximal quality of life preceding a hastened death. Stopping glucocorticoids can also be considered cessation of a life sustaining therapy followed by aggressive palliation of symptoms that might occur.

Huntington's Disease

Huntington's disease (HD) shines the spotlight on a facet of requests to hasten death that we have not explored thoroughly prior to this – psychiatric comorbidities. In a Netherlands study, 64% of patients with HD indicated at some point in their disease trajectory they would wish for PAD or euthanasia. This high prevalence of desire for PAD or euthanasia prompts consideration about the unique aspects of this disease.

Psychiatric symptoms have long been recognized as an early manifestation in HD. Depression is twice as prevalent in patients with HD as the general population, and more than 10% report at least one suicide attempt, more than any other medical or psychiatric condition [44]. Psychosis, personality changes, and other psychiatric abnormalities tend to develop early on in the disease and lead to strained interpersonal relationships. It does not appear that depression continues to increase in prevalence or severity later in the disease course [45–47]. In the late stages the various manifestations of the disease converge on a pattern of severe cognitive impairment and physical disability. All of these considerations make requests to hasten death particularly challenging. While patients with HD certainly have legitimate reasons to fear the deterioration their disease inevitably brings, paranoid thoughts and depression may confound their decision-making process. We recommend involvement of a psychiatric consultant in all cases of persistent requests to hasten death in patients with HD for these reasons. This measure reinforces adequate treatment of psychiatric comorbidities and also potentially provides an independent assessment of whether the request to hasten death stems from depression or more rational thought processes.

Stroke

Applying PAD concepts to stroke patients is fraught with additional complications. First and foremost, of all of the diseases we are specifically discussing, stroke is the only one which is not progressive. Most patients recover after strokes, though recovery can be limited and mortality is a significant risk early in the course of large strokes (See Chap. 2 "Severe Acute Brain Injury"). Age and deficit burden (frequently assessed via NIH stroke scale) are the main determinants of early death. A large German study including over 16,000 patients with strokes demonstrated a jump from 3.3% in-hospital mortality with an NIHSS of 5–15 to 25.5% with an NIHSS of 16–25 and 47.7% in-hospital mortality with an NIHSS >25. A poor outcome (identified as modified Rankin Scale 3 or more) was almost universally present in the latter two groups [48]. The mortality curve with respect to age increases sharply after an age around 80 [49]. Much of the challenge in prognosticating in stroke patients appears to be related to fluctuation within the first several hours and the presence of complications within the 1st week. The persistence of deficits at 7–10 days is a much more reliable predictor of long-term outcome than earlier deficits [50].

These uncertainties raise important points about the care of stroke patients. First, patients who are >80 and have suffered large strokes are extremely high risk for poor outcomes and mortality. Second, prognostic estimates are dramatically more reliable after about 1 week. These data indicate that in the highest risk subset of patients we should have realistic discussions with the patient and family about the severity of the situation and consider withholding aggressive intervention if it would be consistent with their wishes. In the remaining situations where

prognosis is nebulous, we recommend use of time-limited trials with the recognition that typically after 1–2 weeks prognostication will improve [43]. A hastened death in stroke patients will typically depend on withholding of interventions as elderly patients with large strokes are typically incapacitated at the time these decisions must be made. Patients who are capacitated often have a lesser deficit and their ultimate prognosis is typically more dependent on underlying diseases than the stroke itself. Consequently we do not see PAD and euthanasia as highly applicable to the care of stroke patients, though certainly patients who have other underlying progressive diseases and are further debilitated by stroke may have their associated deficits influence their decision to pursue PAD.

Summary

Hastening death is an important contemporary conversation in medicine in the United States as PAD is being legalized in additional states, and as a society we continue to focus on patient autonomy. Requests to hasten death may be seen disproportionately in patients with neurologic disease as our diseases tend to cause severe physical and/or cognitive disability and for many attack the core of what it means to be human – influencing our ability to care for ourselves, hug family members, talk to loved ones, and think about our place in society. While not every physician must be expert in all of the options for hastening death, a foundational knowledge of these issues and comfort in discussing the topic if raised by the patient is essential to the care of seriously ill patients. The initial response to patient inquiries about a hastened death should be exploration, not denial or affirmation. These discussions can clarify the values and fears of your patients and lead to a deeper and more rewarding patient-physician relationship. Many patients may want to consider and explore these options as they face the end of their lives to be sure they understand all possibilities, but relatively few will then pursue them in earnest. For most, the possibility of an escape may be more important than the reality [51]. When a hastened death is adamantly desired and the patient meets agreed upon criteria, the initial discussion should revolve around withdrawal of life-prolonging treatments and withholding further interventions not focused on comfort. If this is not sufficient to alleviate the patient's suffering or if there is uncertainty about evaluating or responding to the patient's request, a palliative medicine consultation should be sought. The next more aggressive interventions are voluntarily stopping eating and drinking for patients whose immediate physical suffering is not overly severe (VSED, an active but almost entirely patient-centered intervention) and palliative sedation for those who need an aggressive response to immediate, severe suffering (an active intervention from the physician). Regardless of which option is being employed, careful discussion to inform the patient and family of what to expect is mandatory. Physician assisted death (PAD) marks passage into more legally and morally nebulous territory, though we anticipate it may be legalized in additional states as time goes on given growing public support. PAD and VAE allow a more rapid alleviation of suffering/hastening of death than other interventions but require regulation for patient safety and to ensure fully informed consent and adequacy of palliative treatments.

The field of neurology brings specific challenges to discussions about hastening death. Perhaps the most perplexing are the questions of (1) hastening death in patients who are sure to have insidious cognitive deterioration and (2) barring voluntary active euthanasia for patients otherwise eligible to access a physician assisted death who are physically incapable of self-administration. We encourage palliative medicine specialists to become seriously engaged as consultants in these decisions as a safeguard to high-quality communication and maximizing more standard palliative interventions before any "last resort" options are pursued.

Caring for dying patients involves a substantial emotional burden, and assisting patients through a hastened death is often reported as particularly intense [52, 53]. Neurologists are already among the highest risk of physician burn-

out by specialty, and rate work-life balance lower than other specialties, so self-care is particularly important in dealing with emotionally taxing situations such as end-of-life care [54]. We strongly recommend communication with colleagues regarding the discomforts, challenges, and joys of treating seriously ill patients. This can be an additional benefit of bringing a palliative care specialist into the treatment team.

Return to Our Initial Patient Presentation

AA had multiple conversations with his treating neurologist about his end of life options, and a palliative care consultant was asked to become involved. Both agreed that AA was not depressed and that wanting the option of a hastened death was consistent with his long standing views and values. Although the patient's preference would have been for PAD, he lived in New York State where the practice is illegal. Even if he lived in a state where PAD was a legal, it was not entirely clear he would meet the terminal illness requirement (death expected within 6 months) and it was also not clear he could self-administer the required amount of medications all at once by himself (meals had become very time consuming and required a lot of assistance.) His acute symptoms were not severe enough for palliative sedation, which left voluntarily stopping eating and drinking as his only realistic choice.

AA appreciated this option but chose not to activate it for another 6 months. He felt less trapped with the knowledge that there could be an escape at a time of his own choosing, and he was still finding enough meaning to live longer. However, his level of dependence eventually became unacceptable to him and he asked for a visit to explore options. He was assessed to be thinking clearly to both the neurologist and the palliative care clinician, but both asked him to be evaluated by a psychiatrist to corroborate his decision making capacity and ensure that all alternatives were considered. The psychiatric consultant agreed he had full decision making capacity and was not clinically depressed. His home health aides on whom he was totally dependent refused to participate despite talking with the clinical team, so he was admitted to the palliative care unit to initiate the process of stopping eating and drinking after carefully exploring the acceptability of the proposed process with the palliative care team and the hospital administration.

After admission, he began the process and was disciplined about not eating or drinking anything. He was visited by a range of friends and colleagues to "say goodbye", and his symptoms of dry mouth were palliated with artificial saliva which he swished and spit out. It was a very meaningful time for all involved. He was fully alert for the 1st week, and then gradually became sleepier and after 13 days died peacefully.

Take Home Messages

- Hastening death is an important contemporary conversation in medicine in the United States as PAD is being legalized in additional states, and as a society we continue to focus on patient autonomy.
- Requests to hasten death may be seen disproportionately in patients with neurologic disease as our diseases tend to cause severe physical and/or cognitive disability and for many attack the core of what it means to be human.
- While not every physician must be expert in all of the options for hastening death, a foundational knowledge of these issues and comfort in discussing the topic if raised by the patient is essential to the care of seriously ill patients.
- The initial response to patient inquiries about a hastened death should be exploration, not denial or affirmation.
- Regardless of which option is being employed, careful discussion to inform the patient and family of what to expect is mandatory.
- Caring for dying patients involves a substantial emotional burden, and assisting patients through a hastened death is often reported as particularly intense.
- We strongly recommend communication with colleagues regarding the discomforts, challenges, and joys of treating seriously ill patients.

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Withholding and Withdrawing Life-Sustaining Treatment

15

Ralf J. Jox

Case

Vincent was a 43-year-old man who was intellectually disabled due to prenatal brain damage in the context of a birth complication. It was not until the age of 8 years that he had learnt to walk and speak. Yet, Vincent managed to lead a relatively independent life, living in an assisted facility and working in a garage for the intellectually disabled. For unknown reasons his health condition started to decline significantly in his 40th year of life. The spasticity of his extremities worsened, he developed dysphagia, needed a PEG tube and had recurrent aspiration pneumonias. As he was hospitalized for pneumonia for the third time in 1 year, he was found in the bathroom of his patient room, in cardiopulmonary arrest. Despite immediate resuscitation measures and optimal critical care therapy Vincent suffered severe hypoxic-ischemic brain damage. The MRI additionally showed acute bilateral anterior cerebral artery infarction. Clinically he remained in unresponsive wakefulness syndrome (vegetative state) several weeks after the event. The consulting neurologist did not see any potential for recovery, which was confirmed by three rehabilitation facilities that declined to take the patient into their care. The ICU staff and neurologists unanimously felt that any rehabilitative or life-sustaining measures would be medically inappropriate as they would not benefit the patient. They therefore suggested withdrawing antibiotic treatment as well as artificial nutrition and hydration. Yet, the two brothers of Vincent who were court-appointed guardians requested adamantly that full life-sustaining and rehabilitative treatment measures be pursued. They were convinced that Vincent was conscious, that he communicated with them and that he would be able to recover at least partially. They suspected some discrimination against him because of his intellectual disability. Vincent had never before talked about his treatment preferences for such a situation and did not have advance directives. Both palliative care specialists and ethicists were consulted, when suddenly one night, Vincent developed respiratory insufficiency and died due to a suspected pulmonary embolism.

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This chapter discusses ethical considerations around withholding and withdrawing life-sustaining treatment with a focus on neurological diseases. I will proceed in four steps: First, I will summarize the available empirical evidence on prevalence and characteristics of this phenomenon in Western health care systems, showing also its relevance to neurology. Second, I will discuss terminology, definition and distinctions from other end-of-life decisions and practices. Third, I will focus on the ethical criteria for guiding decision making about the administration of life-sustaining treatment. Fourth, I will conclude by giving practice recommendations regarding the communication and implementation of these end-of-life decisions.

Describing the Phenomenon of Withdrawing and Withholding Life-Sustaining Treatment

Over the past two decades, several studies have looked at the population-level frequency of end-of-life decisions. One of the methodologically best studies was the EURELD study that analyzed all official death certificates during an 8-month period in 2001–2002 in six European countries [1]. Of all deaths that occurred during that period, between 4% (Italy) and 28% (Switzerland) of deaths occurred after withholding or withdrawing life-sustaining treatment. Other European countries that had not participated in this study have since provided similar prevalence data, such as the UK with 21.8% [2] and France with 18.8% [3]. A more recent study in Germany, using the same methodology as the EURELD study, found that in 2013 even 50.7% of all deaths were preceded by a decision to withhold or withdraw life-sustaining treatment [4]. This study comprised 403 physicians (36.9% response rate) and may not have been fully representative of all German physicians. In Switzerland, however, a similar frequency was recently reported based on a methodologically more robust study: researchers published an increase in the prevalence of "foregoing life-prolonging treatment" from 41.1% in 2001 to 49.3% in 2013 [5].

In intensive care units, up to 90% of all deaths are associated with forgoing medical treatment [6–8], but the frequency varies considerably between countries, cultures, and contexts [8]. Among the factors that influence the frequency of decisions to forgo life-sustaining treatment are not only patient-related factors like prognosis, age, gender or ethnicity, but also the culture of an institution and physician-related factors like their religious and moral attitudes [9, 10]. Most religious groups accept a legitimacy of forgoing life-sustaining medical treatment at least in certain situations. Yet some only accept withholding treatment but prohibit withdrawing treatment (like the Orthodox Jewish community) [11], while others, for example the Catholic church, have problems with withdrawing *certain forms* of treatment, such as artificial nutrition and hydration, in particular when it concerns patients with chronic disorders of consciousness [12–14].

Different forms of life-sustaining treatment may be more or less often withheld and withdrawn. While cardiopulmonary resuscitation, vasoactive drugs, surgery and hemodialysis are rather often foregone, mechanical ventilation, artificial nutrition and artificial hydration are less commonly limited [15, 16]. Factors that seem to ease the limitation of a life-sustaining intervention are its invasiveness, complexity and cost as well as the ease of applying alternative, comfort-focused measures when forgoing this intervention [17, 18].

Forgoing life-sustaining treatment is often regarded as one of the cornerstones of palliative care. The definition of palliative care by the World Health Organization explicitly states that palliative care "intends neither to hasten nor postpone death" [19]. Hospice and palliative care institutions often refuse to administer clearly life-prolonging measures such as chemotherapy or even decline to admit patients who are still receiving disease-modifying treatment with the aim of prolonging life. Nevertheless, there is a vivid discussion within hospice and palliative care whether a rigid stance against life-sustaining treatment can and should be upheld. Even patients who have switched to a comfort-focused goal of care may develop the understandable, legitimate

wish to extend their life span as they may enjoy an increased quality of life or may wish to survive to a certain life event like the birth of a grandchild. Moreover, knowing that palliative care itself (when started early) may in fact have a life-prolonging effect questions a rigid demarcation between life-prolonging non-palliative care and non-life-prolonging palliative care [20, 21].

Withholding and withdrawing life-sustaining treatment also occurs frequently in neurology [22]. Two of the ten leading causes of death worldwide are neurological conditions, cerebrovascular disease and dementias [23]. As dementia is commonly due to an incurable (neurodegenerative) disease, in particular Alzheimer's disease, and as cerebrovascular disease is usually also a chronic progressive condition with recurrent crises, these disorders do in fact limit the life span and prompt questions about the adequacy of life-sustaining treatment. One recent German study found that 34% of patients who died in a stroke unit had decisions to withhold and/or withdraw life-sustaining treatment, often associated with disturbance of consciousness, dysphagia and large supratentorial strokes [24]. A literature review in 2005 reported a wide variation in the frequency of withdrawal of life support in severe stroke patients in the intensive care setting [25].

In dementia, the usual disease trajectory requires decisions about the administration of antibiotics, respiratory support, and artificial nutrition and hydration in the advanced stages of the disease [26]. In addition to cerebrovascular disease and dementia, other chronic progressive diseases like amyotrophic lateral sclerosis, Parkinson's disease and multiple sclerosis, as well as acute severe brain injuries also commonly require such end-of-life decisions [27–31]. The disease-specific characteristics of such end-of-life decisions will be discussed in other chapters of this book.

Clarifying Terms and Meanings

Terminology

The field of end-of-life decisions is fraught with misunderstandings that are often perpetuated by imprecise and emotionally charged terminology. In many languages, withholding and withdrawing life-sustaining treatment is still called "passive euthanasia" or "passive aid in dying", suggesting a close link to terminating life on request (so called "active euthanasia") and allowing associations to a long and complicated history of the term "euthanasia" [32]. Using a descriptive, ideally neutral terminology like "withholding and withdrawing life-sustaining treatment" eschews these problems. This wording may, however, especially when shortened to "treatment withdrawal", be perceived as abandonment by patients and their families. Instead, palliative care professionals often speak of "changing the goal of care" from a curative or life-prolonging intention to a comfort-focused one (easing suffering and enhancing quality of life). In any case, patients and families should be reassured that forgoing life-sustaining measures does not mean forgoing the professional care they so rightly deserve. Another term, easily understandable and capturing the essence of the process, is the term "letting die", "allowing death to occur" or "letting nature take its course". It emphasizes the fact that dying is a natural, physiological process that can be medically impeded and thus can also consciously be allowed to happen.

Definition

The attempt to define "withholding and withdrawing life-sustaining treatment" is less straightforward than it may seem. The first half is relatively clear: withholding a certain treatment measure means not starting an intervention that could in fact be started, i.e. which is technically feasible, practically available and professionally manageable. Withdrawing means stopping a treatment intervention that is continuously administered (such as vasoactive drugs via a syringe pump) or that is administered in regular, short intervals (such as hemodialysis or daily enteral or parenteral medication with a resulting steady state serum drug level). Withdrawing an intervention will result in a more or less rapid

fading of the treatment effect, depending on the kinetics of the administered treatment form.

The second half of the definition is less clear: What is a life-sustaining treatment or, as it is also called, a life-prolonging treatment? Although these two terms may have different connotations, I use them interchangeably, as anything which sustains life (even if it is only for minutes) also prolongs life and vice versa. We can speak of sustaining or prolonging life irrespective of the duration for which life is extended.

Definition of life-sustaining treatment
Life-sustaining treatment is defined as a treatment without which life would, with a very high probability, end within a foreseeable period of time.

This definition takes a particular form that is called *ex negativo* or counterfactual, because instead of positively stating what the notion entails it describes what the notion excludes. Life-sustaining treatment is defined by hypothetically imagining the effects without that treatment, based on solid evidence by science, physiology and experience.

Two elements of the definition need further attention. First, it is said that without the treatment, life would end within a foreseeable period. This will usually be in the range of minutes, hours or days, only rarely weeks or a few months, depending on the kind of treatment forgone and the severity of the underlying disease and co-morbidities. It is difficult to predict the exact time to death after withdrawal of life-sustaining treatment, depending mainly on ventilation, oxygenation, vasopressor use, Glasgow Coma Scale score, and brain stem reflexes [33]. If artificial ventilation is stopped, death will commonly ensue within minutes to a few hours. If a chemotherapy that successfully extends life is stopped, its effects will only gradually subside and, depending on the progression of the disease, it may take months until the patient will die. In any case, there has to be a certain proximity to death and a medical condition causing death if one talks about forgoing life-sustaining treatment.

If someone renounces to use certain preventive measures that statistically extend life expectancy (e.g. some forms of cancer screening or antihypertensive medication to prevent hypertension-induced stroke), we would not speak of withholding life-sustaining treatment, although the measure would quite possibly have prolonged life. As always, there are grey zones: a patient with multiple sclerosis who discontinues disease-specific medication and who therefore may have a faster disease progression and shorter life span may be such a case in the grey zone.

It is also worth noting that therapeutic measures like drugs or surgical interventions can sometimes be used for different purposes. Blood transfusion may be used for the purpose of sustaining life (in a patient with acute hemorrhage) or for the purpose of soothing symptoms (for symptomatic anemia). This will be explained in more detail under point 3 below.

The second element of the definition that deserves particular attention is the statement of probability. In medicine, probabilistic judgments are everyday practice when physicians prognosticate and apply certain treatment measures with more or less likely effects. The same holds true if a physician withholds or withdraws a life-sustaining treatment: death is *expected* to occur earlier than it would have occurred without that treatment. Yet, this effect can never be proven in the concrete case, as we can never let both alternative chains of actions happen simultaneously. We can base our probabilistic judgment on sound collective evidence, but there always remains an uncertainty for the individual case. If a certain treatment had not been withheld, it might have caused an even earlier death due to undesired side effects. In fact, this suspicion is not implausible with regard to aggressive chemotherapy in patients with advanced cancer. Sometimes, patients and their families may be astonished to find out that after withdrawing life-sustaining treatment the clinical situation may in fact improve and the patient may live longer than expected. Therefore, it is crucial that health care professionals communicate this unavoidable uncertainty to patients and families and do not predict exact times of survival in an individual case.

Withholding Treatment, Withdrawing Treatment, and Assisted Dying: Distinctions

An important topic that has to be discussed is the question whether there is a normative difference between withholding and withdrawing life-sustaining treatment. On the face of it, under a purely descriptive perspective, there is in fact a difference relating to the *recent and current* action. In the case of withdrawing treatment, a life-sustaining intervention is being administered up until the present moment (be it for a few days or for decades), in the case of withholding treatment this treatment is not currently being administered (although it may have been done so at an earlier time in the past). Yet, if we only look at the *future* action that is being deliberated and planned, there is no difference between withdrawing and withholding, because in both cases the treatment *will not* be administered in the future.

Obviously, from a practical standpoint, withdrawing a treatment may require a different management than withholding it. Withdrawing artificial ventilation, for example, requires a terminal weaning protocol and concomitant or even preventive medication to treat dyspnea [34, 35]. In most situations, however, life-sustaining treatment can be discontinued abruptly without incurring additional suffering to the patient (e.g. antibiotics, transfusions, chemotherapy, hemodialysis or hemofiltration). If more than one intervention have to be discontinued, as is often the case in the intensive care unit, physicians sometimes use a stepwise approach, but there is no evidence that using stepwise protocols of withdrawing life-sustaining treatment impact time to death or reduce suffering [36].

Psychologically, it can make a huge difference for health care professionals and family caregivers whether one stops a treatment or decides not to start the very same treatment (see Chap. 20 “Caregiver Assessment and Support”). For some it may be more difficult to discontinue treatment than to withhold it because it may have been effective or may be associated with care, love and hope. Moreover, if death ensues immediately after treatment withdrawal, the decision maker will have a strong psychological impression to be the principal (or even sole) cause of death. Others, however, may have more difficulty withholding life-sustaining treatment and not giving it at least a try. This may explain the fact that in some countries and cultures (e.g. in Southern Europe) withholding is more frequent than withdrawing life-sustaining treatment, while in others (e.g. Northern Europe) it is exactly the opposite [6].

Whether there is in fact a *moral* difference between withholding and withdrawing life-sustaining treatment is a controversial question [37]. Most ethics scholars argue that the historical perspective (looking at past actions) is no valid argument in ethics. Usually, withdrawing and withholding life-sustaining treatment have the same consequences for the present and future wellbeing of the patient. As deontological ethics theories (based on duties rather than on consequences of action) prohibit certain actions and allow others, they have problems justifying the legitimacy of withholding but not withdrawing (or vice versa) because both exert the same causal contribution to death and thus have the same relation to the value of life and the right to die. Moreover, there is no reason to believe that the intentions and attitudes of the persons involved will be different between these two actions. Taken together, all major criteria that are relevant to an ethical evaluation do not differ between withholding and withdrawing treatment. In addition, completely prohibiting any kind of withdrawal of life-sustaining treatment runs into serious practical problems and inconsistencies [38]. Most jurisdictions as well as most ethical and medical guidelines regard withholding and withdrawing life-sustaining treatment therefore as equivalent [37].

Before moving on to the decision-making process, a last conceptual distinction needs to be discussed: the crucial distinction between withholding and withdrawing life-sustaining treatment on the one hand (letting die) and the so-called assisted dying that encompasses euthanasia (terminating life on request) and assisted

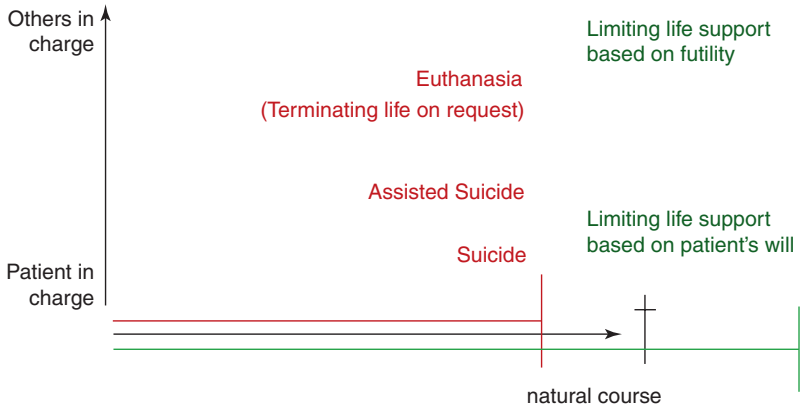

Fig. 15.1 Schematic illustration to demonstrate the difference between actions that hasten death (suicide, assisted suicide and euthanasia) and actions that allow death to occur naturally (limiting life-sustaining treatment). X-axis: life course until death, marked by a cross. Y-axis: degree to which the patient is in charge of the respective decision, as supposed to others being in charge of it. (From Marckmann [39], with permission)

suicide on the other hand (see Fig. 15.1). While it is characteristic for the former that life would spontaneously end without the treatment, it is typical for the latter that life would spontaneously continue without the action that hastens death. The former leads to death at a time when it would have occurred naturally or even later (because of the life-sustaining effect of treatment), the latter is characterized by a death occurring very likely earlier than it would have occurred naturally.

In other words: withholding or withdrawing life-sustaining treatment is a *necessary* condition for death to occur in these situations, but it is *not sufficient*: in addition, there has to be a terminal disease, a devastating injury or another fragile health condition that is physiologically incompatible with life and leads to death if not compensated by a medical intervention. Euthanasia and assisted suicide, however, are *sufficient* conditions of death: they lead to death even if the patient did not have such a medical condition incompatible with life. These are still differences on a purely descriptive level. The highly controversial question of whether killing and letting die should be evaluated differently from an normative-ethical and legal perspective is extremely relevant, but its discussion is beyond the scope of this chapter.

Ethical Criteria for Decision Making

The Range of Options to Act

Deciding about withholding or withdrawing life-sustaining treatment presupposes that the decision maker is aware that there is in fact a decision to be made (see Chap. 13 "Improving Medical Decisions"). Being aware of a decision means thinking in alternatives. Surely, there is always the general freedom to act or to omit an action, to administer a treatment or not to administer it. Yet, for a health care professional with his or her professional ethos it is not a real option to let a patient suffer and just send him or her away. Instead, the professional has to provide an alternative that offers a tangible benefit to the patient. In severe illness scenarios at the end of life, this alternative is commonly comfort-focused care. Thus, if the decision is made to withhold or withdraw life-sustaining treatment, this usually means that it is replaced by a comfort-focused treatment approach (Fig. 15.2). It is crucial to distinguish this change in goals of care from palliative care as a comprehensive approach. Palliative care may in fact begin already at the diagnosis of a severe, incurable disease, going alongside disease-modifying therapy for a long time (as "integrated care"), but at some point in time the goal of comfort may become the only goal of care as shown

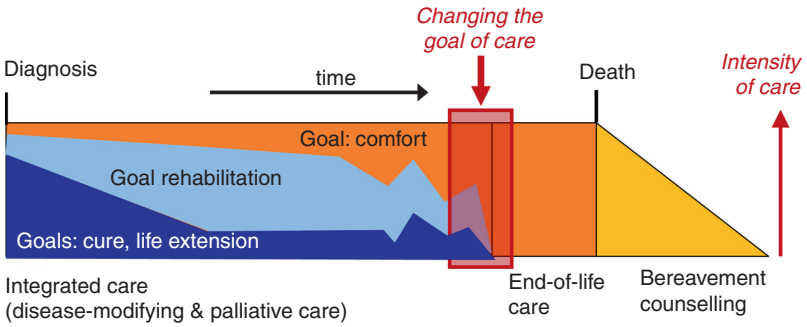

Fig. 15.2 Schematic illustration showing the change of the goal of care. X-axis: time. Y-axis: intensity of care. The diagnosis of a severe and life-threatening disease should prompt a care integrating curative, life-prolonging, rehabilitative/restorative and comfort-oriented goals. As the disease progresses the priorities of goals shift. If the goals change completely towards comfort, life-sustaining treatment is by consequence withdrawn and withheld, but the intensity of care remains unchanged. (Adapted from Murray et al. [40]).

in Fig. 15.2. Hence, every physician and nurse who takes care of these patients should have a good knowledge of both the life-sustaining, curative treatment options and the comfort focused options.

The Goal-Directedness of Decision-Making

The decision-making process will substantially improve and gain clarity if the persons involved do not so much focus on the treatment measures but consider first the overarching goals of care that are logically prior as they justify and direct the treatment measures. This is all the more important as a specific treatment measure can serve different goals. Antibiotic therapy, for example, can be given to save and extend the life of a patient with Parkinson's disease and severe pneumonia, but it can also be given to ease the pain of a patient in hospice with a cystitis whose pain is refractory to analgesics. Blood transfusions can be given with the goal to save the life of a patient with an acute massive gastrointestinal hemorrhage, but it can also pursue the goal to increase quality of life in a patient with leukemia and anemia-related loss of energy.

For these reasons, making decisions about life-sustaining treatment should center on the goal of care. There are various goals of care that can be pursued in medicine: saving and prolonging life, cure, prevention, rehabilitation, easing symptoms, providing comfort, enabling a peaceful, dignified dying – just to name the most common ones.

The Decision-Making Algorithm

In reflecting on and discussing the appropriate treatment, particularly in a patient with a severe and potentially life-limiting disease, we should first ask ourselves what the patient's preferred goals of care are (Fig. 15.3). The patient should be in the center of all attention and his or her goals are the ones that should direct all therapeutic efforts (see Chap. 11 "Communicating Effectively", and Chap. 13 "Improving Medical Decisions"). Sometimes, however, health care professionals and family members are not aware of the patient's preferred goals of care. The various persons involved may pursue different goals of care, which may be divergent, even incompatible with one another, and often not transparent. While a patient with an advanced glioblastoma may have the wish to be free from pain and to ease the bereavement of the family after the expected death, the family may still think that the disease can be cured and should be fought, and the neurologist may pursue the goal of functional rehabilitation and an independent living at home. If they only talk about chemotherapy, radiotherapy and analgesia but do not frankly discuss the goals of care from a patient-centered per-

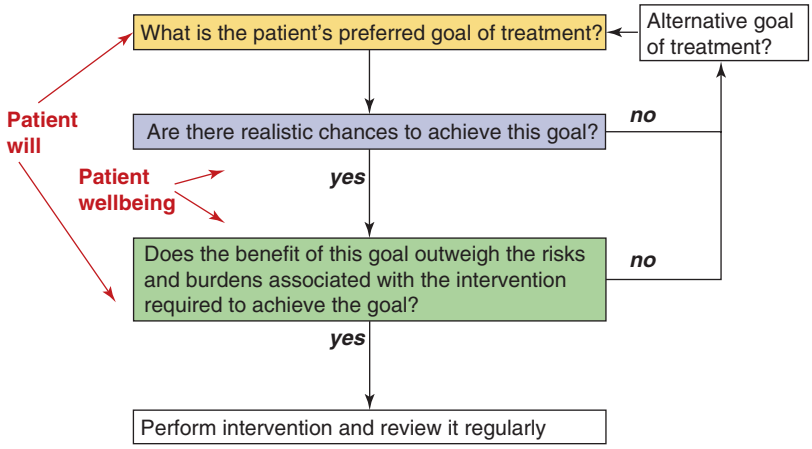

Fig. 15.3 Decision-making process of finding the appropriate treatment in a patient with a severe, life-threatening disease, starting with the question on top. Yellow = question that has to be answered by the patient or based on patient autonomy. Blue = question that mainly requires medical expertise. Green = question that requires both medical judgment and patient autonomy. All questions should ideally be discussed among the patient or his representative, his family and professional caregivers. In red: ethico-legal criteria present at various levels of the algorithm. (Adapted from Jox et al. [41, 42]. From Marckmann [39], with permission)

spective, they miss the point and probably do not reach consensus.

Once the patient's preferred goals of care are clearly established and accepted by all, the question should ensue whether and how this goal can realistically be achieved. Answering this question requires medical expertise, especially regarding prognostication and the chances of available treatment options. For some diseases, there is a relatively good evidence base from clinical studies, literature reviews, meta-analyses, and clinical guidelines to help with that question; for other, rarer diseases, this evidence may be lacking and (more or less) clinical experience may be the only indication.

What, then, is a realistic chance to reach a certain goal? This cannot be expressed in precise percentages but requires a practical judgment. Even if there is appropriate statistical data on prognosis, this may allow a collective statement, but it never permits a precise prediction for the individual case (see Chap. 12 "Prognostication"). You may have two 60-year-old patients with exactly the same kind of stroke, e.g. an infarction of the left middle cerebral artery with the same extent of brain edema. Yet, based on comorbidities, social situation and other personal factors the judgment may be different as to whether you think a hemicraniectomy will realistically allow a "good" outcome or not.

If the proposed goal of care cannot be realistically achieved, it is pointless to continue pursuing this goal, but alternatives goals should be considered instead that can more realistically be achieved. After it has been established that the proposed goal of care is realistic, this is not yet tantamount to a medical indication for the related treatment that would target this goal. The basic ethical principle of beneficence requires that medical actions are more than simply effective: they have to serve the patient's wellbeing and benefit the patient. Thus, we have to ask whether the likely benefit to reach the desired goal of care outweighs all risks and burdens associated with the interventions that are necessary to reach this goal. In a patient with an irreversible unresponsive wakefulness syndrome (vegetative state), a PEG tube may effectively reach the goal of prolonging life, but it may not confer any benefit to the wellbeing of the patient.

Medically Inappropriate Treatment

The latter two questions encapsulate what is in many jurisdictions discussed under the legal term "medical indication" or, if the questions are

answered to the negative, under the controversial term "medical futility" [42–44]. In the so-called futility discussion, a difference has been put forward between a *quantitative futility*, relating to the ineffectiveness of a certain treatment or the inability to reach its proposed goal – and a *qualitative futility*, relating to the unfavorable benefit-risk ratio or the inability to reach a goal that the patient can perceive as a benefit [45]. The term "futility", however, is misleading and inappropriate with its negative and pejorative connotations. Moreover, the discussion on medical futility has been mixed with the ethical discussion on fair allocation of scarce resources, which discredited the term even more. It is therefore suggested to avoid this term and to prefer speaking of "medically inappropriate", "medically not indicated" or "nonbeneficial" treatment [46].

If the patient or the substitute decision maker, based on the patient's will, demand a treatment that is deemed inappropriate by the physician, they should enter into a fair and open dialogue with the aim of clarifying the underlying reasons and reaching consensus (Fig. 15.4). The conflict can generally result from a different evaluation of the patient's wellbeing or from a conflict between different moral values.

In the former case, the dissent can be an epistemic one due to a different appraisal of the facts and the situation (e.g. a lack of information) or a moral one due to a different evaluation of the same information with regard to wellbeing. For example, a patient with a central nervous system lymphoma may demand a chemotherapy considered ineffective by the physicians because he simply does not know about its ineffectiveness (*information deficit*) or because the patient is well informed but refuses to accept the severity of the illness and denies its incurability (*emotional defense*). Patients may also be erroneously informed by unreliable sources of information, which can be rumors, internet information, lay media reports or sometimes even misinformation by health care professionals. It is therefore always crucial to ask the patient what he or she has understood about the disease, the prognosis and the proposed treatment options. Important information should be given in a sensitive, comprehensible and stepwise manner, which may require several discussions.

Sometimes it may be difficult to disentangle whether the patient is just not sufficiently informed or whether the patient avoids information as a coping and defense strategy. Coming to

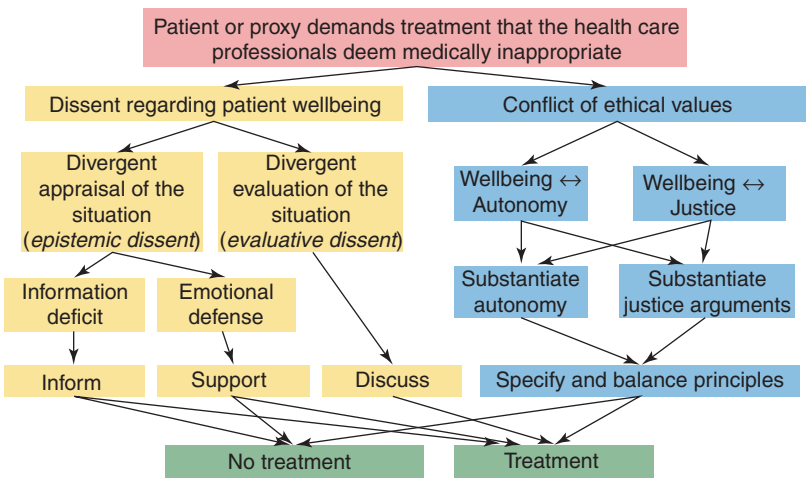

Fig. 15.4 Reflective algorithm suggested for the situation that a patient or proxy demands a treatment that is considered medically inappropriate by the health care professionals. As the figure suggests, the key to moving forward differs across patients and may at times require more medical information or emotional support and at others a more in-depth discussion of the values of the patient or the ethical principles involved

terms with existentially tragic information such as the diagnosis of an incurable disease or the fact that a disease enters the final stage and death cannot be postponed is emotionally daunting. Professionals should first and foremost understand the reactions of their patient, including the ones that try to deny the facts. It may help to enlist the support of psychologists, spiritual care providers, social workers, volunteers, clinical ethicists or others who offer a fresh perspective, adduce specific competencies and may gain better access to the patient. Psychological coping also needs time, which can be very hard to accept in the health care system of today.

In other situations, the patient may be fully informed and cope well with the clinical situation, but he or she simply evaluates the situation differently than the care team (*evaluative dissent*). While the majority of patients suffering from amyotrophic lateral sclerosis refuse invasive ventilation for fear of becoming locked-in, losing control and suffering without an exit option, other patients may evaluate the identical situation differently. They may have less fear of suffering and losing control and may feel well and happy even with an extremely reduced range of daily activities; or they may be even more afraid of dying or want to stay alive for a certain occasion or situation. Studies among patients with locked-in syndrome drastically showed that the self-rated quality of life of these patients differs substantially between some who feel miserably and request euthanasia and others who report a surprisingly good quality of life [47–50].

If there is a real *conflict of values* which lies beneath the controversy, it often concerns a conflict between patient wellbeing (as perceived by the health professionals) or and the autonomy of the patient, a conflict between patient wellbeing and considerations of justice (competing interests of other patients, shortage of ICU beds, competing needs of relatives, high costs for society etc.). If this is the case, the competing values should first be substantiated by specifying autonomy, wellbeing and justice in these particular circumstances. This will then help to balance the specified values or principles against each other, always relating to the concrete situation. If the professional care team and the patient and/or his family do not concur in their ethical balancing, it may be helpful to ask an ethics consultant to moderate a joint reflection (see below).

Patient Autonomy

Let us now return to the general structure of the reflection around changing the goal of care (see Fig. 15.3). In addition to the value of patient wellbeing, the model also incorporates the fundamental value of patient autonomy. It is crucial to see that patient autonomy is relevant both on the general level of care goals and on the more specific level of certain treatments and their benefit-risk analysis. Thus, the patient is both the one who defines the goal of care in the first place and the one who ultimately decides whether to consent or not to a certain treatment offered by the physician. The first principle stems from the fact that it is the patient's own life that is at stake and that the patient is the one who conducts his or her own life and makes life plans. The second principle results from the fact that the patient is the expert about the own subjectivity, knowing best what promotes his or her own wellbeing.

In neurology, however, patients often cannot realize their autonomy because they do not possess decision-making capacity due to diseases or injuries to the brain, reducing their cognitive or communicative capacities. The most frequent examples are advanced dementia, major stroke, intracranial hemorrhage, brain tumor, status epilepticus, severe encephalopathy and acute confusional state. When decision-making capacity has thoroughly been investigated according to legal and medical standards and has been found to be lacking [51], others have to decide on behalf of the patient using surrogate criteria of patient autonomy. In most jurisdictions, the surrogate decision maker will either be a person with durable power of attorney for health care matters (designated by the patient before), a family proxy automatically authorized to decide based on family bonds or a legal guardian appointed by the court. This decision-maker is supposed to give voice to the person who cannot speak for him- or

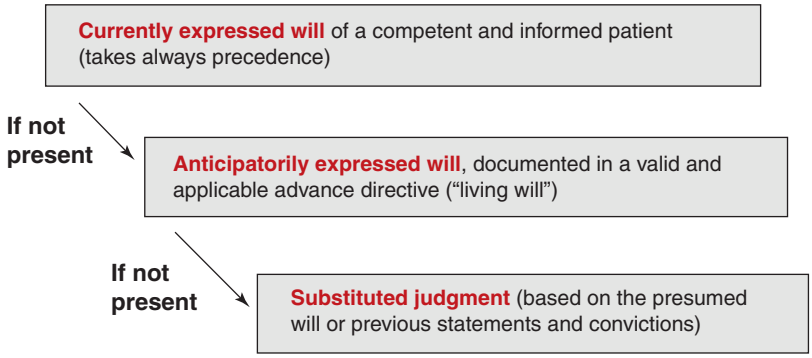

Fig. 15.5 Cascade of criteria for patient autonomy (from top to bottom). If the patient does not have decisional capacity to express his current will, respect for autonomy first requires looking at the anticipatorily expressed will (precedent autonomy). Should this not be possible, then substituted judgment should be used (substitutive autonomy). (From Marckmann [39], with permission)

herself any more. The criteria that surrogate decision makers have to follow are rather similar in most jurisdictions: precedent autonomy (valid and applicable living will/advance directive) and substitutive judgment (Fig. 15.5).

Some Practical Considerations

A plethora of international data shows convincingly that treating patients who lack decisional capacity according to their own autonomous choices is very difficult and often fails. Even advance directives (living wills) and substituted judgment by the closest relatives often do not lead to care in accordance with the patient's wishes and preferences [52–54]. Advance care planning, understood as a more comprehensive, systems-level approach that includes professional facilitation of patient-led anticipatory decision making and a regional implementation of change management, is demonstrably more successful in realizing patient autonomy at the end of life [55–59]. This demanding, rich model of advance care planning is to date only practiced in some pioneer regions like Australia, New Zealand, some areas of Canada, the USA and England. There is data indicating that the approach is also applicable to neurological patients [56, 60–63]. Neurologists are encouraged to start advance care planning programs for their patients and evaluate them systematically.

Another practical point merits consideration. We have seen that decisions about withdrawing and withholding life-sustaining treatment in neurological patients need certain knowledge in palliative care. Therefore, it does not come as a surprise that one of the main tasks of palliative care consultations in neurology concerns difficult decisions about the goal of care [64, 65]. Most hospitals nowadays also have clinical ethics support services that offer particular help in complex ethical decision making [66, 67]. Although both services are of course not exclusive and it may be prudent to use them both in a complex situation, health care professionals may need some orientation as to when call which service (Table 15.1).

In the introductory case of Vincent, both a specialized palliative care consultation and a clinical ethics consultation were sought by the care team. This was done sequentially, because the case presented in fact so many complexities calling for the expertise of both the palliative care team and the clinical ethicist: On the one hand, the unclear course of dying after withdrawing nutrition and hydration and the extreme emotional suffering of the family, on the other hand the intricate ethical problem of deciding about life-sustaining treatment in a patient who was presumably but not certainly unconscious. For the health care professional, this was a clear case of "medical futility", but for the patient's brothers there was still hope for recovery. It seemed that they cognitively knew the relevant medical information, but did

Table 15.1 Specific triggers for specialized palliative care or clinical ethics consultation in a situation where withholding/withdrawing life-sustaining treatment is in question

	Specialized palliative care consultation[a]	Clinical ethics consultation
Source of consult	Uncertainty or controversy on palliative care options	Moral uncertainty, value conflicts or value-related dissent
Expertise needed	Information on palliative care options, prognosis, end-of-life trajectory, dying process, grief	Ethical analysis, information on guidelines or legal framework, facilitation of decision making
Additional support	Psychosocial or spiritual support for patient or family	Support for patient or family in making a difficult decision, issues of guilt and responsibility
Educational goal	Educate the care team about comfort-focused approach and options	Educate care team about ethical analysis and decision making

[a]After generalist palliative care provision has been exhausted or needs have been identified as complex

not believe the reported prognosis, partially as a way of coping with the distressing situation. Moreover, they probably evaluated the tiny glimpse of hope differently than the professionals did. The discussions between the persons involved did not solve the quandary and the dissent persisted. Maybe an early advance care planning at a situation when the patient was still communicating, for example after his second hospitalization, integrating his brothers, his treating physician and maybe others who knew him, may have prevented a situation like the one that ensued after resuscitation.

Take Home Messages

- Decision making about the withholding or withdrawing of life-sustaining measures is very common in neurological disorders, so that each neurologist has to be familiar with the basic medical, ethical, and legal aspects of it.
- When withholding or withdrawing life-sustaining measures, health care professionals should make sure that patients and their families are not abandoned but continuously cared for, although the goal and the measures change, and they should clearly convey this message to patients and families.
- Despite clear differences in psychological coping and practical management of the two, there is no ethical and commonly no legal difference between withholding and withdrawing life-sustaining measures.
- Treatment that, from the perspective of the health care professionals, either cannot realistically achieve the intended goal of care or would involve more harm than benefit to the patient should be considered medically inappropriate.
- If patients or proxies demand treatment considered medically inappropriate, it should be established whether the underlying reason for conflict is misinformation, problems with emotional coping, a different evaluation of the treatment's effect on patient wellbeing, or a conflict between ethical principles.
- In neuropalliative care, many patients lack decision-making capacity so that respecting their autonomy requires advance care planning and substituted judgment.

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Part III

Crosscutting Issues in Palliative Care

Hospice and End of Life Care in Neurologic Disease

16

Farrah N. Daly and Mara M. Lugassy

Case

Mr. Jay, a 74-year-old man with Parkinson's disease, visits your office for routinely scheduled follow-up. He has moderate dementia related to Parkinson's disease, and his spouse provides the history. Since your last visit with him 3 months ago, he has been hospitalized twice, once for urinary tract infection and once for pneumonia due to aspiration. On his last visit with you, he was ambulating slowly with a walker. Today, his family brings him to the office in a wheelchair. His spouse says "the second time we were in the hospital, he had a difficult time and got very confused and agitated. One of the doctors mentioned we should think about hospice; what do you think?"

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Origins of Hospice Care

The word hospice originates from the Latin word *hospitum* for hospitality, initially referring in medieval times to a house of rest for pilgrims, travelers, and the sick [1]. By the nineteenth century, the concept of a hospice had evolved to a site for the care of the terminally ill. Founded and run by religious orders, notable early hospices included the Our Lady's Hospice in Dublin, established in 1879, the Hostel of God in London established in 1891, and St. Joseph's Hospice, established in the East End of London in 1905.

The modern concept of hospice as a medical model of care is largely credited to Dr. Cicely Saunders, a nurse and social worker turned physician in Great Britain, who established the basic principles of hospice care which continue to this day: focus on symptom control, emphasis of the clinical team, and utilization of research to support clinical interventions. Dr. Saunder's 1967 establishment of St. Christopher's hospice in South London marked the integration of a medical hospice model with the emotional, spiritual and social aspects of care [2].

Increased interest in hospice care spread to the United States in the 1960s−1970s, fueled in part by the publication of *On Death and Dying*, by Swiss-American psychiatrist Elizabeth Kubler-Ross in 1969, who advocated for dying at home as opposed to institutional care and for increased

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patient choice and participation in end of life conversations.

The first hospice in the United States, Connecticut Hospice, was established by Florence Wald in 1974 as an inpatient facility. In 1982, the United States Congress established the Medicare hospice benefit, making it permanent in 1986 [3]. While the first hospice in the United States was an inpatient facility, the majority of hospice care in the United States is provided in the patient's own residence. As of 2015, approximately 60% of hospice patients died in their own home or long term care facility, 30% in inpatient hospice facilities, and 10% in hospitals [4].

The Hospice Benefit

You are surprised by Mrs. Jay's question. It has been a while since you thought about hospice for one of your patients. Over time you have cared for patients who have had hospice services, but the referral was usually made by the primary care physician or the hospital. As you take a moment to think about what services hospice care would add for your patient, you gather some more information from Mrs. Jay. "What did they tell you about hospice when you were in the hospital?" you ask. "Well," says Mrs. Jay, "they said that we might get more help at home, that hospice could send a nurse to visit us at the house and help with equipment, too. But there was so much happening, I couldn't take it all in. It is really hard at home now, with the wheelchair and everything. I'm not strong enough to get him in and out of our bed."

Hospice is a medical model by which patients with advanced illness can receive interdisciplinary, specialist level palliative care with a focus on the comprehensive management of physical symptoms, as well as psychosocial and spiritual concerns. While palliative care is available and appropriate for people at any stage of disease, hospice care is limited to those who are expected to die within months.

In the United States, hospice care has been established as a government entitlement, administered through either Medicare or Medicaid, the federal social insurance programs. Through the hospice benefit, a patient who meets the medical eligibility guidelines for their specific illness (see below) is admitted to a specific hospice agency under the diagnosis of this terminal illness, and through the hospice agency and its associated interdisciplinary team, receives a package of benefits directed toward management of that terminal illness, which comprehensively addresses the relevant physical, psychosocial, spiritual and emotional needs of both the patient and their family [5].

Benefits under the hospice program include:

- Regularly scheduled visits by members of the interdisciplinary hospice team. The nurse coordinates visits from other members of the interdisciplinary team, including the physician, chaplain, social worker, and volunteers.
- Coverage of all medications and other therapies related to the patient's terminal illness.
- Coverage of medical supplies and durable medical equipment related to the patient's terminal illness (e.g. oxygen concentrator, bipap machine, hospital bed, wheelchair, walker, catheter, commode, feeding tube supplies, suction devices, etc.)
- Availability of home health aide services as needed
- Physical, occupational, respiratory or speech therapy as appropriate for supporting the patient's individual goals of care.
- 24 h availability to patients and family members for phone support and after hours or urgent nursing visits
- Bereavement Services for the family for up to 13 months after the patient has passed away.

It is a common misconception that hospice is a place rather than a service. As stated earlier, the majority of people who receive hospice care in the United States do so in their

own home. Care can be provided in the home, nursing home, or other long-term care setting as well as in the hospital. Intensive symptom management may also be provided in a hospice inpatient setting if appropriate and available. Inpatient hospice care is different from residential hospice care, which is a dedicated long-term care setting for hospice patients and is rare in the United States.

The Hospice Team

The core members of the interdisciplinary hospice team are the nurse, physician, social worker, chaplain, and volunteer. The majority of hospice teams also include certified nursing assistants and physical, occupational, and speech therapy (Table 16.1).

In addition, a number of hospices provide access to a variety of complementary and

Table 16.1 The hospice team

Team member	Role	Typical visit frequency	Included in service
Nurse	Serves as the case manager through regular patient visits and collaboration with the rest of the hospice team and maintains the hospice plan of care. Provides ongoing clinical monitoring and skilled care, as well as education to the patient, family members, and other caregivers	Typically once per week, may increase to daily during times of need, minimum once per 2 weeks	Always
Physician	Oversees the medical aspects of the patient's hospice plan of care and provides certification and recertification of the patient's terminal illness. The hospice medical director or team physician may serve as the patient's primary physician while on hospice or may work in collaboration with the patient's own primary care physician or neurologist	Home visit availability and frequency is variable by organization; 24/7 support by phone is standard	Always
Social worker	Provides ongoing psychosocial support and counseling to patients and families, as well as assistance with other practical matters including financial concerns, transitions of care, referral to other community based resources, advance care and funeral planning	Typically monthly, may increase during periods of need	Always
Pastoral care/ chaplain	Provides spiritual support and counseling to patients and families consistent with the patient's belief system and spiritual practices. May explore anticipatory grief, life review, dignity therapy, and other spiritual issues in a non-denominational manner	Typically monthly, may increase during periods of need	Always
Volunteer	Provide companionship to patients and assistance with a variety of tasks to provide respite to family members	As needed based on patient needs and organizational availability. 5% of direct patient care hours are provided by volunteers	Always
Certified nursing assistant	Provides hands on care to promote patient's health and hygiene, for example assisting with bathing, changing bed linens, and incontinence care	Availability varies by organization, scheduling varies by patient need. Typically a 1-h visit 2–3 times per week	Variable
Physical, occupational, and speech therapy	Administer therapies to maximize patient independence in a manner consistent with the individual situation and goals of care. Often training for safety in transfers and using new durable medical equipment	Varies by organization	Variable

alternative therapies designed to enhance the quality of life for both patients and family members, including but not limited to: music and art therapy, supportive group therapy, acupuncture, massage therapy and other therapeutic touch, aromatherapy, and pet therapy [6].

Hospice agencies operate on a capitated system, through which they are reimbursed a set per diem rate by federal or private insurers for each person under their care. Out of this per diem rate, the hospice agency is then responsible for financially covering all elements related to the patient's hospice plan of care, including medicines and durable medical equipment. Most hospices supplement their per diem rate through philanthropy to provide optimal services to higher need patients.

U.S. Hospice Eligibility Guidelines

You can see how it has been difficult in the past for Mr. Jay to get out to office visits, and in addition to the recent hospitalizations you are noticing signs of strain in Mrs. Jay. You think that additional support in the home would be helpful, and wonder if he is actually eligible for hospice services at this time.

In the United States, eligibility for hospice services is based on expected prognosis. The Medicare-covered hospice benefit is available to patients who have "a terminal illness and a life expectancy of six months or less" [7]. Two physicians, usually the attending or referring physician and the hospice medical director, must certify that they believe the patient's prognosis is 16 months or less if the disease takes a typical course. Determining prognosis is quite difficult, particularly for people with neurologic disease. Long periods of severe disability and sudden declines in the setting of illness can make it difficult to predict when patients are nearing the end of life [8, 9]. In addition, the term "terminal illness" is not clearly defined and may be used differently in different settings [10].

Guidelines were developed to assist with determining hospice eligibility, and disease specific guidelines exist for people with stroke, amyotrophic lateral sclerosis, and dementia, as well as for other non-neurologic conditions such as cancer, congestive heart failure, chronic obstructive pulmonary disease, and renal failure. These expert consensus guidelines attempt to define severe disease but they do not definitively determine a short prognosis or rule out a long prognosis [11]. Though the guidelines have many acknowledged limitations, they have been adapted by CMS and Fiscal Intermediaries to guide eligibility for the Medicare Hospice Benefit. Guidelines for specific neurological diseases, as written by NHPCO are listed in Table 16.2 (fiscal intermediaries may not follow these exactly).

It is critically important to realize that the guidelines listed in Table 16.2 are not rigid criteria. For example if someone has a progressive dementia and is still communicating verbally, they may not fulfill the guidelines as listed above. However, if they also have had a rapid recent decline in ambulatory ability or if there are multiple comorbid conditions contributing to frailty, then they may still be considered to have a prognosis measured in months and as such are eligible for hospice care as defined by the U.S. hospice benefit. In addition to considering the above guidelines, it is useful to consider the question "would I be surprised if this person died in the next 6 months?" If the answer to that question is no, then refer the patient for hospice service and describe the clinical reasons that indicate frailty. As indicated in the chart above, general complications that may indicate frailty include recurrent infections, decubitus ulcers, multiple emergency room visits or hospitalizations, and rapid decline in functional status. Once a person begins receiving hospice services, their eligibility is reassessed by the hospice medical director on a periodic basis. Under the Medicare hospice benefit, as long as the prognosis is still expected to be 6 months or less, the person will remain eligible for hospice care for an unlimited period of time.

Table 16.2 Guidelines for hospice eligibility in selected diagnoses

Dementia	Functional assessment of staging in Alzheimer's disease (FAST) stage 7C:
	Unable to dress or bathe without assistance
	Occasional or frequent urinary and fecal incontinence
	Unable to have meaningful communication
	(<6 intelligible and different words in an average day)
	Complications such as: aspiration pneumonia, urinary tract infection, multiple stage III–IV decubitus ulcers, septicemia, recurrent fever after antibiotics
	Difficulty swallowing leading to poor intake and weight loss with no artificial means of nutrition OR weight loss 10% despite artificial nutrition
Stroke (acute)	Coma or vegetative state >3 days post stroke
	Dysphagia preventing adequate PO intake, and not pursuing artificial nutrition
Stroke (post-acute)	Age >70
	Poor functional status with palliative performance score <40%
	Post-stroke dementia with FAST score >7
	Unintentional weight loss >10% in the last 6 months, whether receiving artificial nutrition or not
	Complications such as: aspiration pneumonia, urinary tract infection, multiple stage III–IV decubitus ulcers, septicemia, recurrent fever after antibiotics
Amyotrophic Lateral Sclerosis (ALS)	1. Critically impaired ventilatory capacity
	Vital capacity less than 30% of predicted
	Dyspnea at rest
	Requiring supplemental oxygen at rest
	Declines mechanical ventilation
	OR
	2. Rapid progression, with most disability occurring in the last 12 months, for example:
	Ambulation decline from independent to wheelchair bound
	Speech decline from normal to barely intelligible
	Diet decline from normal to puree
	Functional decline from independent to major assist with activities of daily living
	AND
	A. Critical nutritional impairment
	Continued weight loss
	Dehydration or hypovolemia
	OR
	B. Life-threatening complications
	Aspiration pneumonia, urinary tract infection, multiple stage III–IV decubitus ulcers, septicemia, recurrent fever after antibiotics
General decline (may be applied to chronic progressive diseases like Parkinson's disease)	Life limiting condition due to a specific diagnosis OR a combination of conditions
	Goals of care directed at relief of symptoms rather than cure
	Progression of disease
	Multiple emergency department evaluations
	Recent decline in functional status
	Palliative performance score <50%
	Dependence on 3 of 6 ADL'S
	Recent impairment in nutritional status
	Weight loss >10% in the last 6 months

Stuart [12] and Boersma et al. [13]

The Neurologist's Role

There are no disease specific guidelines to determine hospice eligibility in Parkinson disease. Spurred by Mrs. Jay's question, you consider the question "would I be surprised if Mr. Jay died in the next year?" You would not be surprised and so you reference the hospice eligibility guidelines for general decline. Mr. Jay has had a rapid decline in ambulatory ability over recent months. He has had three hospitalizations for complications of disease. He looks more frail than in prior visits and a check of his weight in the office confirms weight loss of >10% over the last 6 months. "You know, Mrs. Jay, I do think your husband could benefit from the additional home support of hospice service. And since he has lost weight, had repeated infections, and lost his ability to walk, I think he is eligible for more support. The hospice system is designed to support people who have decided to focus on their comfort and quality of life and who want to avoid returning to the hospital. Tell me what you think about that." Mrs. Jay again relays the trials of the recent hospitalizations, focusing on how difficult it was for both her and her husband. She also references prior advance care planning discussions in which her husband had defined his own goals of care in advanced disease. "Doctor, we definitely don't want to go back to the hospital, but I would like to see if he might still get stronger." You review the hospice benefit with Mrs. Jay including that you expect some physical therapy as a part of the plan. You make a referral to a local hospice organization for significant decline with a primary diagnosis of Parkinson's disease. The representative that you speak to asks if you intend to remain the attending physician.

Neurologists or physicians of any other specialty involved in the care of a patient on hospice can be reimbursed for their services through several different routes, depending on their role in the patient's hospice plan of care, and whether their services are directly related to the patient's hospice diagnosis.

There are several ways in which a neurologist might interact with a hospice team (Table 16.3). The most common is serving as a consultant, seeing the patient periodically and making recommendations back to the attending and to the hospice team regarding neurologic conditions and medications. If the neurologic condition is the patient's greatest problem and the likely cause of their decline, then it may be more appropriate for the neurologist to serve as the attending physician of record on the hospice system. As the attending, the neurologist will attest to the patients expected prognosis at the time of admission to hospice, and will periodically review the medications and plan of care as documented by the hospice team. Alternatively, a neurologist who is subspecialized in palliative medicine either by formal training or by clinical experience might serve as a hospice medical director, overseeing the medical care provided by the hospice team for all people who are admitted to services. While this is still rare, increasing numbers of neurologists are seeking subspecialty training in hospice and palliative medicine, either with intent to augment their primary neurologic practice or to practice fully within the subspecialty of palliative medicine [14].

The past several decades have seen marked growth in the number of patients receiving hospice care in the United States; 25,000 in 1982, compared to 1,656,000 in 2014 [4]. Correspondingly, the number of hospice programs serving these patients has also increased, with 1545 hospice programs in 1985 compared to 6100 in 2014.

While cancer is the most common primary diagnosis for patients admitted to hospice (36.6% of all people receiving hospice care in 2014), patients with a primary non-cancer diagnosis now make up the majority admitted to hospice programs. Dementia (including both Alzheimer's

Table 16.3 Potential roles of the neurologist for a patient with hospice services

Role	Example
A neurologist who wishes to serve as the patient's attending physician while the patient is on hospice is reimbursed for services related to the patient's terminal hospice diagnosis by billing Medicare Part B directly.	A patient with advanced Parkinson's disease opts to keep his neurologist as his attending physician when he enrolls in hospice. The neurologist continues to manage the patient's care through both office visits and collaboration with the hospice team. A primary physician may consult on other health care problems unrelated to the neurologic condition
A neurologist or other specialist who provides consultative services related to the patient's terminal hospice diagnosis is reimbursed by billing the hospice agency directly for related services after establishing a contract with hospice agency with an agreed upon rate	A patient with advanced Parkinson's disease maintains his own primary care doctor, a family medicine practitioner, while on hospice. However, the patient opts to see a movement disorders specialist for advice regarding further titration of his Parkinson's medications
A neurologist or other specialist who provides services for a problem unrelated to the patient's hospice diagnosis is reimbursed for services by billing Medicare Part B directly, specifying that the services are unrelated to the patient's hospice diagnosis	A patient admitted to hospice under a diagnosis of metastatic pancreatic cancer, who also has Parkinson's disease, opts to continue seeing his neurologist for management of his Parkinson's symptoms

disease and non-Alzheimer's dementia) is the most common non-cancer hospice diagnosis (14.8% of hospice cases in 2014) and is expected to continue to increase. Other neurologic diagnoses which figure among the twenty most common hospice diagnoses are stroke and coma, Parkinson's disease, Non-ALS motor neuron disease and ALS [15]. Other neurologic diseases which may be less common but often receive hospice care in the end stages include glioblastoma, Parkinson's plus syndromes, multiple sclerosis, Huntington's disease, and prion diseases.

Although there has been a progressive increase in the number of patients referred to hospice, and an increase in the number of patients with neurologic diagnosis who receive hospice care, patients with neurologic diseases, are both under-referred to hospice, and referred later in disease course than they are eligible [16–18].

Hospice International Perspective

While in the United States the term hospice connotes a specific government entitlement, with set benefits and criteria, internationally there is wide variation in how end of life care is conceptualized and delivered within the field of palliative care. The term "hospice" itself is much less clearly defined in an international scope with some countries and health systems using the terms hospice and palliative care interchangeably, and others defining hospice care by the setting in which the care takes place or the type of services provided [19].

This variation results from significant structural differences within health care systems in terms of funding of health care services, availability of specialist level palliative care, and access to opioid pain medications. Additionally, variations in delivering end of life care have been influenced by cultural taboos in discussing death and dying [20]. Historically, greater integration of palliative and end of life care has been associated with higher income countries, with initial availability of hospice services occurring throughout Western Europe in the 1980s. However, the twenty-first century has seen increased initiatives to expand end of life care on a broader international scope [21].

In the United States, a person is eligible for hospice when they have both a terminal diagnosis and an expected prognosis of 6 months or less. In the United Kingdom, however, hospice services may be received at any point after a terminal diagnosis is received, with no stipulations as to the duration of service, and individuals have multiple episodes of hospice care throughout the course of their illness depending on their needs at

the time. In the United Kingdom, hospice services are administered through individual hospice organizations which are funded through a combination of the National Health Service as well as private donations and other fundraising efforts [22]. Hospice services may include home based care focusing on symptom management, inpatient care, as well as hospice day care and respite care. While hospice services are free of charge to patients, available space in individual hospices may be limited [23].

In Canada, hospice is not viewed as separate entity within the broader field of palliative care; rather, the term "hospice palliative care" broadly refers to care aimed toward the relief of suffering and improving quality of life for any person or family living with life threatening illness, regardless of the prognosis or the other types of treatment being received concurrently [24]. In addition to hospice palliative care provided in hospitals, individual hospice palliative care organizations may provide either facility or home based interdisciplinary hospice palliative care. Funding of services may come from a variety of sources, including provincial health care plans, private insurance, and charitable donations [25].

While considering the variation in end of life care systems, it remains important to consider that much of the world's population resides where there is no end of life care system. The great majority of deaths occurring across the world occur in developing countries that may have no access to medications or expertise for symptom control [26].

Initiating Discussions About Hospice

Mr. and Mrs. Jay leave your office with plans to meet representatives from two of your local hospice organizations. Mrs. Jay understands that both organizations offer home visits from nurses, doctors, certified nursing assistants and volunteers. She wants to compare what each organization offers for physical therapy and occupational therapy since she is hopeful that Mr. Jay will regain some strength. You plan to remain the attending physician for the duration of their hospice care, since they are closer to you than to their primary care physician. Later in the same day, you see a different patient with advanced disease, and (probably since it's on your mind since seeing Mr. Jay) you notice a pattern of increasing complications with several infections, weight loss, and a decline in function over the last year. You wonder if you should initiate a discussion about hospice care.

Clinicians may shy away from discussing hospice services for many reasons. Because the hospice benefit in the United States is tied to prognosis, discussing hospice requires also discussing the end of life. Talking about the end of life can be emotional even when the situation is uncomplicated, and the clinician's own emotional response to death can inhibit their ability to fully engage with patients on the topic. In addition, clinicians may not feel skilled in opening the discussion or in responding to the patient's possible emotional response (see Chap. 11 "Communicating Effectively"). As a result, many patients are referred for hospice service late or not at all. Delay in enrolling with hospice is considered a disservice to the patient and family, who could otherwise benefit from access to 24-h emergency support in the home, as well as medications and equipment related to their terminal diagnosis. Potential triggers for a hospice conversation are listed in Table 16.4 and mirror the events listed in hospice eligibility guidelines (Table 16.4).

A conversation about hospice generally involves exploring the patient's goals of care, explaining hospice services, and discussing the signs that indicate eligibility for hospice. If conversations about goals of care or advance care planning have happened earlier in the relationship,

Table 16.4 Hospice conversation triggers

Diagnosis	Conversation triggers
Dementia	Recurrent hospitalizations for infections or failure to thrive
	Decision to forgo feeding tube placement in setting of decreased oral intake
	Ongoing weight loss with or without artificial nutrition
	Significant functional decline in ADLs
	Loss of ability to speak or ambulate
Stroke	Ongoing weight loss with or without artificial nutrition
	Decision to forgo artificial nutrition or hydration in the setting of dysphagia
	Development of nonhealing stage III and IV wounds
	Recurrent hospitalizations for infections
ALS	Decision to forgo feeding tube placement or mechanical ventilation in the setting of dysphagia
	Increasing dyspnea at rest
	Bipap dependence
	Dependency for all ADLs
	Development of aspiration events
Malignant brain tumors	Decision to forgo further disease modifying therapy such as chemotherapy or radiation
	Progression of disease seen on imaging despite therapy
	Significant functional decline with dependency for ADLs
	Dysphagia with declining nutritional status
Parkinson's disease	Worsening dysphagia with aspiration events
	Decision to forgo feeding tube placement
	Ongoing weight loss with or without artificial nutrition
	Recurrent hospitalizations for infections
	Markers of significant functional decline (frequent falls, loss of ambulation, dependency for ADLs)
Coma and other disorders of consciousness	Repeated hospitalizations for infections
	Nonhealing stage III and IV ulcers
	Decision to withdraw mechanical ventilation or artificial nutrition
Other neurologic conditions	Declining nutritional status with decision to forgo artificial nutrition or hydration
	Repeated infections (aspiration pneumonia, UTIs, wound infections)
	Dysphagia with frequent aspiration events
	Functional decline progressing to total dependency for ADLs or bedbound state

then there is an easier approach to the conversation. For example, it may be possible to say "in the past you have said that you value your independence most; and now your independence is limited. How do you feel about your quality of life? What is most important to you now?" If the conversation or the relationship is new, then it will be necessary to explore goals from a fresh perspective. If the patient's goals align with the goals of hospice, namely wanting to stay at home, maximize comfort and avoid future hospital stays or other aggressive care, then the next step is to explore the gaps in the patients support. For example, "what is most difficult for you to do at home?" "How long does it take to get out of the house for a doctor's appointment?" Describe how the hospice interdisciplinary team could address those gaps in support. Finally, explain the factors that indicate eligibility for hospice, but also reassure the patient and family that prognostication is

difficult and that patients may live in hospice for well over 6 months or even improve in condition and graduate from the program. Through the course of discussion, barriers to acceptance of hospice care may arise; encourage the patient to talk about their concerns. Concerns are often based in misunderstanding of the program or its goals. Provide education as appropriate. Practical approaches to common situations surrounding the hospice discussion are included in "I'm not ready for hospice: strategies for timely and effective hospice discussions" by Casarett and Quill in the Annals of Internal Medicine, 2007 [27].

Medical Symptom Management at the End of Life

The pharmacologic management of symptoms near the end of life is grounded in physiology and pharmacokinetics as it would be at any other point in disease trajectory. Major differences for care near the end of life are a heightened need for attention to the burdens versus the benefits of a treatment plan, the need to make decisions without complete diagnostic testing, and limited routes of medication delivery. In addition, there is a relative lack of strong evidence base for treatments as people near end of life are often excluded from studies.

Mr. Jay has been at home with hospice care since your visit with him 4 months ago. He initially improved with physical therapy and was able to resume use of a walker with assistance for transferring in and out of bed. He had one additional urinary tract infection which manifested symptoms of agitation and was treated at home without any transfer. Overall, despite improvement in ambulation, he continued to show gradual decline with continued dysphagia, steadily increasing time to consume meals, decreased appetite for meals, decreased speech, and weight loss. Mrs. Jay has felt well supported and feels confident that she is fulfilling her husband's goals to avoid returning to the hospital and to have a peaceful death at home. Mr. Jay's hospice nurse case manager calls you reporting that Mr. Jay has had a change in condition. This morning his wife discovered that he was difficult to rouse. The nurse describes him as minimally responsive, with a heart rate of 110, respiratory rate of 16, and pulse oximetry 88%. He appears comfortable with no facial grimace, no restlessness and no moaning.

For any symptom management, the expected benefits of an intervention should outweigh the expected burdens. This is true at any point in the process of a disease, but at the end of life when burdens of basic interventions are higher this analysis needs to be an active, thoughtful process. Benefits are defined in the context of the patient's individual priorities and goals of care. Burdens are those that are direct to the patient, such as creating discomfort to perform a laboratory test, as well as to the caregivers, such as adding stress and responsibility in an already difficult situation. For example, in the case of Mr. Jay, he has a reported change in mental status and the nurse assessing him found tachycardia and hypoxia. His previously defined goals of care emphasized his physical comfort and minimal medical interventions at the natural end of his life. Consider the intervention of supplemental oxygen via nasal canula, which at most points in disease trajectory would be a fairly innocuous and automatic intervention for hypoxia. Expected benefits of this therapy might be to improve the hypoxia which might improve his mental status and possibly prolong his life. However, life prolongation was not one of Mr. Jay's personal goals and therefore this benefit, which would be nearly automatic at any other point in disease trajectory, is negligible for this particular patient near the end of life. Burdens are the addition of a medical intervention, adding a piece of medical equipment and medical noise to an already crowded

bedroom. Remember that Mr. Jay was unresponsive but comfortable-appearing. Now consider the case slightly differently. What if Mr. Jay had a respiratory rate of 30 breaths per minute and grimacing? In that case, there would be evidence of discomfort as well as documented hypoxia, and the assessment of benefits and burdens of oxygen therapy could be different.

Medical Decision Making Without Diagnostic Testing

Most physicians in developed countries are accustomed to guidance from readily available laboratory and imaging data. It would be very rare in our training to experience decision-making without also having a full complement of diagnostic studies. At the end of life, however, the burdens of obtaining this information may be greater than the benefits. Patients may only be able to transfer or travel with great difficulty. Obtaining phlebotomy or urinalysis in the home may be technically feasible but the time required to get a staff person to the home to obtain the sample, and then deliver that sample to a laboratory site, and then receive results from the laboratory site may take a day or more. Phlebotomy and urinary catheterization are mildly invasive and create some discomfort. Finally, in most end of life situations, testing should only be obtained only if the result is expected to change management. In the case of Mr. Jay, laboratory testing might indicate if the cause of the change in mental status is hypoxia, metabolic disarray, dehydration and renal failure, or infection. However, if this particular patient wanted no further medical interventions, hospitalization, or artificial nutrition/hydration, then knowing these results does not change the management plan. Remember that Mr. Jay's clinical change had been preceded by persistent worsening of his overall condition. Now consider the case slightly differently. What if he had been steadily improving over the four months of hospice care? What if he had returned to walking with his walker, was eating well, and the prior trend of weight loss had been reversed? In that case, empiric antibiotics might have potential benefits (treatment of infection, reduction of dyspnea, improvement in mental status) that outweigh potential benefits (increased pill burden, medication side effects). Now consider if Mr. Jay had comorbid congestive heart failure. In that case, a portable chest radiograph obtained in the home might change the management plan, helping to distinguish infection from volume overload as a cause of hypoxia. A physician might feel some pressure to be able to tell a patient's family definitively what is happening. However, most families do understand the uncertainty, with a description of the thought process and how the treatment plan is aligned with the patient's goals.

You speak to Mrs. Jay on the phone. She asks what has happened to her husband. You say, "First, let's go over the signs that Mr. Jay is comfortable. He is not restless, his face is relaxed, and he is breathing slowly. Although he seems sicker, he also seems to be comfortable. It is impossible for me to tell you with certainty what has happened. From the nurse's examination and the history, I think that the most likely cause is aspiration pneumonia." You offer support and answer her questions about what to expect next.

Specific Symptom Management

Seizures

Factors near end of life such as metabolic disarray, fever, or dysphagia leading to altered medication schedule may contribute to lowered seizure threshold. Burdens to patients include post-ictal pain/myalgia, risk of injury, and risk of aspiration. Burdens to caregivers include causing fear and anxiety, and possibly perception of an uncomfortable death. Principles of non-pharmacological and pharmacological measures in the event of seizure are the same as at other points in disease management. It is most impor-

Table 16.5 Selected anti-epileptics: potentially available routes

	Routes available					
Medication	Oral	Rectal	Intravenous	Intramuscular	Subcutaneous	Intranasal
Phenytoin	Yes	No	Yes	No	No	No
Valproic Acid	Yes	Yes	Yes	No	No	No
Levetiracetam	Yes	Yes	Yes	Yes	Yes	No
Phenobarbital	Yes	Yes	Yes	Yes	Yes	No
Carbamazepine	Yes	Yes	No	No	No	No
Midazolam	Yes	Yes	Yes	Yes	Yes	Yes
Lorazepam	Yes	Yes, but slow	Yes	Yes	Yes	Yes

Anderson and Saneto [28]

tant to be familiar with a variety of medications and the routes by which they can be utilized, so that the medical treatment plan can adapt as needed to the patient's condition (Table 16.5). The patient may lose or gain the oral route, intravenous access is unlikely to be available, community pharmacies may or may not have the first choice medication in stock, and novel delivery mechanisms, such as for intranasal delivery, may be cost prohibitive. If a patient in hospice care is thought to have a high risk of breakthrough seizure or status, it is important to consider the plan, coordinate with local pharmacies, and investigate available resources in advance.

It is also important for the neurologist to advocate for continued seizure prevention in a patient with high likelihood of recurrent seizure. Most hospices create an individualized care plan and do not arbitrarily discontinue chronic medications on admission. However, it is important for the neurologist to be familiar with the practices of their local hospice organizations, and advocate for medication maintenance as necessary.

Delirium

Delirium can be a significant source of distress to both patients and families. Typical symptoms include acute onset, waxing and waning course, altered level of consciousness (either hyperactive or hypoactive), inattention, and cognitive impairments such as alterations of orientation, thought processes, and perception [29].

Delirium may result from low cognitive reserve in the setting of the underlying illness (patients with brain pathology such as from dementia, stroke, or brain tumors are particularly susceptible), combined with additional exacerbating factors such as infection, hypoxia, medication side effects, constipation or urinary retention, uncontrolled pain, electrolyte or other metabolic disturbances, or environmental factors such as sensory deprivation or a change to an unfamiliar environment such as hospitalization [30]. Delirium occurs in up to 88% of patients in the last hours to days of life [31] and this proportion is likely higher in patients with neurologic disease.

Although addressing reversible causes is an important step in management of delirium, consideration should be given as to what degree such causes should be sought, particularly in the last hours and days of life, as investigations such as searching for and treating electrolyte abnormalities and underlying infections may place an undue burden on patients, without necessarily altering the clinical course or relieving suffering [32].

Delirium may be present without causing discomfort, for example if a patient is pleasantly confused, and in this case treatment is not required. When treatment is required, whenever feasible non-pharmacological therapies should be attempted first. Use natural light cycles, music, and gentle reassurance or distraction to create a calm environment. Seek and remove any triggers that add to confusion, such as nighttime noise or bedside interventions that interrupt sleep. Pharmacotherapy for delirium in the end stages of illness typically involves use of antipsychotics- most commonly haloperidol [33], which has the advantage of administration availability

through a variety of routes (orally, sublingually, parenterally, rectally). The use of another antipsychotic, chlorpromazine, which has more sedating properties, may be adventitious in cases of delirium associated with significant agitation [34]. A typical antipsychotics including risperidone, olanzapine and quetiapine can also be used if not contraindicated by the underlying primary diagnosis. Use of antipyschotics for delirium is an evolving science. A recent randomized clinical trial found no benefit of haloperidol or risperidone for agitated delirium and called into question current practice [35]. Quetiapine is the first line antipsychotic for patients with extrapyramidal disorders such as Parkinson's disease as it has a significantly lower antidopaminergic profile than other typical or atypical antipsychotics.

Benzodiazepines are best reserved as a second line therapy for refractory agitated delirium, or when the delirium is associated with significant anxiety given the risk of worsening the underlying delirium, particularly in the setting of dementia [32]. Benzodiazepines may also be considered as an intervention for delirium when there is a recent history of or high risk of seizures and there is concern about lowering the seizure threshold with increasing doses of antipsychotics.

A sudden escalation in delirium known as terminal agitation may herald the last hours or days before death and is discussed below under "signs of approaching end of life".

Myoclonus

Myoclonus describes the brief involuntary contractions of muscles and occurs with increasing prevalence at the end of life. As a highly visible symptom that can continue despite sleep or declining levels of consciousness, it may be a cause of concern for family members [36]. Myoclonus can be a feature of multiple neurodegenerative conditions, including Alzheimer's disease, Parkinson's disease and other Parkinsonian conditions such as multiple system atrophy, Huntington's disease, and Creutzfeldt-Jakob disease [37]. It may also feature prominently following anoxic brain injury, both in a generalized form in comatose patients, indicative of poor prognosis, and in a more chronic form in patients who recover consciousness, known as Lance-Adams Syndrome [38]. Myoclonus can also be caused or exacerbated by a number of conditions which develop with increasing frequency in an end of life setting, including hypoxia/hypercarbia, worsening renal or hepatic failure, and hyponatremia [36]. Finally, medications commonly used in patients with neurologic disease, as well as in patients with advanced illness may cause or exacerbate myoclonus, including levodopa, dopamine agonists, amantadine opioids, antipsychotics, metoclopramide, selective serotonin reuptake inhibitors, tricyclic antidepressants and antibiotics including quinolones, cephalosporins, and penicillin [39]. The first step in management of myoclonus is addressing reversible causes; for example, if myoclonus were thought to be induced by high doses of morphine, rotation to another opioid for control of pain may both control the pain and reduce the myoclonus. In other cases investigations into reversible causes, such as renal failure or hepatic failure, might have limited utility and unacceptable burden at the end of life stage. When patients with myoclonus are unresponsive and not thought to be experiencing distress directly related to it, the most beneficial intervention is to minimize family distress and concern by providing education to the family about the symptom. There is limited evidence for pharmacotherapy for myoclonus; however, for cases in which pharmacotherapy is felt to be indicated, levetiracetam, valproate, and clonazepam are the first line therapies [37].

Dyspnea

Dyspnea is one of the most common symptoms at end of life in multiple neurologic diseases [40]. It is particularly common in ALS and other neuromuscular diseases [41] due to the direct impact that the disease has on the muscles of respiration but also occurs with increasing frequency in other neurologic condition such as dementia as end of life approaches [42]. Management of dyspnea should first involve

consideration and management of underlying causes, such as pulmonary edema, bronchoconstriction, pulmonary embolism, anemia, or aspiration. Targeted pharmacological therapies such as diuretics, bronchodilators, and supplemental oxygen may improve comfort in the right clinical circumstance. Use of non-invasive ventilation such as Bipap plays a particular role in the dyspnea commonly associated with ALS and other neuromuscular disorders [43]. For dyspnea of a variety of causes, or that associated with the last hours and days of life, opioid therapy is a mainstay of treatment in reducing the sensation of breathlessness. Morphine is typically the first choice for the treatment of dyspnea, as it can be administered not just orally, but parenterally and sublingually as well; other opioids, such as oxycodone, hydromorphone, and fentanyl, can also be used. The dose of the opioid is escalated systematically to achieve comfort. The titration amounts and frequency are determined by the level of discomfort, the effectiveness of prior doses, and the degree of urgency. Protocols for rapid opiate titration exist for severe discomfort. While benzodiazepines such as lorazepam are not a first line therapy for management of dyspnea itself, they can be added to manage the panic and anxiety frequently associated with severe dyspnea [32].

Pain

An extensive review of pain management is provided in Chap. 17 “Pain Assessment and Management”. Pain management at the end of life is similar to pain management in other stages of life, including assessment for easily reversible causes, initiation of nonpharmacologic measures, and escalation of pharmacologic measures through the pain ladder. Where end of life pain management differs is in the relative urgency with which pain should be reduced to an acceptable level and in the consideration of long term side effects. Side effects that occur over months to years of use of a medication are not a concern if the patient is expected to live only weeks to months. Similarly, concerns about tolerance or dependence on opiate medications should not interfere with immediate treatment of pain when prognosis is short. Pain near the end of life should be treated expediently. Signs of pain when a person is in the final hours or days of life should be treated as an emergency and may require rapid titration of opiate medications. Palliative medicine specialists and pain specialists have specific training in emergent rapid titrations of opiates; typically the neurologist’s role in this setting will be to know that rapid titration is possible and to make sure the right specialist is involved.

Signs of Approaching End of Life

Recognition of signs and symptoms that portend the approaching end of life is central to effective end of life care in neurologic disease, both in terms of maximizing patient comfort and in adequately preparing family members and other caregivers for the approaching death. Educating family members about physical changes that occur at the end of life can help alleviate some of the fear and concern that frequently surrounds the witnessing of a loved one in the actively dying phase. Reduction in oral intake, increased agitation, increased upper airway secretions, and changes in respiratory pattern may occur in isolation at other points in the disease process. However, when these changes occur together they typically herald the last hours to days of life.

Reduction in oral intake As a person approaches end of life, there is commonly a marked decrease in the desire for any sort of oral intake, and many people stop eating and drinking all together. Family should be reassured that this is part of the normal progression at end of life, and that attempting to forcing their loved to eat or drink will likely do more harm than good, particularly as in many neurologic conditions, an already present dysphagia will continue to worsen as death approaches. It is important to remember that at this point the lack of eating is a symptom of dying rather than the cause of dying. Therefore, artificial nutrition and/or hydration at this stage are not expected to have any benefits

for life prolongation. Family who remain focused on trying to feed their loved one can be redirected to focus their efforts on keeping the patients' mouth and tongue moist, by way of oral sponges, swabs, and artificial saliva substitutes.

Terminal agitation An abrupt escalation in agitation may manifest with rapidly fluctuating restlessness, moaning, and hallucinations. When prognosis is measured in months or years, a thoughtful assessment of reversible causes should be considered. However, when prognosis is measured in hours or days the goal is suppression of the symptom. Calm, reassuring presence of family and clinicians is important. Identify and minimize triggers of increased agitation. For example, are there many visitors creating a lot of noise in the room? Is the TV on and loud? Is there any way the room could be a more calming environment through music, light, and voice? With these factors addressed, if pharmacologic management is required, lorazepam and haloperidol administered via sublingual concentrate can lead to sedation and reduction of outward signs of agitation.

Terminal secretions Terminal secretions, sometimes referred to as 'death rattle" are audible, gurgling sounds that frequently occur in the last hours or days of life and result from the accumulation of oropharyngeal secretions in the airway due to the loss of normal swallowing reflexes. It has been demonstrated to predict death in 48 h in 75% of patients [44]. Terminal secretions are particularly common in patients with neurologic disease, in part due to the dysphagia associated with many neurologic conditions. One study demonstrated increased prevalence of terminal secretions in the last week of life in stroke compared to cancer patients, (60.7% compared to 40.2% respectively) [45].

The most commonly prescribed pharmacologic interventions for terminal secretions are anticholinergic medications such as atropine, glycopyrrolate, and hyoscine bromide. Evidence for their effectiveness, however, is limited, and while they reduce production of further secretions they cannot remove secretions that are already filling the airway [46]. Although deep suctioning is best avoided in dying patients in the interest of minimizing disruptions to the patient's overall comfort, in some cases gentle suctioning of the oropharynx should be attempted to remove already present secretions prior to initiating anticholinergic therapy. Non pharmacologic interventions for terminal secretions including repositioning the patient either with the head of bed elevated, or on the side to mobilize secretions, and holding IV fluids and enteral feeds in the last hours of life, which if continued can contributed to excessive secretions. Noisy secretions can be of particular distress to family members who may perceive that the noise indicates choking or suffocating. Education and reassurance are important [47].

Changes in respiratory pattern Changes in respiration are another salient finding at end life, and a frequent cause of concern for family members. In the last hours to days of life, noisy breathing, with gasping or sighing sounds can occur, as well as slowing of the respiratory rate, with increasingly longer episodes of apnea. Families should be reassured that these are normal changes that occur in the dying phase.

In patients with neurologic disease, in particular with intracranial pathology, such as brain tumors, hemorrhages, and large ischemic strokes, changes in respiratory status might result not from pulmonary pathology, but from a change in neurologic status. Cheyne-Stokes breathing, marked by cyclical fluctuations in both the depth and rate of respirations interspersed with periods of apnea, may result from metabolic causes, bilateral hemispheric damage, or as an early sign of brain herniation. Very rapid breathing, at rates from 40 to 70 breaths per minute, can result from pulmonary or metabolic causes, but can also indicate central neurogenic hyperventilation, associated with pontine lesions or increased intracranial pressure. Cluster breathing, presenting as periods of regular rapid breathing interspersed with periods of apnea, and ataxic breathing marked by irregular rhythm and rate of breathing, are both associated with brainstem injury and can be a sign of herniation [48]. Bedside recognition of

these respiratory changes in the end stage of neurologic disease can help to identify, and thus keep the family apprised of changes in the patient's clinical status.

Other changes which mark a transition to the actively dying phase are a decreased interaction and level of responsiveness, declining urine output, and dropping body temperature, with cooling and mottling of the extremities.

Mr. Jay remains unresponsive for the next 36 h. He develops intermittent tachypnea and facial grimacing which both resolve with low and intermittent doses of morphine. His wife feels empowered to continue his care at home through the natural end of his life. Her grief is powerful but uncomplicated, and after his death, she takes advantage of bereavement support over the next year.

Research and Educational Agenda

There is much work to be done to improve care for people with neurologic disease at the end of life. Educational efforts must be bidirectional, with neurologists requiring more education about hospice and end of life and hospice providers requiring more education about specialized care for neurologic diseases. Research questions include: (1) Developing more accurate predictive tools for 6-month prognosis; (2) Defining the appropriate time to discontinue medications in advanced disease; (3) Improving our evidence base for symptom management at the end of life; and (4) Exploring the costs, benefits and effectiveness of various models of end of life care, for example comparing prognosis based system of care (as exists in the US) versus models based on need.

Take Home Messages

- In the United States, hospice is a system of care including an interdisciplinary team, durable medical equipment, and medications for people with prognosis expected to be 6 months or less if the disease takes a typical course.
- Across the world, end of life care services carry different names, definitions, and structures; and in some places do not exist at all.
- Strong, evidence based guidelines for determining prognosis of 6 months or less are not established for neurologic diseases. Guidelines based in expert consensus to define advanced disease are in use for stroke, ALS, and dementia.
- General signs of decline that are widely accepted include recurrent infections, weight loss, multiple hospitalizations or emergency room visits, and rapid deterioration in functional status.
- Symptom management is based on physiologic and pharmacologic principles, with a goal to use minimum effective dose to achieve the patient's comfort and to meet the patient's individualized goals of care.

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Pain Assessment and Management

17

Christina L. Vaughan and Alan C. Carver

A key focus of the neuropalliative care approach is aggressive symptom management. Despite the publication of numerous national and international guidelines on how to manage pain effectively, under-treatment of pain remains a significant public health problem. Chronic pain affects 20–40% of patients with primary neurological diseases [1]. Many barriers remain that prevent patients with moderate to severe pain from receiving the care that they deserve including physician discomfort with prescribing pain medications, lack of clinician training in pain management, patient reluctance to discuss pain or take pain medications, and difficulties obtaining certain pain medications from pharmacists.

Pain Mechanisms

Chronic pain is often a direct result of a neurologic disease including traumatic injury to the central nervous system (CNS), neurodegeneration, neuroinflammation, and peripheral nerve damage (Table 17.1) [1]. Identification of the underlying pain mechanisms provides a more targeted treatment [2–4]. It is helpful clinically to broadly place a complaint of pain into either of two categories – *nociceptive* or *neuropathic*.

Table 17.1 Common causes of pain in neurologic disease

I. CNS damage
(a) Post-stroke
(b) Traumatic brain injury
(c) Spinal cord injury
(d) Multiple sclerosis
II. Neurodegenerative disease
(a) Parkinson disease/atypical parkinsonisms
(b) Huntington disease
(c) Alzheimer's disease and other dementias
III. Neuromuscular disease
(a) Amyotrophic lateral sclerosis
(b) Guillain Barre syndrome
IV. Neuro-oncologic disease
V. Head and face pain
(a) Primary and secondary headaches
(b) Trigeminal neuralgia
VI. Peripheral nerve disorders
(a) Peripheral neuropathy
(b) Complex regional pain syndrome
(c) Post-herpetic neuralgia
(d) Back pain
(e) Post-surgical pain

Nociceptive pain emanates from tissue damage whereas neuropathic pain arises from damage or dysfunction of the central or peripheral

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nervous system. Nociception may be further subdivided into either a *somatic* or *visceral* etiology:

- *Somatic pain* is due to the activation of nociceptors on cutaneous or deep tissue sites, and described by patients as aching, throbbing, or gnawing. Somatic pain is sharp, well localized, and due to muscle, bone, or soft tissue damage.
- *Visceral pain* is due to the activation of nociceptors on visceral organs, and described by patients as a "crampy", pressure-type pain. Visceral pain is poorly localized, and may be referred from one location to another.
- *Neuropathic pain* is due to direct neuronal involvement and described by patients as burning, tingling, shooting, itching, lancinating, electric-like pain. Well-localized, neuropathic pain may be secondary to toxins such as poorly controlled blood glucose, alcohol, or chemotherapy, leptomeningeal or cranial neuralgias, traumatic peripheral neuropathies, central pain syndromes, mononeuropathies, or paraneoplastic peripheral neuropathies, among others. The prevalence of neuropathic pain in the general population has been estimated at 6.9–10.0% [5].
- *Central pain* is a type of neuropathic pain that arises from the central nervous system (CNS). One example of central pain is the thalamic pain syndrome following thalamic stroke (Dejerine–Roussy syndrome). Thalamic pain is driven by multiple mechanisms and often patients require more than one analgesic that targets more than one mechanism.

Examples of Pain in Major Neurological Disease Categories

While the management of neurodegenerative disease has historically focused on motor and cognitive symptoms, many of these patients report pain. For example, pain is common in Parkinson disease (PD) and occurs in 30–95% of patients [6–9]. Pain is very heterogeneous in the PD population and may be categorized as directly related to PD, indirectly related (aggravated by PD), or unrelated (attributed to any other health problem) [10, 11]. Musculoskeletal pain in PD originates from abnormal postures, dystonia, rigidity, and akinesia, and can result in cramps, shoulder disturbances, spinal or hand/foot deformity, or nonradicular back pain [12–14]. Neuropathic pain in PD can be peripheral (radicular or peripheral neuropathy), or central with otherwise unexplained pain often worse in the more affected parkinsonian limbs, or rarely, unexplained oral, abdominal, or genital pain. Restless legs syndrome in PD can also contribute to discomfort [12, 13]. Akathisia pain is a subjective restlessness or painful impulse to move continually which may improve with levodopa [15]. *(*See also Chap. 5, "Parkinson's Disease and Related Disorders").

Prevalence rates of both dementia and pain increase with age [16] and people with dementia often suffer from various comorbidities associated with pain such as osteoarthritis or sequelae from falls. Although individuals with dementia are often unable to communicate their suffering [17], studies using observational tools to assess pain suggest that about 50% of patients with dementia living in nursing homes are suffering from pain [18, 19]. The etiology of pain among patients with dementia living in nursing homes include genitourinary infections, musculoskeletal pathology [20], pressure ulcers [21], and skin diseases, the latter of which is described as one of the most prevalent health problems in this population [22]. Studies of community-dwelling patients with dementia also suggest at least 50% are suffering from pain [14, 23–27]. Accurate pain assessment in advanced dementia is challenging and requires less reliance on self-report and more on behavioral indicators of pain such as facial expressions [14] (see also Chap. 6, "Dementia").

Several small to moderately sized studies have reported a prevalence of pain in Huntington's disease (HD) ranging between 11% and 62% [28–30] with a more recent large cross-sectional study suggesting a prevalence of 40% that is fairly stable across stages [31]. A recent retrospective cohort study of HD patients enrolled in hospice

found that pain was the most common symptom at the time of enrollment [32]. Notably, areas of the brain that modulate pain perception are affected by HD [33, 34]. As in dementia, the management of pain is challenging due to communication difficulties, cognitive difficulties, and apathy [31].

Amyotrophic lateral sclerosis (ALS) is the most common neurodegenerative disorder of the motor system in adults, and pain can occur in up to 80% of patients [14]. In a small case series of ALS, pain was the first symptom manifested in over 20% of patients, with the arms as the primary affected region [35]. In general, pain is commonly reported in the back and shoulders, followed by neck, buttocks and hip(s), feet, arm(s), and hand(s) [36]. Inactivity, joint inflammation, or points of pressure in ALS contribute to atrophy, muscle cramps, spasticity, or pressure sores [37, 38]. A recent cross-sectional study revealed that pain of musculoskeletal origin with an axial distribution in the body (i.e. head, neck, lower back) was found in most patients [39]. The neuropathic components of ALS-related pain can be present even in the early phases of the disease and worsen musculoskeletal pain [40]. (See also Chap. 8, "Neuromuscular Diseases").

There is a high incidence of pain syndromes in patients with multiple sclerosis (MS), with a significant prevalence of craniofacial manifestations, including trigeminal neuralgia and migraine [41] in addition to lower back pain, neuropathic pain and painful spasms. Chronic pain is estimated to occur in 30–85% of those with MS [42–45]. Damage within the central or peripheral nervous system, inflammatory, and musculoskeletal mechanisms, such as immobilization of parts of the body, may all contribute to pain in MS [45, 46]. Conflicting findings of associations between pain and relapses have also been reported, with some showing associations of pain with higher relapse rate [47] while others report increased relapses associated with lower prevalence of pain [48]. While it seems logical that the presentation of pain correlates with sites of demyelination, a study evaluating CNS pathways in patients with MS with and without pain found no association between chronic pain and the site of demyelination [47]. Instead, increased pain in MS is found to correlate with depression, spinal cord involvement at onset, and the presence of spinal cord lesions [47]. (See also Chap. 7, "Multiple Sclerosis").

Chronic pain occurs in 11–55% of patients with stroke [49], often due to infarcts along the spino-thalamocortico-tract (spinothalamic tract, lateral thalamus, thalamic–parietal projections), which result in central pain syndromes [50]. The mechanisms underlying the severe, spontaneous, burning pain that occurs with thalamic stroke remain unclear [1]. (See also Chap. 2, "Severe Acute Brain Injury").

Patients with brain tumors typically exhibit head pain, which is localized, progressive, worse in the morning, and aggravated by coughing or bending forward. The headache is said to develop in temporal, and often spatial, relation to the neoplasm and resolves within 7 days of surgical removal or treatment with corticosteroids [51]. Headaches due to intracranial neoplasm can be caused by obstruction of CSF flow and secondary intracranial hypertension, direct mass effect by the neoplasm, inflammatory effect of neoplasm, or neuroendocrine changes related to tumor [52].

Pain Assessment and Communication

Comprehensive pain assessment starts by establishing a trusting relationship with the patient by providing a safe space where their complaint is taken seriously and thoroughly investigated. Pain is often more than simply physical symptoms. Dame Cicely Saunders, founder of the modern hospice movement, introduced the concept of "total pain" as the suffering that encompasses all of a person's physical, psychological, social, spiritual, and practical struggles [53]. In addition to obtaining a complete history and performing a detailed and directed medical and neurologic evaluation, gaining understanding of *what the pain means to the patient and the psychological impact of the pain* are critical components of the assessment. Useful questions could include, "In what parts of your life do you most notice the

pain?" "How do you make sense of this pain?" "How are you able to carry on with your day with this pain?" "With better pain control how would your life look differently?"

Identifying the cause(s) of pain is essential to guide treatment. Pain caused by tissue injury to visceral structures is often poorly localized and referred to cutaneous sites while neuropathic pain may be accompanied by additional sensory phenomena (such as allodynia or hyperpathia) [54]. Some situations will require a detailed goals-of-care or serious illness conversation to explore what is most important to the patient, and what his/her expectations are. A patient who wants pain controlled regardless of side-effects (such as drowsiness) would require a markedly different approach than a patient who wants to maximize wakeful productivity. As part of this discussion, the clinician should determine the network of support patients have available and, if there is a lack of support, facilitate access to needed services or appropriate support groups. Prior to considering analgesic therapy, it is vital for the clinician to ask about the location of the pain, to understand what makes it better and what makes it worse, and to ask the patient to describe in as much detail as possible the nature of the pain. By asking these few questions, the clinician will begin to understand how to categorize the pain, what mechanisms drive the problem, and make the best possible choice of therapy based upon those mechanisms. Key points of pain assessment are summarized in Table 17.2.

There are several validated pain scales that can be used to track pain, assess the efficacy of therapies and improve communication across providers such as the Brief Pain Inventory [55], the McGill Pain Questionnaire [56], the Memorial Pain Assessment Card [57], and the Memorial Symptom Assessment Scale [58]. Asking a patient to rate his/her pain on a scale from 0 (no pain) to 10 (worst pain imaginable) offers the patient the opportunity to quantify the complaint and gives the clinician a benchmark to measure severity and treatment response. Given the high prevalence of communication and/or cognitive impairment in patients with neurological disease, verbal scales (mild/moderate/severe) can be substituted by a Visual Analogue scale (bisecting a horizontal line to mark the pain intensity) or, as

Table 17.2 Pain assessment algorithm [96]

1. Believe the patient's complaint of pain
2. Take a careful history of the pain complaint to place it temporally in the patient's history of neurologic disease
3. Map the characteristics of each pain, including its site, its pattern of referral, and its aggravating and relieving factors. Assess the functional impact of pain
Clarify the temporal aspects of the pain – acute, subacute, chronic, episodic, intermittent, breakthrough, or incidental
OPQRSTU mnemonic: onset, palliation/provocation, quality, region/radiation, severity, temporal pattern, useful therapies
4. If there is more than one pain complaint, prioritize appropriately
5. Evaluate the response to previous and current analgesic therapies
6. Evaluate the psychological state of the patient and whether or not there are emotional factors that exacerbate the pain complaint
7. Ask if the patient has a history of alcohol or drug dependence – whether illicit or by prescription
8. Perform a careful medical and neurologic evaluation
9. Order and personally review the results of the appropriate diagnostic tests
10. Treat the patient's pain as you are proceeding with the necessary work up
11. Design the diagnostic and therapeutic approaches to suit the individual patient
12. Provide continuity of care, from evaluation to treatment, to ensure patient compliance and reduce anxiety
13. Reassess the patient's response to follow up within a short and appropriate interval
14. Remember the 4 A's – affability, affordability, ability, availability. The success of any pain management strategy suggested by the clinician will be predicated upon the patient feeling he/she is cared about by the clinician, the expertise of the clinician, and the availability of the clinician and/or the team of providers in between office visits

Modified from Carver and Foley [96], with permission of Elsevier

commonly used in children, a scale of various facial expressions [59]. For nearly the past two decades, The Joint Commission on Accreditation of Healthcare Organizations (JCAHO) has included clearly visible pain assessment measurement as an accreditation standard [60, 61].

Pain Management

A multidisciplinary approach is recommended to investigate all possible options for optimal management: (1) non-pharmacological measures, including psychological support and physical therapy, (2) pharmacotherapy, and (3) interventional procedures.

Non-pharmacologic Management of Pain

Non-pharmacologic therapies can help minimize polypharmacy which is of particular concern in older populations. Non-pharmacologic measures include [62]:

- Treatment of reversible cause(s)
- Application of heat or cold to affected area
- Elevation of extremity, providing range of motion
- Music, aromatherapy, distraction, pet therapy, journaling, acupuncture, mindfulness techniques
- Physical therapy
- Therapeutic massage
- Hypnotherapy
- Assessment and management of spiritual, emotional, social, financial concerns

Some patients may expect that pain will automatically be treated with pharmacologic interventions, and thus it is important to introduce the possibility that *non*-pharmacologic therapies may be useful either as monotherapy or in conjunction with medication. Taking the time to educate patients about the etiology of their pain often allows for a discussion of the breadth of interventions that may address their specific pain.

Mindfulness-based interventions, cognitive behavioral therapy, and hypnosis are psychotherapies that can reduce perception of pain and increase mobility and functioning [63–65]. In a study of mindfulness-based stress reduction (MBSR) vs cognitive behavioral therapy (CBT) or usual care on back pain, clinically meaningful functional improvement was achieved by a significantly greater proportion of participants in the MBSR and CBT groups at 26 weeks compared with usual care recipients, and improvements in the MBSR group persisted at 52 weeks [66]. Some reports have indicated that physical treatment methods like massage, heating pads and transcutaneous electrical nerve stimulation (TENS) are useful for pain management [67]. One study revealed that increasing amounts of time per day spent in light-intensity physical activities were significantly associated with less incident disability and less disability progression in patients with osteoarthritis, even after controlling for socioeconomic and clinical factors [68]. Regular physical therapy can help treat pain with movement and stretching, as well as sometimes prevent contractures and worsening of pain.

Targeted Pharmacologic Pain Management

By properly categorizing the pain complaint, the provider can then ask "What are the first-line therapies that are most likely to be successful in relieving pain by targeting the identified mechanisms?" In general, patients are most likely to respond to evidence-based therapies. The WHO approach to managing cancer pain provides some helpful tips which may be generalizable to multiple pain types (Table 17.3). Second or third-line approaches should only be offered once the pain has proven refractory to first line choices. The American Pain Society, AHCPR, and WHO have published specific guidelines for the management of pain [69–71] and all agree that analgesic drug therapy is the mainstay of treatment. In 1986, the WHO first proposed an analgesic ladder [70] (Fig. 17.1), which has remained useful to assure the proper linkage between pain severity and

Table 17.3 A useful approach to managing cancer pain [70]

1. *The oral route* is preferred first for simplicity and efficacy
2. *By the clock* – for persistent pain, analgesics should be offered around the clock in order to stay ahead of the pain either by offering short-acting analgesics at appropriate daily intervals or with timed, extended release medication, with a shorter-acting provision for breakthrough pain
3. *By the ladder* – It is essential to be certain that the severity of the pain is matched with the appropriate analgesic (See Fig. 17.1)
4. *For the individual* – The right dose is the dose that provides effective pain relief with minimal or manageable side effects. Patients with similar disease states may require widely varying amounts of pain medication in order to provide satisfactory relief
5. *With attention to detail* – pain must be assessed, understood, and treated, in all of its determinants. Emotional, spiritual, or other components, when present, must be thoroughly assessed and treated for a satisfactory result to be achieved

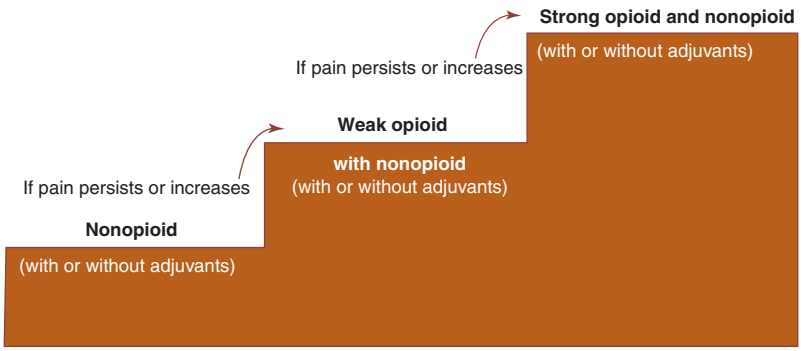

Fig. 17.1 The World Health Organization analgesic ladder for treating cancer pain [123], [124]with permission Vargas-Schaffer G. Is the WHO analgesic ladder still valid. 24 years of experience, Canadian Family Physician, Vol 56, June 2010. (Adapted from the World Health Organization)

choice of analgesic (i.e. to help the clinician avoid making the error of treating severe pain with acetaminophen, or mild pain with morphine).

If pain is acute it is usually related to an easily identified event or condition and resolution is anticipated within a period of days or weeks. Chronic pain may or may not be related to an easily identified pathophysiologic phenomenon and may be present for an indeterminate period [72]. To manage constant pain, the WHO recommends scheduling medication every 3–6 h, instead of prn use only.

Neuropathic Pain

Neuropathic pain is not a single disease, but a syndrome that can be caused by a number of diverse etiologies [73] and its clinical manifestations vary greatly [74]. Given the unrelenting chronic nature of neuropathic pain, it is important to ensure other comorbidities are addressed (such as depression) and that assessment of sleep and overall quality of life are not overlooked. Less than 50% of patients achieve pain relief of at least 50% with any drug or combination of drugs [2]. Clinical practice guidelines have been published by many international and regional professional associations, and three drug classes have received strong recommendations for first-line therapy: tricyclic antidepressants, particularly amitriptyline; the serotonin-norepinephrine reuptake inhibitors (SNRIs) such as duloxetine; and the calcium channel alpha-2-delta ligands gabapentin and pregabalin [75], (Table 17.4). Of note, while gabapentin and pregabalin are structurally related agents with similar spectra of antinociceptive activity, pregabalin has a linear pharmacokinetic profile which makes the suggested dose

Table 17.4 First line neuropathic pain medications

Medication	Starting dosage
Pregabalin	50 mg BID or TID
Gabapentin	100 mg BID or TID
Duloxetine	30 mg daily
Amitriptyline	10 mg at bedtime

Tramadol (starting dose 50 mg BID-QID) a weak opioid and an SNRI, is generally considered to be a second-line agent. The guidelines of the National Institute for Health and Care Excellence (NICE) of the UK recommend tramadol only for use in rescue therapy as it has been generally associated with higher rates of withdrawal due to adverse events compared with other treatments and that the clinical studies that investigated its efficacy included small numbers of patients and short observation periods [125]

(300 mg/day) and the dose increments meaningful and the results far more predictable compared to gabapentin [76]. Therefore, in daily clinical practice, pregabalin may be a better choice than gabapentin [75]. While most clinical trials have shown that the efficacy of SNRIs is lower than that of tricyclic antidepressants [77], the safety profile of SNRIs is superior to that of tricyclic antidepressants, and are probably preferable in elderly patients [75].

Carbamazepine (200–800 mg/day) and oxcarbazepine (600–1800 mg/day) are generally recognized as effective treatments for trigeminal neuralgia, and the 2008 AAN/European Federation of the Neurological Societies practice parameter identified several randomized controlled trials that found these to be equally effective [78]. Topical lidocaine can be used for localized neuropathic pain [79], while low concentrations of topical capsaicin, though commonly used to treat neuropathic pain does not have significant data to support its benefit [80]. There have been some results suggesting that capsaicin 8% treatment may be effective in managing the dynamic mechanical allodynia of neuropathic pain [81].

Tramadol and lower potency opioid analgesics (such as hydrocodone or codeine, or acetaminophen-combined opioids) are recommended as second-line treatments for moderate to severe neuropathic pain. Tramadol is a weak opioid agonist and mimics some of the properties of the TCAs as it inhibits reuptake of norepinephrine and serotonin [82]. Drugs recommended for third-treatment now include cannabinoids, and fourth-line treatments include methadone, topical lidocaine, and anticonvulsants with lesser evidence of efficacy.

The use of medicinal cannabis has become gradually more accepted in the United States and globally and between 45% and 80% of those who seek medical cannabis do so for pain [83–85]. Recent systematic reviews found low-strength evidence that cannabis preparations may alleviate neuropathic pain and muscle spasticity in MS, but overall quality of evidence was low to moderate and there was insufficient evidence in populations with other types of pain [85, 86]. It is important to remember that cannabis use has potentially serious mental health and adverse cognitive effects, although data are insufficient to characterize the degree of risk or in whom the risk is highest [85]. Although the literature does not reveal strong, consistent evidence of benefit, clinicians should be prepared to engage in evidence-based discussions with patients requesting to use cannabis; up to date literature reviews such as that from Nugent et al. (2017) [85] may be a good starting point for the clinician.

The combination of different pharmacological treatments in the management of pain ("combination therapy"), typically using two drugs with different mechanisms of action, is compelling as many patients have insufficient pain relief on monotherapy. Furthermore, the drugs used for treatment of neuropathic pain may have dose-dependent side effects and tolerability issues that often lead to discontinuation of high-dose monotherapies [87]. A recent review using a Delphi process completed by Danish pain specialists [87]

revealed that the combination of pregabalin or gabapentin with tricyclic antidepressants was commonly documented and experts had good clinical experience with this combination in the management of neuropathic pain. The combination of pregabalin or gabapentin with a SNRI (mostly duloxetine) was also reasonably well documented with good clinical experience and fewer side effects than high-dose monotherapy. Despite the fact that combination therapy is widely used in clinical practice with generally beneficial results, existing guidelines do not contain much information or recommendations on combining pharmacological pain therapies to improve pain management in neuropathic pain [87].

Opioids

If an immediate-release opioid is chosen and the pain is constant, the medication should be given every 4 h (on the half-life). Optimal pain control is expected to occur once a steady state is achieved, which is after 4–5 half-lives, or nearly a day later. As-needed doses of the same medication should be available as a rescue dose for breakthrough pain (see Breakthrough pain section below). If pain remains uncontrolled after 24 h, the scheduled dose should be increased by 25–50% for mild to moderate pain, by 50–100% for severe to uncontrolled pain, or by an amount at least equal to the total dose of rescue medication used in the prior 24 h. Immediate-release opioids are characterized by a rapid rise and decline in serum levels, which may be beneficial for the treatment of acute pain and breakthrough pain, whereas chronic pain is more effectively managed by sustained-release formulations. Opioids with long half-lives or extended-release formulations are preferred for the management of chronic pain. These drugs may facilitate patient adherence with treatment regimens, increase convenience for caregivers, provide consistent levels of analgesia, and allow the patient to focus less on pain and dosing [88]. Taking a sustained-release opioid in the evening is more likely to provide better sleep at night, as compared with repeated dosing of a short-acting opioid [89]. Depending on the product, sustained-release oral opioids are specifically formulated to release drug in a controlled way over 8, 12, or 24 h. The best possible pain control for the dose will be achieved once steady state is reached, within 2–4 days. As such, doses should not be adjusted any sooner than once every 2–4 days. Care must be taken if using methadone as it has a long and variable half-life which approaches a day or longer. Methadone is generally started at 5–10 mg tid, and given the often unexpected potency and variable half-life, the dose should not be increased sooner than every 4–7 days.

In general, the right dosage of an opioid is the amount of medication that provides maximal pain relief with minimal or easily manageable side effects. As there is no ceiling effect for opioids, patients should be titrated until dose-limiting side effects occur or satisfactory pain relief is achieved.

Breakthrough Pain

Data from several clinical trials suggest that up to 93% of patients with successfully treated around the clock pain still have breakthrough pain (i.e., pain that breaks through the daily extended-release provisions) [90–94]. Patients therefore who are prescribed timed-release around the clock analgesics, whether opioid or non-opioid, must be offered a short acting provision for breakthrough pain. The dosage of the short-acting medication for breakthrough pain should represent 15–20% of the total 24 h dosage. The goal of treatment is NOT to eliminate breakthrough pain. Instead, it is to minimize the frequency of breakthrough pain that requires a short acting analgesic to one to three doses of pain medicine per week or to the frequency most satisfactory to the patient. If the breakthrough incidence is significantly more frequent, it is reasonable to adjust the chosen dosage of around the clock medication to reduce the frequency of breakthrough pain. It is neither a realistic nor a desirable goal to eliminate breakthrough pain entirely as this risks the patient becoming overly sedated, sometimes leading to an inappropriate reduction of the long-acting analgesic.

If a patient with well-controlled chronic pain and relatively infrequent breakthrough pain notes an increase in the breakthrough incidence and/or requires a higher dose of around the clock analgesic, the most likely cause is a new site of disease or progression of the prior site of disease. Psychological dependence (i.e., addiction, see below) or loss in potency of the previously effective medication are less likely. Should a patient receiving pain medication request a higher or more frequent dosage, it is essential to obtain an appropriate history, perform a physical and neurologic examination, and order the appropriate tests to best identify the pathology that is most likely to be at the heart of the request for a medication adjustment.

Tolerance, Addiction, and Pseudoaddiction

Tolerance is defined as a change in the dose-response relationship induced by exposure to the drug and manifests as a need for higher dose to maintain effect. Clinically, it is important to realize that there is no limit to tolerance [95]. Wide ranges of opioid requirements in individual patients have been reported and concern about tolerance should not thwart the administration of opioids when necessary for the management of severe pain [96]. Physical dependence is the phenomenon of withdrawal when an opioid is abruptly discontinued, or when an opioid-mixed agonist-antagonist or antagonist (such as naloxone) is given [96]. To prevent withdrawal, those receiving opioids for greater than 1 week should be tapered off the opioid rather than discontinued abruptly. Psychological dependence (i.e., addiction) is a behavioral pattern of drug use characterized by continued craving for opioid effects rather than for pain relief. This often entails preoccupation with drug use and procurement, legal, marital, and employment difficulties associated with drug use, and lack of improvement in quality of life with the use of the drug [96]. It is important not to confuse these behaviors with "pseudoaddiction" which is proposed to be an "iatrogenic syndrome that mimics the behavioral symptoms of addiction" in patients receiving inadequate doses of opioids for pain [97].

Assessment of Opioid Abuse Potential

Misuse of opioids is common in patients with chronic pain and early recognition of misuse risk could help physicians offer adequate patient care while employing appropriate levels of monitoring to reduce aberrant drug-related behaviors [98]. Validated measures have been developed to screen patients with pain for addiction risk potential. The 5-item Opioid Risk Tool (ORT), a brief checklist completed by the clinician, is such a validated questionnaire that predicts which patients will display aberrant drug-related behaviors [99]. Scores of 8 or higher suggest high risk for opioid medication abuse, and this information can direct the physician to provide closer monitoring with more frequent clinic visits, urine screens, self-report questionnaires, and behavioral observation. Regularly using the state's prescription drug monitoring program can be critical in watching out for abuse in individual patients. Controlled-substance agreements are often used in clinics to explain the roles of the patients and providers and to ultimately improve patient compliance with opioid medication. These documented agreements provide education and mutual consent among patients and providers and inform patients of their responsibilities when using prescribed pain medication [98].

Opioid Rotation

Familiarity with the widely available opioid equianalgesic table (Table 17.5) is essential to offer patients the best chance for sufficient pain relief should a particular opioid analgesic require substitution. Many patients experience far fewer side effects and notably better pain relief with opioid rotation. The starting dosage of the new drug should generally be one-half the equianalgesic dosage of the prior drug to account for the phenomenon of incomplete cross tolerance. However,

Table 17.5 Opioid analgesics commonly used for moderate to severe pain

Medication	Parenteral (mg)	Oral (mg)	Half-life (h)	Comment
Morphine	10	30	2–4	Usual 1st choice in opioid naïve pts. without renal or hepatic insufficiency
Hydromorphone	1.5	7.5	2–3	Shorter acting
Oxycodone	–	20	3–4	
Fentanyl	0.05-0.1		1–2	Short half-life, transdermal and transmucosal
Methadone			15–120	Good bioavailability, may accumulate with repetitive dosing, biphasic half-life
Meperidine	75–100	300	2–3	Not recommended for chronic cancer pain, impaired renal function, or if receiving MAO inhibitors (due to toxic metabolites)

Modified from Carver and Foley [96], with permission of Elsevier

if a patient's pain is poorly controlled and an opioid rotation needs to occur, the starting dosage of the new drug may be as high as 75–100% of the prior opioid and as noted previously, the new drug should be titrated until successful analgesia or dose-limiting side effects are achieved.

Opioid-Induced Side Effects

The successful management of moderate to severe pain with opioids is predicated upon the comfort level of the clinician not only with the use of opioids, and rotation from one to another if needed, but also with the aggressive treatment of side effects. Patients are often undertreated due to their fears of opioid-related side effects and the clinician's lack of confidence or comfort with how to manage these side effects successfully. As a general rule, if a patient's pain is being managed successfully yet he/she is bothered by a particular side effect, the best management strategy is to treat the side effect. If the patient is experiencing multiple side effects the medication should be changed to an alternative opioid analgesic.

Constipation

Opioid-induced constipation (OIC) is the most common and bothersome effect reported by patients, and is present in 40–90% of patients who use opioids chronically [100]. Opioid receptors line the gastrointestinal tract and spinal cord decreasing peristalsis and intestinal secretions. This is the only opioid-induced side effect that patients do not become tolerant to no matter how long the opioid is administered. Treatment of OIC is complex and stepwise in nature, involving dietary modifications, lifestyle changes, and laxative use [101]. Laxatives are generally classified according to their mode of action: bulk-forming laxatives, osmotic laxatives, stimulant laxatives, and stool softeners and lubricants. Generally, a combination of a softener and a stimulant is recommended for the management of constipation in palliative care as peristalsis stimulants have a tendency to cause colic pain unless accompanied by an agent that will soften the stool [102]. A starting regimen of 300 mg of docusate sodium and two tablets of Senokot is often recommended.

Most over-the-counter laxatives do not target the underlying mechanism of OIC, specifically, the peripheral effects on enteric μ-receptors. A new class of peripherally acting μ-opioid receptor antagonists (PAMORAs) have emerged over the past decade to combat this gap in treatment. Patients should fail non-pharmacological (adequate hydration, increase in dietary fiber, and mobility) and over-the-counter treatment options before initiating one of these more-expensive prescription alternatives [101]. Presently, PAMORA agents available to treat OIC include methylnaltrexone, naloxegol, naldemedine, and

alvimopan, although alvimopan is not approved for OIC. In addition, lubiprostone, a chloride channel activator, is FDA approved for the treatment of OIC in patients with chronic non-cancer pain [101].

Sedation

If a patient is sedated but receiving adequate pain relief, the sedation is best managed with caffeine, methylphenidate, or a similar psychostimulant. Caution is advised in taking these later in the day, as these can produce insomnia. Respiratory depression is a relatively uncommon side effect when opioid dosing guidelines are properly followed. The adage, "no one ever died of respiratory depression while awake" is helpful to remember. Unless hemodynamically unstable, the initial approach to a patient with respiratory depression should include vigorous stimulation of the patient, a lowering of the dose of opioids, and consideration of alternative analgesics. The specific opioid antagonist, Naloxone, should be reserved for use in the setting of the unstable patient to assure the safety of the patient and to avoid precipitating a pain crisis unnecessarily.

Encephalopathy

While opioid medications can induce confusion, it is essential to be certain, when evaluating a patient with a mental status change, that he/she undergoes an appropriate, comprehensive work up, and that the clinician not make the error of assuming the culprit is the opioid because the patient is receiving an opioid analgesic.

Myoclonus

Uncontrollable twitching and jerking of various muscle groups may occur in patients who receive chronic opioid therapy and it appears to be dose-related in an unpredictable manner. The incidence of opioid-related myoclonus varies widely, ranging from 2.7% to 87% [103]. Opioids and their metabolites affect multiple receptor systems with variable effects in patients. Sometimes myoclonus is subtle and non-bothersome and may be monitored. Reversible causes including metabolic derangements should be appropriately treated and the hydration status should be assessed. Metabolic or other drug-induced encephalopathies should be considered, acknowledging that the primary neurologic disorder could also be a culprit. If myoclonus is likely opioid-induced, persists and impairs function or prevents sleep, a reduction in opioid dose, a symptomatic approach, or a switch to a different opioid should be considered in the face of refractory or severe myoclonus [103].

Urinary Retention

Among many other drugs, opioids can contribute to impaired emptying of the bladder resulting in post-void residual urine [104]. This can lead to bladder/suprapubic pain and tenderness and new onset overflow incontinence. Certainly many neurologic conditions can also cause or contribute to urinary retention, but if this is (sub)acute and coincides with change or start of opioid, then decrease or discontinuation of the offending agent should be considered.

When Managing a Pain Crisis

Corticosteroids remain a highly effective choice in providing immediate relief of a patient in 10/10 severe, crisis-level pain due to spinal cord compression, increased intracranial pressure, superior vena cava syndrome, bone pain, visceral pain (obstruction and/or capsular distension), or severe neuropathic pain in the setting of cancer. While guidelines vary widely, it is worth remembering that a single high dose of intravenous corticosteroids can provide suffering patients with rapid-onset of relief and rarely if ever has toxicity been described following a single dose of up to 100 mg of IV dexamethasone or its equivalent. Corticosteroid side-effects occur with repeated administration and so clinicians should not fear a

single intervention that can be uniquely helpful in eliminating the crisis as a diagnostic work up is initiated.

Neuropathic pain which becomes resistant to high dose opioids may respond to NMDA-receptor antagonists such as dextromethorphan, ketamine, lidocaine, and methadone. Intravenous ketamine infusions have been used extensively to treat often intractable neuropathic pain conditions, but there is a relative paucity of evidence in the current literature to guide ketamine infusion therapy and no consensus on an optimal IV protocol [105]. Lidocaine infusion can be successful in controlling pain where other agents have failed, but there is also a dearth of studies that have assessed differences in dose, infusion protocol and adverse effects of lidocaine administration [106].

Procedural Methods of Pain Relief

Interventional procedures may be indicated in some patients with advanced disease, with 8–10% of patients benefiting from peripheral nerve blocks and 2% from a central neuraxial block [107]. Epidural or intrathecal infusion can be considered in cases refractory to medical management, especially in patients with inadequate analgesia despite increasing opioid use/rotation, those with intolerable side effects despite aggressive management, and those with visceral pain associated with abdominal or pelvic malignancies [87, 107].

Radiotherapy can be very effective for painful bone metastases, to manage obstruction caused by tumor compression of blood or lymphatic vessels, of airways or the gastrointestinal tract. Neuropathic pain due to nerve or plexus invasion or headache by intracranial hypertension secondary to brain metastases may also be good indications for palliative radiotherapy [107].

Botulinum neurotoxin (BoNT) has been used for the treatment of many clinical disorders by producing temporary skeletal muscle relaxation and has been useful in pain management with its demonstrated reduction in muscular hyperactivity. It has been used in many painful diseases such as myofascial syndrome [108], headaches [109], neuropathic pain [110], spasticity [111–113], and dystonia [114]. Although the precise mechanism of analgesia is not well understood, it has been hypothesized that BoNT may reduce neuropathic pain symptoms by altering the peripheral mechanism of neuropathic pain transmission and ultimately reducing central sensitization [115–119]. In particular, BoNT-A may inhibit the release of proinflammatory agents, such as cytokines, substance P, bradykinin, serotonin, adenosine, and prostanoids, which can sensitize muscle nociceptors and alter neural transmission and central processing [120, 121].

Public Health Challenges

There is undoubtedly a crisis of opioid misuse that has sadly taken the lives of many and dominated the headlines over the past several years. The CDC Guideline for Prescribing Opioids, published in JAMA in 2016 [122], and many other growing restrictions will undoubtedly with time help stem the tide of the challenge prescription drug abuse that has garnered so much of the attention of government officials and the media over the past several years. There are published data as recently as 2015 to suggest that opioid diversion and abuse may be reaching a plateau, and possibly decreasing undoubtedly as a result of all of the public attention, and increasing regulatory controls.

Since the 2009 revision of the Clinical Practice Guidelines for Quality Palliative Care, there have been several positive steps which have been encouraging in the fields of hospice, pain and palliative medicine. The Accreditation Council for Graduate Medical Education has recognized Hospice and Palliative Medicine as a subspecialty of eleven different parent boards, lending significant legitimacy to a field in the United States that has been well established in several other nations for decades. The World Health Assembly issued its first global resolution on palliative care in 2014 which called upon the WHO and its member states to improve access to palliative care “as a core component of health systems.”

The Prague Charter in 2013 urged governments worldwide to focus upon improving palliative care and widening access to pain medication.

These efforts among many others, are encouraging indications that internationally there is a growing insistence that the under-treatment of pain must come to an end, and that it is violation of Patient Rights not to receive adequate analgesic medication and to be cared for by clinicians whose training does not include competency in the basic principles of pain and palliative medicine. Redefining competency in neurology, among other specialties in clinical medicine, to include expertise not only in the treatment of disease, but in best practice standards of patients suffering from such diseases, is on its way, and offering a hopeful response to the many frightening events that have captured the attention of professionals as well as the lay public in recent years.

Take Home Messages

- Chronic pain affects up to 40% of patients with primary neurological diseases
- A trusting patient-doctor relationship is paramount in the comprehensive assessment of pain, with compassion at the forefront
- Accurate pain assessment in dementing illnesses is particularly challenging and requires less reliance on self-report and more on behavioral indicators of pain
- Pain assessment requires a detailed goals of care discussion seeking first to understand what the pain means to the patient and the psychological impact of the pain, followed by what his/her expectations are
- Identification of the underlying pain mechanisms provides a more targeted treatment (i.e. nociceptive vs neuropathic)
- A multidisciplinary approach is recommended to investigate all possible options for optimal management, both non-pharmacological and pharmacological
- Opioids are the mainstay of treatment of severe pain and in general, the right dosage is the amount of medication that provides maximal pain relief with minimal or easily manageable side-effects
- Troublesome side-effects of opioids must be addressed and may require use of adjuvant drugs or opioid rotation
- Safe prescribing of opioids requires assessment of abuse potential and regularly querying the state's prescription drug monitoring program

Suggestions for Research and Education

Neurology training programs must incorporate a palliative approach to pain management into the curriculum to mitigate the potential for under-treatment of pain while not contributing to the current opioid abuse epidemic in the U.S. Disease-specific pain assessment tools are needed particularly in dementia populations where communication is impaired or unreliable. Pain management at end of life in neurologic diseases is a particular area with a paucity of guidance requiring further study.

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Spiritual Care

18

S. Judith Long

Case

When researcher and professor A.L. was first diagnosed with Progressive Supranuclear Palsy (PSP), she was concerned but still confident that she could continue her research and her teaching. Her professional success had always depended upon her insistence on doing her best, and she expected that her determination would serve her now. As she learned more, first from her neurologist and then from her own online search, she felt both fear and shock. How could this be happening to her, and why? Her children needed her and looked up to her as their role model. Her elderly parents and many members of her extended family in El Salvador depended on her emotional and financial support. What would become of them? And who would take care of her?

Spirituality is the aspect of humanity that refers to the way individuals seek and express meaning and purpose and the way they experience their connectedness to the moment, to self, to others, to nature, and to the significant or sacred. [1]

Spirituality is also the way individuals seek and express their capacity to choose how they relate to their experience, even in the face of circumstances outside of their control. Spiritual care supports those who struggle with feelings of meaninglessness, isolation, and helplessness, whether they identify as religious or not. All people, in this context, have a spiritual or existential dimension, and serious illness *inevitably* challenges spiritual well-being. whether or not one is part of a formal faith tradition, our spiritual nature yearns for peace in the face of serious illness.

The chaplain, who is the team's spiritual care specialist and helps patients, families and staff discover and use their own spiritual resources in the service of their healing [2]. When living with serious illness, many people turn to their religious or spiritual tradition [3]. Some look to other personal resources.

It is important to recognize that many patients want their health care providers to be aware of their spiritual needs [4]. The wish to be understood as a whole person extends to the full constellation of patients' lives, including family and friends, culture, ethnicity, and religion. These multiple aspects influence how

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the patient and family cope, communicate, and view treatment decisions. *Even within a busy clinical practice, it is possible for clinicians to express interest in the spiritual well-being of their patients without lengthy spiritual discussions. One does not need to be a chaplain or a saint to offer spiritual comfort.* Table 18.1 offers examples of phrases that might be used in particular situations. A chaplain can then continue the conversation as needed to support the patient and help the team understand these aspects of the patient's life. The chaplain's role includes "completing spiritual assessments, functioning as the 'cultural broker', and leading cultural and spiritual sensitivity assessments for staff and physicians" [5]

Table 18.1 Suggested words for providing spiritual support ('What can I say?')

Spiritual challenge	Support strategy	Sample words
Meaninglessness: *how could this be happening to me?*	Joining	*This is unfair. Sometimes things happen that don't make sense. You didn't do anything to make this happen. It's not your fault.*
	Neutralizing guilt/ blame	
Isolation: *I'm fine*, or *I don't want people to know.*	Shining light on community and providing community	*Tell me about who you connect with. Tell me about your closest confidantes.*
Hopelessness: *There's nothing I can do. It's hopeless.*	Shifting to realistic hopes	*I wonder what you hope for today.*
		I wonder what is possible for you now.
Shock 2: immediate reaction to diagnosis or other bad news	Silent presence	*No words…*
		Have water and Kleenex in the room, but let them be.
		Arrange for your devices and computer to be temporarily muted.
		Be willing to stay in the room with them, sitting quietly.
		If you like, you can silently wish for them to find peace, even if it's not possible yet. "May you know peace".
Shock 2: a few minutes after diagnosis or other bad news	Asking permission to re-engage in conversation	*Would it be okay to talk about what's happening now?*
		I wonder what's given you strength in the past when things were tough?
Agitation	Somatic grounding *(See also* Table 18.3 *for details)*	*I wonder if it would be okay to show you some simple practices you can also do at home to help you calm your nervous system and your emotions?*
Difficult emotions	Naming emotions *(See also* Table 18.4 *for details)*	*Some people say that a serious illness feels like an emotional rollercoaster. I wonder what it's like for you?*
		Some people can notice when they feel a strong emotion
		I wonder if you could notice when you feel a strong emotion and silently name it, in a neutral or kind voice (e.g., "Oh, this is anger".) [6, 7]
Grief and loss	Naming losses of expectations	*Some people say there are many losses with serious illness. I wonder what losses you are noticing.*
	Naming the grief associated with the losses	*It's natural to grieve when we lose things we care about. I wonder how that is now for you.*
Loss of social identity	Naming losses of social roles	*Some say they notice the loss of many of their usual roles.*
		I wonder how that's been for you
Loss of personhood	Naming loss of relationship or consciousness and related confusion	*Some say a change in consciousness (or communication, or personality) profoundly changes their relationship with their loved one. I wonder how that's been for you.*
Uncertainty	Naming fear of uncertainty	*When you look to the future, what's your biggest concern?*
Hope for a miracle	Acknowledging faith and shifting to other hopes	*I understand your faith is important to you. While you continue to pray for a miracle, I wonder what else you hope for* (Table 18.5)

Table 18.1 (continued)

Spiritual challenge	Support strategy	Sample words
Cultural diversity	Cultural humility and respect	*'What do I need to know about you as a person to take the best care of you that I can?'* [8]
Patients in the caregiving relationship: *I feel like a burden*	Appreciate and love caregivers rather than shutting them out 'for their own good'	*I wonder how it would be for you to let your family know how much you appreciate and love them*
Family caregivers: when caregiving feels a burden	Reconnect with reasons for being a caregiver	*Studies have shown that caregiving can be a positive experience, even though difficult, if we recall a positive reason we chose to offer this care.* *I wonder why it is important for you to be X's caregiver.*

Table 18.2 Triggers for referral to a chaplain

Patient identifies as religious and would like to see a chaplain
Patient indicates cultural needs or care team suspects cultural issues may be interfering with effective communication
Patient or family experience spiritual or existential struggle such as meaninglessness, fear of death, social isolation, loss of identity or hopelessness
Patient of family are struggling with difficult emotions such as grief, anger, guilt
To conduct a memorial/provide contemplative space and time/lead a ritual
Provide support for clinicians

Table 18.2 outlines triggers that may suggest a need for the services of a chaplain.

Challenges to Spiritual Well-Being

Spiritual or Existential Struggle

As patients and families look for balance in the midst of serious illness that rocks their world, they often find themselves in the midst of spiritual or existential struggle around meaninglessness, isolation, and helplessness. When feelings of meaninglessness predominate, you may witness attempts to make sense of what's happening. Some people may ask questions, such as: *"How can this be happening to me?" or "Why has God let this happen?" or "It must be my fault!" or "What did I do to deserve this? It isn't fair", or simply, "What did I do wrong?"*

Acknowledging the unfairness of this illness is a supportive response to such a question, as is a simple statement acknowledging that others may do the same kinds of things without getting a serious illness [9].

Another challenge to spiritual well-being is the sense of isolation that can arise in the face of seemingly impossible difficulties. Some may have the habit of turning inward while others may have the habit of 'powering through'. Yet humans are wired to connect when things are difficult [10]. Clinicians might ask their patients to tell them about their confidantes or who they connect with in their lives. You can help them understand that it is possible to do both, to 'power through' when it is needed and also to reach out and connect with others.

When feelings of helplessness predominate, you may encounter difficult behaviors associated with strong emotions such as fear or anger. It can be challenging for clinicians to empathize with an angry patient or family. Remember that this is usually not personal, no matter how it seems, and that you can ground yourself even in the middle of the encounter (Table 18.3, Somatic Grounding). As long as the behavior is reasonably acceptable, an empathic response may provide a much needed link to safety in the midst of the seeming chaos [11, 12]. Such a response might include validating or normalizing strong emotions at a time when the ground feels like it's being pulled out from under them (see Chap. 11, "Communicating Effectively").

Table 18.3 Somatic grounding exercises

Grounding
A. Bring your attention to the soles of your feet (sitting or standing)
Notice the physical sensation of the support of the floor beneath your feet
Sustain your attention on the sensation of the support of the floor beneath your feet (3 seconds)
B. Gently shift your attention to the sensation of the chair supporting your body.
Sustain your attention on the sensation of the support of the chair beneath your body (3 seconds)
Paced breath
Inhale slowly and deeply, expanding your torso, on a silent count of 4
Exhale slowly and fully, on a silent count of 8
Repeat this paced breath for 60 seconds
Note: Shorten the count if that's better for you or patient (e.g., 3::6 or 2::4)
Focused attention with grounding in one breath [13]
"*Inhale and gather your attention"*
(Inhale and notice the sensation of air entering your nostrils)
"*Exhale, and drop (your attention) into your body."*
(Direct your attention to a physical sensation in your body that has a sense of stability for you: your hands, or the support of the floor beneath your feet, or the support of the chair beneath your body)

Handling the Diagnosis and Other Bad News

Although clinicians may feel that the diagnosis or news they are giving is relatively good news compared to other possible clinical scenarios, patients and their families usually feel otherwise and are often reeling from the news. It is important to stay present following the delivery of bad news. A silent, caring presence (for example staying in the room without looking away at your computer or cell phone) allows patients and their families to begin to absorb what they have just learned while the clinician is still there in the background as a safety net. Strong emotions can temporarily block cognitive understanding and dialogue for the patient [14]. Their reactions may also default to how they and their families have reacted to threats in the past. Again the clinician's willingness to offer a caring, non-judgmental presence may be what matters most.

After allowing a few minutes for the news to sink in, the clinician might wish to ask for permission to continue, for example, "Would it be all right to talk about what's happening now?" You might then start with an expression of your own natural empathy, acknowledging that it's a lot to take in, or that you can't imagine how they must be feeling now. You could also ask them what's given them strength in difficult situations in the past. Later, you can reassure them regarding when you'll see them again and who to call when they have questions.

If they seem especially distressed, you might also ask them if it would be all right to show them some simple practices they can do later, on their own, to help calm their emotions and their nervous systems. Somatic grounding may be an effective way to help them regulate their emotions (Table 18.3). The team's chaplain (or you) can guide them in some of these brief practices. Whether leading or participating, know that you also steady yourself, creating a sense of safety that your patients can trust.

Difficult Emotions

Difficult emotions and frequent extreme mood swings are common in serious illness for both patients and families [9]. It is important to validate such emotions and mood swings as a common reaction to serious illness rather than to pathologize them as psychiatric illness. Patients and family caregivers are often relieved to learn that it's possible to recognize difficult emotions and learn to meet them skillfully. Clinicians may find it helpful to understand that while people experience a strong emotion, their perception is temporarily gated so they only perceive what is congruent with that emotion. Strong emotions might reflect a spiritual crisis, the day-to-day difficulties of these illnesses, or concerns about what the future may hold. The chaplain or other counselors can help patients and families work with these emotions and, depending on their nature and severity, may suggest various forms of psychotherapy or recommend courses that teach emotion regulation and coping strategies.

Most human beings have alternative emotional systems to choose from, such as the drive (challenge) system that helps people focus and achieve goals or the soothing-affiliation system that helps them create safety and extend empathy. However these alternative ways of responding are developed differently in different people, and some may respond to every challenge as though it threatens their survival, so they are more likely to cope by fight, flight, or self-criticism [14, 15]. The more patients can notice and recognize their emotions, the more likely they can choose ways to respond that cause them less suffering. Clinicians can help patients recognize these emotions.

Thoughts alone can also give rise to storms of emotions, even when the thoughts aren't accurate. Although thoughts are not realities, they do create realities, and they have an emotional charge, both for ourselves and for others. It is helpful to realize that a thought, which is an internal event, can be just as triggering as an external event. By noticing our thought patterns, we can consider whether the thoughts are actually true or helpful. If not, we can choose to tell ourselves a different story.

Grief and Loss

Many people think of 'grief' as the feeling of loss that accompanies the death or impending death (anticipatory loss) of a loved one, yet there are *many kinds of loss* that contribute to grief. In neurologic illness, losses may occur quickly or over the course of months. Many kinds of losses erode resilience, such as loss of the ability to communicate, loss of the ability to take care of personal hygiene, or a change or loss in identity.

It may not occur to patients that these kinds of losses are actually *grief*, so it can be helpful to introduce the word 'grief' into the conversation. Grief is the common physical, emotional, cognitive, and spiritual response to an actual or threatened loss of someone or something to which we are emotionally attached. You might ask your patients and their families what losses they are noticing now. Naming these losses can help people start to regain control. Simply speaking of the losses aloud can be empowering [16]. You can acknowledge and normalize their grief as one of their predominant experiences at this time. You can also help them understand that there is no right way to grieve and that no single process fits all. Even social withdrawal can be a form of grief. There's no need to insert something positive into the conversation. People need to grieve.

> *As the weeks passed, A.L. reported continuous waves of anger and sadness at this illness that "robbed her" of her expectations of a normal life, of seeing her children grow up and have families of her own, of caring for her parents, of continuing her research. She found it helpful to realize she felt a deep need to grieve these losses.*

In neurologic illness, successive losses may build up over time as the illness worsens. Family members also feel the loss of their former lives and former relationships. Often everyday rituals, such as family mealtimes, are interrupted and superseded by the impact of the illness on the patient's and the family's lives, causing family members to feel like their lives are no longer normal, and contributing to a sense of isolation. Yet connecting and sharing experiences has been shown to be one of the most effective ways to find support and begin to stabilize and normalize grief [16]. Your recognition and normalization of grief helps build trust and safety for your patients and their families. Sometimes the health care team may be the only support for them, and the team's capacity to empathize/grieve with them can be highly validating.

Because many people feel uncertain about how to respond to the news of someone's illness or feel afraid to get too close, friends may fall away from the patient's life. Patients often express disappointment in their friends and may react by holding themselves apart. You can help them understand how common these responses are, and that they can feel safe to build bridges back into relationship with others. Over time you might help the patient explore

what other sorts of things still have some degree of normalcy for them, or even what is going well, what is healthy. That may need to happen later though, after the illness becomes more managed, or as natural coping mechanisms emerge.

Differentiating ***depression from grief*** is also important for those who treat people with serious neurologic illness. You can help your patient and their family understand that there is a difference between the acute grief or anxiety that are a common part of the adjustment to a serious illness and actual clinical depression.

Anger and Fear

Anger is a defensive emotion that attempts to keep us safe by removing obstacles, while fear is a protective emotion that attempts to keep us safe by removing ourselves from danger. Anxiety is the flavor of fear that anticipates what might happen in the future. Since both anger and fear are uncomfortable emotions, many people avoid them or express them blindly. Although these emotions are different from one another, each is a survival strategy that comes from the wish to be safe, so it is helpful to notice them.

Guilt and Shame

Guilt and shame are different flavors of feeling bad about oneself. Guilt comes from the thought "I have done something wrong" or "I made a mistake", which focuses on our behavior. Shame comes from the thought, "I am bad", which focuses on our self-worth, so that we feel that we are inherently bad or unworthy [6, 7]. With the onset of serious illness, these emotions may occur in unaccustomed ways, for example shame may occur with visible symptoms, such as a tremor, freezing gait, impairment of speech, or wheelchair dependence and lead to social anxiety. In some illnesses, the shame and anxiety can even worsen the physical symptoms, leading to a cycle of increasing shame and isolation. The clinician can help the patient notice and understand how this can happen and consider using grounding, for example, as a way to interrupt this cycle (Table 18.3).

Meeting Difficult Emotions

Mindfulness and compassion allow people to notice whatever emotions arise with kindness, so they can find a middle path. When we bring a kind attitude to these emotions, we are more likely to feel safe enough to try again. Having emotions is not optional, but we do have the option to notice them. Emotions are designed to be experienced briefly. Noticing them with kindness allows us to manage and regulate our emotional patterns by becoming aware of their distortions and adjusting for them. Mindfulness creates cognitive space and perspective around difficult emotions, which also helps patients and caregivers to soften self-conscious or judgmental thoughts about themselves [17]. Although we may be accustomed to believing we can't affect our difficult emotions, the powerful takeaway message is that we can learn skillful means to meet them; Table 18.4 offers suggestions.

Treatments for grief and other difficult emotions span a wide range of therapies and treatments, such as supportive therapy, client-centered therapy, meaning-oriented therapy, narrative or bibliotherapy, cognitive behavioral therapy (CBT), and interpersonal therapy (IPT) [18]. Other modalities might include life review, storytelling, and creative expression such as poetry, art, or music. Many grief therapists like to start where the client is, focusing on a strengths-based approach and a person-in-the-environment context. They may explore what the client feels is the presenting problem and what his/her intrinsic/natural coping strategies are. Humor and laughter are also a normal and natural response to loss, so

Table 18.4 The RAIN acronym to notice and acknowledge emotions

***R**ecognize – Silently recognize these emotions in a kind voice. "Oh, this is anger"*
***A**ccept – Accept it as it is. "I have a system that does this"*
***I**nvestigate – What's the wisdom in this? "What's triggering me? What can I learn from it?"*
***N**urture – Nurture myself with kindness (not harshness) and choose a wise response. "I can see what's happening, and I appreciate that I'm doing the best I can"* [14]

you might recognize and normalize them too when they occur [19]. Be aware as well of your own personal tolerance for distress, tears, and strong emotions, so you can adjust as needed, rather than allowing it to bias your interaction.

Changes and Threats to Social Roles, Identity and Personhood

The word 'identity', in this discussion, refers to the quality of being a social individual with unique social roles, whereas the word 'personhood' refers to being a conscious or cognitive individual. The loss of social roles or consciousness or both is not uncommon for patients with serious neurologic illness. Although loss of roles may not sound as dramatic as loss of cognition, when we pause to consider how social roles define us, loss of our accustomed roles profoundly impacts our basic identity, for example:

- *Family roles, such as parent, sibling, spouse, child*
- *Professional roles, such as teacher, carpenter, researcher*
- *Social roles, such as best friend, or parent club leader*
- *Physical activity roles, such as walker, swimmer, or bicyclist.*

> *A.L. was profoundly distressed by her loss of identity, both her professional identity as researcher and preceptor and her family identity as mother, confidante, caregiver, friend. She also expressed grief, anger, and humiliation at the decline of her cognition, the loss of her visual, manual, and verbal dexterity, and the loss of her balance.*

Patients wonder who they are when they are no longer able to participate or contribute in the ways that make them who they feel they are. This may be even more confusing, for both the patient and family, when the patient still looks much the same, especially early in the disease process, yet the patient may feel profoundly changed and afraid of what lies ahead. You might invite your patients and their families to brainstorm creative adaptations or encourage them to develop new social roles or activities around what is meaningful and brings them joy. In a more acute setting, such as after severe acute brain injury, families are often faced with a drastic change in their loved one's abilities and identity. In extreme cases, they may need to consider life-and-death treatment decisions for a loved one who 'will never be the same'. It is important to help families understand that human beings can adapt and to encourage them to identify those aspects of life that could still be meaningful.

In contrast, loss of personhood, refers to alteration of the patient's cognition that often changes the patient's personality or presence beyond recognition, including loss of self-awareness, communication and cognitive impairments, behavioral and personality changes, and changes in level of arousal, including coma. The extreme changes that occur with loss of personhood affect both patient and family.

The patient may be unaware or only peripherally aware of these changes. It is important in these cases for both family members and clinicians not to assume the patient cannot hear or understand, we can't know that's true with certainty. For example, the patient may be conscious, but unable to communicate readily, as with expressive aphasia. In such situations, it may be helpful to name what is happening and to take the time to allow the patient to express him or herself in adaptive ways. Because patients and their families are usually not familiar with these kinds of losses, they can seem particularly distressing and frightening. Your grounded presence and your normalization of what they are experiencing can be deeply reassuring for them.

Uncertainty

Uncertainty is another type of loss that occurs throughout neurologic illness. Some uncertainty

is long-term, such as the prognosis for patients with severe acute brain injury (SABI). Some uncertainty is short-term, as in the day-to-day and even minute-to-minute fluctuations of symptoms in Parkinson's Disease or the behavioral changes of frontotemporal dementia. Uncertainty can be fraught with questions for patient and family caregiver alike:

> *"Will I live long enough to see my children marry?" "…to see my first grandchild?" "…to care for my dog?" "Will I become demented, and when?" "Will I know that I'm changing?" "Can I do anything to prevent it?"*

Patients and their families are profoundly affected by the changes inherent in these illnesses. Some have confided that they feel that they are "always waiting for the other shoe to drop". This uncertainty contributes to a state of hypervigilance which, when chronic, is depleting and can intensify feelings of anxiety and helplessness. Uncertainty is likely a predominant part of your patient's and their family's experience. Your willingness to explore and name what's happening with kindness can help counter the sense of isolation in these illnesses.

Hope and Hope for a Miracle

Families who experience severe acute brain injury (SABI) describe the importance of maintaining hope in the face of prognostic uncertainty [20]. This is true as well for almost all neurologic illnesses, including Parkinson's Disease, dementia, and other chronic illnesses. Although the hope for a cure is pervasive, providers can help patients and their families explore what else they can hope for, encouraging them to re-frame their hope to a more realistic goal, such as the best possible quality of life for their loved one today or for a personal goal. This new kind of hope engages the patient and family in continually re-defining hope as conditions change [12, 20].

While language about hope for a miracle can be difficult for some clinicians to respond to, a similar approach is recommended. When a patient or family asks for miracle, the clinician can explore what a miracle might look like to them and validate their position. One suggested tool to help patients, families, and clinicians continue the conversation and remain engaged with one another is the Johns Hopkins AMEN protocol (Table 18.5) [21]. Using these simple methods helps the clinician remain a partner and prevents an unequal competition between doctors and God.

Table 18.5 The AMEN acronym for responding to hope for a miracle

***A**ffirm the patient's belief: "Ms. X, I am hopeful, too"*
***M**eet the patient or family member where they are: "I join you in hoping (or praying) for a miracle"*
***E**xplore what miracles mean to the patient and family and **E**ducate from your role as a medical provider: "What would a miracle look like to you?" and "I want to speak to you about some medical issues"*
***N**o matter what: "No matter what happens, I will be with you every step of the way"* [21]

Cultural Sensitivity

In today's world, cultural diversity is more the norm than the exception. Diversity has many aspects, such as cultural ethnicity, sexual orientation, socioeconomic background, education, disability, and mental health. When speaking of cultural ethnicity, identity may include: "country of origin, language, education, spiritual traditions, family traditions, diet and nutrition, traditional medical practices, attitudes about illness and death, and migration [or immigration] experiences" [22]. As health care providers, we can gather information that may be useful in the plan of care and maintain awareness of our own reactions to cultural differences.

Even with the best of intentions, clinicians may not recognize what is essential for a particular patient. For example, a team of well-intentioned pediatric health care providers initially assumed that a Latino family was Catholic, when the family actually belonged to a Charismatic faith group that relied heavily on their faith tradition's rituals, herbs, magic, and miracles, which impacted the parents' treatment decisions for their child.

In this situation, strong adversarial feelings became a distraction from the primacy of cultural

respect and cultural humility, the very qualities that were most needed to assure the best care possible. Recognizing the importance of cultural respect and cultural humility from the start can help establish a mindset of seeking to understand and appreciate cultural differences of every kind.

The Patient Dignity Question from Dignity Therapy, though developed for end of life care, offers language to begin the conversation in a respectful way for both clinician and patient: "What should I know about you as a person that will help me take the best care of you that I can?" [8] Caring and respectful interest in the patient's culture lets us help patients and families make meaning, connect, and feel they have some capacity to make choices within an unfamiliar dominant culture that they can trust and where they can feel safe.

Special Issues for Family Caregivers

Caregiving can be both deeply stressful, and also helpful and enriching. It is important for family caregivers to recognize that they can experience benefits from their caregiving behaviors, [23] which can help make their caregiving sustainable. From the perspective of spiritual well-being, protective factors in caregiving are associated with the caregivers' capacity to offer care for an altruistic purpose that is meaningful and aligned with the caregiver's highest values in caring, thereby protecting the caregiver both psychologically and physiologically [24]. This mindset can be intentionally cultivated for the good of both caregiver and patient [25].

Patients may also feel less of a burden to their families and find it easier to welcome and appreciate their family caregivers when they understand that caregiving can benefit their family members, protecting the health and well-being of their loved ones. They can then support their family caregivers by inviting them into their world with kindness and love rather than rejecting them and pushing them away out of fear of becoming a burden.

Both patients and family members often say that their loved ones are what matters most to them, so when the patient and the caregiver agree to this mutual kind of caring, they each fulfill their deeply held wish to support the well-being of the other. You can help your patient and their family understand that it's possible and preferable to do both: to accept and to offer care from their most meaningful sense of love and caring, even when it's difficult. This in turn helps balance the difficult aspects of caregiving with its nurturing and loving side (see Chap. 20, "Caregiver Assessment and Support").

Building Resilience for Patients and Families

Even in the face of serious neurologic illness, patients and their families can still strengthen their resilience. It is important to understand that patients are caregivers, too. They care for themselves in the midst of serious illness, and they care for their loved ones and feel concern for their well-being. Well-intentioned family members and clinicians often insist that patients not concern themselves with the care of others. Yet patients may benefit greatly from being encouraged to contribute in whatever ways are still possible for them.

Family members and close friends may also have a far wider circle of care than they realize. In addition to caring for the patient, they often care for other family members and close friends and for themselves. Building resilience includes discovering and using personal resources as well as strengthening purpose, connection, and choice.

Discovering Personal Resources

People have many kinds personal resources that sustain them, such as strong religious or spiritual ties, a love of nature, participation in a choral group, a weekly card game with friends, or volunteering to help those in need. Although some of these familiar activities may need to give way to a particular illness, you might ask your patients and their families what is still possible in their lives or what else brings

them joy and peace. You can also encourage them to reflect on this question in the days ahead and continue to discuss it with one another to learn what works for them at any given time.

Some clinics maintain a list of resources that they share with patients and their families (e.g., www.neuropalliative.org). Sharing a list of resources can stimulate thought and offer ideas for patients and families to explore. Simply looking through such a list can help create a more positive mindset, which is an important intervention in itself at a time when the patient's world is shrinking.

Qualities of Resilience

Purpose/Intention Beyond Self

Studies show that recalling intention for the greater good strengthens resilience [24]. Your patients and their families can develop this practice by setting a positive intention at the beginning of each new day (e.g., kindness, patience, courage, love, presence), bringing their intention to activities throughout the day as opportunity arises, and reflecting on their intention at the end of the day [26].

Connection

Although most people appreciate the importance of meaningful relationships, in times of stress, they may push others away. Yet humans have, for millennia, affiliated and collaborated with others to to solve problems, to seek safety, and to care and be cared for [10, 27]. You might ask your patients to recall a time when they connected closely with others, either to receive or to offer care. By asking in this way, you can help them recognize how common this can be and possibly suggest alternatives, such as support groups. Your willingness simply to broach the subject of relationships can serve as a temporary relationship in itself and opens the door to further discussion or to possible referrals later.

Choice

Choice (other terms include self-efficacy, sense of agency, or sense of control) is the feeling that people can affect their own destinies, even in the face of circumstances they can't change [28]. Choice was characterized by Viktor Frankl, author of Man's Search for Meaning: *Everything can be taken from a man but one thing: the last of the human freedoms—to choose one's attitude in any given set of circumstances, to choose one's own way.*

One simple yet powerful way to introduce the concept of choice is somatic grounding (Table 18.3). Patients who struggle to keep themselves from panicking have found this practice to be one they can choose to stabilize themselves and regulate their own emotions. It also serves as an introduction to mindfulness that teaches people they can direct and sustain their attention where they choose. Once they learn to direct and focus their attention, they can continue to develop mindfulness to bring perspective to their experience and regulate strong emotions [14].

As you recognize the kinds of challenges that most affect your patients, you can better understand how to support their spiritual needs or when it might be helpful to refer them to a chaplain (Table 18.2). Either way, know that your willingness to be present with their distress and to share how common it is in these circumstances is an intervention in itself.

Another simple, yet powerful, practice that patients and families can choose is to maintain a gratitude journal. Studies have demonstrated the benefit of cultivating positive thoughts and, specifically, developing a gratitude practice [29]. Writing down three or more specific things one is grateful for in a gratitude journal may be an appealing way for many patients to develop this practice.

Selected Mindfulness-Based and Compassion-Based Interventions

In recent years, evidence-based interventions and courses have been developed to help people find balance and emotion regulation in the presence of serious illness, such as:

- The Halifax GRACE training (https://www.upaya.org/social-action/grace/)
- Mindfulness-Based Emotional Balance (http://www.margaretcullen.com/)

- Compassion Cultivation Training (https://www.compassioninstitute.com/)
- Mindful Self-Compassion (https://centerformsc.org/)
- Mindfulness-Based Stress Reduction (https://www.umassmed.edu/cfm/).

Finding balance protects people from the extremes of overwhelm on the one hand, or disconnection on the other. Balance also allows people to connect in the midst of suffering and have confidence that they are safe.

Education and Research Agenda

Education for clinicians should include discussion of spiritual care, distress and resilience as an essential element of primary palliative care. Specialist training in palliative care may include more in depth explorations of these topics and chaplaincy training programs should consider more attention to the unique challenges facing persons affected by neurologic disease.

Research is needed to better understand the specific spiritual and existential challenges patients and families face, to validate appropriate outcome measures, and to test the effectiveness of interventions to address these issues. Similar efforts should also be made to better understand factors associated with robust spiritual well-being and interventions to build resilience.

Take Home Messages

- Spirituality refers to the way individuals seek and express meaning and purpose and the way they experience their connectedness to the world as well as how they exercise their capacity to choose how they relate to their experience.
- Spiritual care supports those who struggle with existential challenges and difficult emotions whether they identify as religious or not.
- Challenges to spiritual well-being include challenges to meaning, connection, and choice. Strengthening these qualities builds resilience.
- Spiritual care helps people discover and use their own spiritual resources in the service of their healing.
- Patients and families prefer that their health care providers understand their spiritual needs, so you can express caring interest, and then triage the patient and family to the chaplain for more in depth conversations.
- Chaplains are the spiritual care specialists on the team who can support patients and families, interpret their spiritual needs to the team, and support the team's spiritual resilience.

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Clinician Self-Care

19

S. Judith Long

Case

One of four neurologists in a busy community practice, AB was successful among her peers and popular among her patients. But at 46 years old, she could no longer find joy in her profession and dreaded going to work. Every night, she spent extra time finishing up her notes and responding to electronic patient messages that she hadn't gotten to during the day. When she viewed her next day's patient list, she noticed that her previously felt excitement for an interesting case or her empathy for a patient with a tragic disease, was being replaced by a feeling of resentment for the increased time these patients were going to require.

Self-care is not a luxury. It is an essential core competency that protects clinicians from the adverse effects of burnout. In this chapter, I define burnout and offer direct practices that can help clinicians build and strengthen their resilience. This chapter focuses on individual clinician self-care and less on the changes that are necessary on a systems level to prevent and manage clinician burnout. Although the effects of burnout are harmful, it is important to realize that the feelings of burnout are meant to keep us safe by convincing us to limit 'toxic' input and conserve energy. If we can recognize the signs of burnout early, we can choose skillful practices that sustain us in our professional and personal lives.

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Burnout

Definitions

Burnout is defined as a chronic occupational (workplace) hazard that is characterized by:

- *Emotional exhaustion* – tired of feeling frustrated, stressed, scared, angry, unappreciated, or sad. Clinicians who are emotionally exhausted typically note a loss of interest and enthusiasm for their patients and their daily practice.
- *Depersonalization* – feeling isolated, alone, and without meaningful connection. Depersonalization leads to cynicism and a loss of empathy for one's patients.
- *Career dissatisfaction* – feeling a diminished sense of personal accomplishment, self-value or control, and feeling that there is no choice [1, 2].

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Engagement is the opposite side of the coin and is characterized by commitment, connection, and satisfaction with work [3].

In the literature, burnout is commonly measured by the validated Maslach Burnout Inventory scale, a 22-item questionnaire, which measures the three dimensions of emotional exhaustion, depersonalization, and personal accomplishment [1].

Burnout Symptoms

Burnout and engagement exist along a continuum, and it is possible to feel more or less burned out or engaged at any point in time. Burnout may show up as chronic exhaustion, chronic irritability, reduced interest in life and in one's career, feelings of cynicism, detachment, ineffectiveness, or resignation [3].

Burnout, like all emotions, can be contagious. Our natural empathy predisposes us to be affected by the emotions of others, so we are affected by the feelings of burnout of others, and they are affected by ours. Burnout is sometimes confused with simple exhaustion, with empathic distress, or with depression. While it may overlap these conditions, it is not synonymous with them. Rather it is a common response to difficult work conditions that need to be addressed on a personal level and, when possible, on an institutional level [3].

Burnout in Neurology and Palliative Care

According to a national survey in 2011, burnout is more common among physicians compared to the general US population, and higher among neurologists compared to most other physician specialties [4]. A recent survey by the American Academy of Neurology (AAN) of over 4000 American Neurologists found that 6 in 10 neurologists experience burnout [5]. In a survey by the American Academy of Hospice and Palliative Medicine (AAHPM), palliative care physicians were found to have a similar burnout rate, with a higher rate (66%) among non-physician clinicians [6].

Risk Factors

The etiology for physician burnout is likely multifactorial and includes reasons that are internal and external to the individual. The AAN survey identifies several risks factors for burnout, such as higher number of work hours, nights on call, patients seen, as well as hours of clerical work. They also note lower rates of burnout among academic neurologists compared to private practice neurologists, potentially owing to more effective staff support, professional autonomy, and older physician age. The largest driver of career satisfaction is reported to be the meaning neurologists find in their work [5, 7]. One of the main drivers of burnout in the medical profession is the mounting clerical burden. Studies have shown that "for every hour physicians spend with patients, they spend one to two more hours finishing notes, documenting phone calls, ordering tests, reviewing results, responding to patient requests, prescribing medications, and communicating with staff" [7]. Other risk factors include conflicting institutional pressures; lack of control; lack of meaning; lack of support; intense commitment; younger age, less experience; and workplace stress.

Many factors in health care settings can act as workplace stressors. Experiencing these as stressors is not pathologic, but is rather a healthy response to difficult circumstances that is intended to keep you safe. It's crucial to understand, though, that allowing them to become chronic is maladaptive and can lead to burnout. Working with patients with serious physical illness and pain can be stressful, especially when accompanied by time pressure and competence pressure in the face of an irreversible diagnosis. Clinicians also report conflicted stressors, such as:

- Work vs family
- Healer vs bureaucrat (both the larger bureaucracy and/or needing to become a bureaucrat)
- Idealized job vs actual job,
- Being asked to 'do the impossible' (for example, being forced to discharge patients too quickly so the system can save money and have more favorable statistics)
- Moral distress

Moral distress is the feeling that institutional or hierarchical constraints prevent one from doing what one feels is 'the right thing to do' [3, 4, 8]. Finally, there is also the vicious cycle of isolation and burnout, where feelings of isolation generate poor social interactions, which lead to negative professional evaluations, which contribute to further feelings of inadequacy and further burnout. We may do better to identify and analyze the components of bad situations in which good people function [3].

De-bunking a Popular Myth

Myth – That practicing medicine with an open heart puts clinicians at risk of overwhelm and burnout.

Fact – That empathy is a natural part of a healthy clinical relationship, as one's long as emotions are balanced.

By learning and practicing skills to keep their hearts open while remaining emotionally balanced, clinicians are actually more resilient and better sustained in offering care. Table 19.1, GRACE, provides an an intervention to foster these skills.

Preventing and Reducing Burnout

The first step in preventing and reducing burnout is to recognize its signs either within oneself or a colleague. Table 19.2 lists signs and symptoms to watch for.

Several suggestions have been made regarding interventions to prevent or reduce physician burnout, though little evidence of their effectiveness exists. The AAN survey reports personal engagement as an important preventive to burnout. Methods used by neurologists to mitigate their own burnout have included reducing work hours, patient numbers and retiring early. Neurologists also identified the need to change systemic factors affecting burnout, the most important of which may be increasing the number of skilled support staff to reduce clinician's clerical burden, as well as:

Table 19.1 G.R.A.C.E. [9] training overview, so that compassion and resilience can emerge

1. ***G**ather your attention* *"Inhale, and gather your attention."* *(Notice the sensation of the breath entering the nostrils.)* *"Exhale, and drop into your body."* *(Notice the sensation of the support of the chair beneath your body or the ground or floor beneath your feet.)* *Purpose →Collect your attention and ground yourself, which clears the mind*
2. ***R**ecall your intention* *"Inhale and recall your intention in doing this work to serve others."* *"Exhale and affirm it."* *Purpose →Bring your highest intention to the forefront of your awareness* *If you notice a sensation that may accompany this wish, see if you can remember the sensation, so you can return to it easily.*
3. *Attune first to yourself, and then to the other* *Do a quick mental sweep of your own body, heart (emotions), and mind (biases/opinions) [i.e., Put on your own oxygen mask first.]* *As you then engage with your patient, silently scan their body, heart (emotions), and mind (biases and views), as best you can.* *Purpose →Empathic resonance: Notice your biases, so you can adjust for them* *Notice your patient's biases, so you can take them into account*
4. ***C**onsider what will really serve* *Allow what you just learned as you entered the room to join with your expertise and experience* *Purpose →Trust your clinical expertise and experience and also welcome your clear, discerning mind and intuitive awareness*
5. ***E**ngage and then **E**nd* *Engage on the basis of your knowledge and experience and your clear awareness of what is needed in this moment* *You can mark the end of the encounter silently with an exhale of kindness for both your patient and yourself.* *Purpose →Engage wisely, notice when the encounter is ending, then end wisely with your patient (e.g., "Before I go, is there anything else you want me to know?"), and with yourself ("I did my best. What do I want to learn?", so you can set it down and move cleanly on.)*

- Reducing time with the electronic health record (EHR)
- Reducing time with insurance mandates
- Increasing face-to-face time with patients
- Increasing reimbursement [7]

Table 19.2 Burn-out (signs to watch for) [10]

Physiologic
Fatigue, headaches, insomnia, gastrointestinal disturbances, weight loss
Emotional
Boredom, cynicism, frustration, irritability, low morale, depression
Performance-related issues
Staff turnover
Impaired job performance (decreased empathy, increased absenteeism)
Deterioration in clinician-patient relationships
Less satisfaction, desire to reduce clinical time, more likely to order tests, increased interest in early retirement
Inability to leave work (working longer and longer hours)
Decreased sense of personal accomplishment

Changes in the system and in individual practices call for senior administration to recognize and measure the extent of this problem. One encouraging step forward has been the National Academy of Medicine's recent launch of its Action Collaborative on Clinician Well-Being and Resilience. The collaborative will focus on solutions at the organizational, systems, and cultural levels [11].

Individual Skills and Workplace Factors (Fig. 19.1) [12]

Building Resilience

One simple and effective way of looking at burnout and self-care at the individual level is that burnout is a depletion of physical, social/emotional, mental, and spiritual energy. To create balanced self-care, clinicians can choose to draw personal and professional boundaries around their need for restorative sleep cycles, physical activity and recreation, and evidence-based interventions for stress reduction, including meditation, yoga, gardening and walking in green environments. Building resilience includes a wide range of practices and methods that clinicians can adopt. The following section provides guidance for brainstorming personal resources, followed by a listing of some additional practices and links. It can be helpful to create your own individual resilience plan that is personally realistic and enjoyable. *By keeping this list somewhere that's easy to see, it can remind you of what you enjoy and care about most.*

Personal Resources (Tables 19.3 and 19.4)

You might begin by brainstorming a written list of your personal resources. Many clinicians already have a rich array of meaningful personal resources to choose from, such as family, friends, colleagues, religious or spiritual practices and communities, enjoyment of the natural world, participating in sports, art, or music. Yet when stress and exhaustion are at their peak, these resources may seem

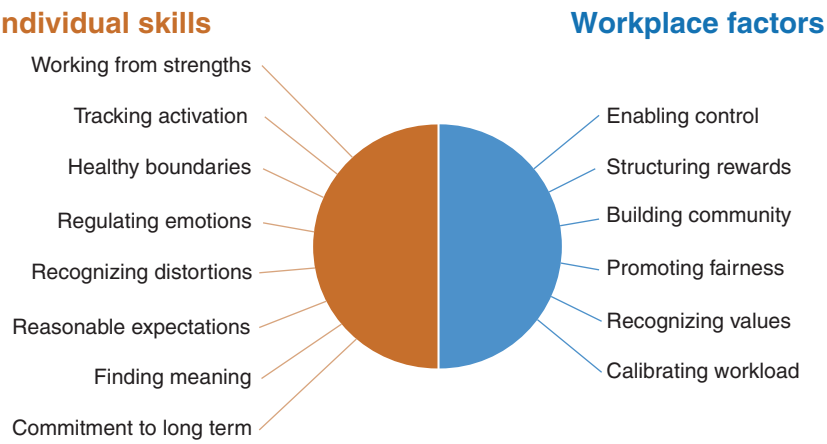

Fig. 19.1 Individual skills and workplace factors. (From Back et al. [12], with permission of Elsevier)

Table 19.3 Examples of coping strategies for burnout [10]

Institutional – Interdisciplinary team (IDT), support groups, Schwartz rounds (structured forums where all staff come together regularly to discuss the emotional and social aspects of working in healthcare), critical incident debriefings
Personal – time alone, journaling, setting limits on workload, using vacation and leave, supportive community within and/or outside of your work environment
Overall – brainstorm/share, inventory your strategies, are some new strategies needed

Table 19.4 Examples of lifestyle management techniques (adapted) [10]

Physical
Maintenance of good nutrition, adequate sleep, exercise (aerobics, yoga, tai chi)
Energy work: reiki, healing touch, therapeutic touch
Decreased overtime work
Emotional/social
Time in meaningful relationships
Effective grieving of losses, rituals
Mental/social
Discussing work-related stresses with others who share the same problems. Visiting counterparts in other institutions; looking for new solutions to problems
Lifelong learning – studying Spanish, music, art, poetry
Seeking consultation if symptoms are severe
Spiritual [9]
Spiritual life: meditation, spending time in nature, rituals

out of reach just when they're most needed. When that happens, it may help to reflect on what gives you joy, and what brings you peace. It can be something very simple, such as:

> *– a good run – a spa day – prayer or spiritual community – a walk on the beach –an evening with friends—playing with children*

It is also helpful to reflect on your highest values and intentions, your most meaningful connections, and what kinds of proactive choices are possible for you, even in the midst of your busy practice.

Recalling What Matters Most

The happiness we derive when we act on behalf of the greater good for all, it shows up as a better immune profile. What values do you really care about? What matters most? While we might feel just as happy eating ice cream, happiness derived from meaningful service to others is correlated with positive health benefits [13, 14]. It is possible to recall your intention frequently, as a normal part of your clinical practice. When you do, you remain clearly focused on why you care about your work and what really matters to you.

Connection

Although many clinicians have an understandable need for solitude after the demands of a busy work-day, our biology also expects connection [15], so we need to find a way to balance solitude and connection. Connection may be experienced as connection with ourselves, with our loved ones, with our colleagues, or even with our work. Perhaps you find solitude while running, taking a walk on the beach, and perhaps you find connection by talking with a sibling, having lunch with a friend. The idea is to avoid unintentional chronic isolation, which carries with it a cascade of deleterious effects that are unwanted and unnecessary [15]. It is crucial to notice your experience of both connection and solitude, so you can balance them in your life.

Choice

Many clinicians may wonder what 'choice' could mean in a world of life-limiting illnesses they can't reverse, or in a clinical schedule determined by others. Clearly we can't change many things we wish we could, yet we can affect our lives in ways that matter. Choice occurs when we recognize what's happening so we can choose *how* we wish to respond. For example, when a patient is feeling shock upon hearing a difficult diagnosis, we can choose to stop speaking and instead sit silently attentive and present while the patient can have the time to begin to absorb what he or she has just heard. Our skillful choices benefit others as well as ourselves [16, 17]. Self-efficacy is our ability to affect our destinies by exercising choice and is a component of core confidence that can be learned.

Selected Practices to Build Resilience

- Re-activate one of your personal resources (see above). Is there something you've allowed to lapse that would bring you joy or peace? Make a list of your personal resources you can turn to whenever you like. Choose one or two you like, and decide when, where, and how often. (Additional ideas for exploring personal resources: Finding Balance in a Medical Life, Lee Lipsenthal (https://tuwarm.com/finding-balance/)).
- Ground yourself in the midst of stressful interactions. Grounding engages your parasympathetic nervous system and provides mental training in directing your attention where you choose. The benefit is reduction of stressful distraction and a clearer mind (See Table 19.5, Directed Attention Practices).
- Every morning, set a daily intention for the good of others (a pro-social intention). During the day, see if there are times when you can bring this intention into your day. Each evening, think back on your day in broad terms, to recall if you had the chance to practice your intention. If so, celebrate it. If not, allow yourself to look forward to trying it again the next day. Practicing intention before and at the end of each day makes your intention serve as bookends for your day [18].
- Keep a gratitude log to build positive emotions. One to three evenings a week, before bed, think back over your day in broad outlines, until you recall three to five things you are grateful for. Let each memory be specific for that day. It can be something relatively simple like the memory of the sunlight through the kitchen window, the feeling of your child giving you a goodnight hug, or a call from your friend. Then jot it down in your log. It's been found that writing it down is important. It's also been found that doing this practice just one to three times per week (rather than every day) brings the greatest benefit [19].
- Notice the possibility of growth in adversity. A brief but powerful practice that can strengthen this skill is an adapted version of the Self-Compassion Break from the Mindful Self-Compassion program [20, 21].
  1. Notice when something is hard. Silently, in a kind or neutral voice, acknowledge the difficulty in a brief phrase, such as, "This is hard."
  2. Then acknowledge that it's part of the human condition, with a phrase such as, "It's part of being human for things not to be perfect all the time."
  3. Offer yourself a kind, self-mentoring message, just like you would to a dear friend. "I know this is hard, but I believe in you. I know you'll learn from this and be able to do it differently the next time.
- Meet strong emotions skillfully. Noticing and naming a strong emotion brings perspective

Table 19.5 Directed attention practices (Pause after reading each line)

Grounding
A. Bring your attention to the soles of your feet (sitting or standing)
Notice the physical sensation of the support of the floor beneath your feet
Optional: Expand this experience:
Direct your attention to the toes, press your toes towards the floor, notice the support of the floor beneath your toes
Repeat with the outsides of the feet, the insides, the heels, the entire soles
Sustain your attention on the sensation of the floor supporting your feet (3 seconds)
B. Gently shift your attention to the sensation of the chair supporting your body
Sustain your attention on the sensation of the support of the chair beneath you (3 seconds)
Paced breath
Inhale slowly and deeply, expanding your torso, on a silent count of 4
Exhale slowly and fully, on a silent count of 8
Repeat this paced breathing for 60 seconds
Note: Shorten the count if that's better for your patient (e.g., 3::6 or 2::4)
Focused attention with grounding in one breath [9]
On the inhale, gather your attention
(Inhale and notice the sensation of air entering the nostrils)
On the exhale, drop your attention into your body
(Drop your attention to a physical sensation in your body that has a sense of stability for you: your hands, or the support of the floor beneath your feet, or the support of the chair beneath your body.)

These practices focus the attention and engage the parasympathetic nervous system. Some have been used extensively in trauma therapy. Directing the attention also clears the mind of distraction, which allows clearer thinking [22]

and clears the mind (Table 19.6 *RAIN*). Notice where the emotion rests in the body, and soften, soothe, and allow the emotion. Adapted from the Mindful Self-Compassion program [20, 21]. (See Table 19.7, *Soften, Soothe, Allow*)

- Practice 'GRACE' using the the Halifax GRACE protocol [9] in the midst of stressful interactions. GRACE is an evidence-based model designed for end-of-life clinicians but useful in any stressful situation. This model enacts purpose, connection, and choice, and it strengthens the trainable elements of compassion, so that principled compassion and resilience emerge. (See Table 19.1 GRACE)

G.R.A.C.E. also helps us maintain a soft front (open heart) and a strong back (grounded equanimity), and it rests on the tenets of not knowing, bearing witness, and compassionate action [24]. Although many believe that burnout is inevitable for clinicians whose clinical work repeatedly exposes them to serious illness, clinicians can instead intentionally create renewable resilience.

- Re-engage Skillfully. The RENEW model guides clinicians in re-framing a sense of helplessness into a reading on a barometer of their engagement with patients and families, so they can balance and re-set themselves to engage more skillfully [25].
- In recent years, evidence-based interventions and courses have been developed that help people find balance and emotion regulation in the presence of suffering. Choose to participate in a training intervention, such as:
  - The Halifax GRACE training (https://www.upaya.org/social-action/grace/)
  - Mindfulness-Based Emotional Balance (http://www.margaretcullen.com/)
  - Compassion Cultivation Training (https://www.compassioninstitute.com/);
  - Mindful Self-Compassion (https://centerformsc.org/)
  - Mindfulness-Based Stress Reduction (https://www.umassmed.edu/cfm/)

Table 19.6 RAIN – a popular acronym to help us notice emotions

1. *Recognize – Silently recognize emotions in a kind voice. "Oh, this is anger"*
2. *Accept – Accept it as it is. "I have a system that does this"*
3. *Investigate – What's the wisdom in this? "What's triggering me? What can I learn from it?"*
4. *Nurture – Nurture yourself with kindness (not harshness) and choose a wise response. "I can see what's happening, and I appreciate that I'm doing the best I can"* [23]

Table 19.7 Adaptation of soften, soothe, allow [21, 22]

Notice any strong emotion, and silently name it in a neutral or kind voice: "Oh this is anger"
Briefly let your attention scan your body to see if you can notice where you might feel some tightness that you associate with this emotion (e.g., tight jaw, shoulders, or belly)
Direct your attention to this area of your body or to the area surrounding it
Silently repeat the word 'softening' while your attention is directed to that area
Now soothe yourself, appreciating that this situation really is difficult, silently repeating the word 'soothing', while you place a soothing hand on that area or offer yourself a soothing message, such as, "I'm so sorry this is happening, and I know you'll be okay."
Then let yourself silently repeat the word "allowing", to remind yourself that it's okay to allow the emotion to be as it is until it naturally dissipates

How to Build Lifelong Habits and Practices of Self-Care

You can turn to your own personal resilience plan whenever you feel it would be helpful to remind yourself of practices and habits that sustain you. As time goes by, you may find new practices to add to your plan or old ones that no longer serve you. It can be useful to re-visit your plan and adjust it once every 6 months or once every year, so it reflects what really works for you now.

Some find it helpful to divide their plan into the following four domains: physical, social/emotional, mental, and spiritual. It also helps to be specific. The following plan is just one example. Your own plan needs to work for you.

- Physical – Walk uphill: from home on 10th Avenue, Tuesday and Friday, 30 minutes, 6-6:30 am
- Social – Farmers market for breakfast with Bill and Ann and kids, Saturday, 10-11:30 am
- Mental – Practice clarinet, Wednesday, 8-8:30 pm
- Spiritual – Walk on the beach, Sunday, 4-5 pm.

What kinds of routines or connections will encourage you to follow through with your plan? Some people prefer a regular routine, like an early morning run or meditation. Some like to have a buddy who will exercise with them or check in to compare notes. It helps to choose practices that are truly aligned with your highest values, so you'll be more interested in giving them a try, even when you're not 'in the mood'.

While the practice of self-care allows you to see for yourself what works for you, it is also crucial to understand that it is not optional. Every clinician can find practices that work for him or her. Burnout is like a 'sneaker wave' that can take you by surprise. The idea is to implement your own personal resilience plan long before you need it, so make it fun and satisfying now.

It will only enrichen your life when you do.

Education and Research Agenda

Several future directions suggest themselves from this chapter:

1. Study the effectiveness of various methods to enhance, cultivate, and sustain the practice of personal resources.
2. Study the effectiveness of different clinician balanced resilience courses and follow-up practices to sustain improvements.
3. Study ways to shift workplace culture so that it values and rewards clinician well-being.

Take Away Messages

- *Self-care is a core competency.*
- *Burnout is an occupational hazard that occurs along a continuum from burnout to engagement.*
- *Awareness of the signs of burnout can trigger skillful practices to build resilience.*
- *Building resilience includes personal resources, purpose, connection, and choice.*
- *There are a wide range of skills and practices to help build these qualities.*
- *There are also many short courses now available that foster resilience* [10].

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Caregiver Assessment and Support

20

Timothy S. Sannes and Benzi M. Kluger

Case

The neurologist entered the exam room, knowing that he had bad news to deliver. The patient, a 67-year-old man, had just undergone a workup confirming a diagnosis of amyotrophic lateral sclerosis (ALS). The patient's wife was slouched over with her head in hands. "I'm sorry sir, but you have ALS." His wife burst into tears. They had been married for 48 years – they were high school sweethearts and shared their entire lives. Transitioning into new roles - he as the patient and she as the caregiver – would be one of the biggest emotional challenges of their relationship. The clinician tried to comfort the patient and his wife, telling them that he likely could still be comfortable as his disease progressed, spend time with his grandchildren and, at least for the next few months, safely ride his motorcycle, which the patient had identified as one of his greatest joys.

Over the next year, the patient progressed in terms of weakness, dysphagia, fatigue and some cognitive impairment. He was no longer able to perform household chores, manage his family's finances, or ambulate to the few social functions that he and his wife used to enjoy. While he received some financial support given his disability, his wife was forced to take on an additional part-time job as she transitioned to becoming the primary breadwinner with mounting medical bills. At this follow-up appointment, she looked despondent, "I would do anything for my husband. But it seems like all I do these days is his chores around the house." She was seen alone immediately after the visit and reported anhedonia, sleep problems, feelings of guilt, fatigue, and anxiety. The neurologist referred her to a community mental health care clinic and gave her the schedule of a local caregiver support group but she did not make it to either of these resources.

Three years following their initial meeting and 1 month after starting hospice, the patient passed away. The patient's wife agreed to attend a support group focused on bereavement offered at their hospital and later thanked the neurologist and social worker running the group about how much she benefitted from this support. "I realize I'm not completely alone in this journey. I never even thought to get help before, but am so glad I have now."

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Neurologic illnesses do not just affect patients but also their families, friends and communities. When these illnesses impair a patient's ability to care for themselves, family members and friends often assist with care. As this case illustrates, assuming the caregiving role for a loved one represents a significant role change whether the patient is a spouse, parent, child, other family member or friend. Caregivers must learn the basics of medical care, manage medications, and help with activities of daily living; all while continuing to provide emotional support for their loved one facing neurologic illness. Accordingly, these informal caregivers[1] [1] face significant emotional, psychological, financial and physical health challenges. Typically, they are left to manage these burdens on their own, as most clinicians caring for these patients are neither trained nor comfortable in assessing and managing caregiver burden, and many do not consider it their responsibility to care for persons other than the primary patient.

The neuropalliative care approach (see Chap. 1, "Neuropalliative Care – Introduction") has the potential to improve caregiver stress in two important ways. First, by providing patient-centered care including complex symptom management, discussions of goals of care, advance care planning, and spiritual support so the caregiver may be relieved of issues they feel obligated to try to manage on their own under traditional models of care. Second, and the focus of this chapter, palliative care goes beyond the traditional patient-clinician dyad to recognize and address the many ways that serious illnesses affect a patient's close relations and relationships [2, 3]. In this chapter, we will discuss the importance of informal caregivers in the care of patients with neurological diseases, the impact of caregiving responsibilities on the caregiver, the needs of caregivers for neurologic patients, clinical assessment of caregivers and interventions to improve caregiver support. Of note, much of the literature on caregivers related to neurologic disease has focused on patients with dementia [4]. While we feel this literature is relevant to other neurologic illnesses we have tried to pull in literature from other illnesses when relevant and feel that this is an area where further research is needed.

The Importance of Caregivers in Neurologic Disease

As the age of the U.S. population increases, so will the need for reliable caregivers, especially within the context of age-related conditions such as stroke and neurodegenerative illnesses [5]. Since 2009, the need for informal caregivers has risen 49%, [6] and will continue to rise as improvements in medical technology allow more people to live into older age with greater health issues. While estimates vary, the proportion of caregivers dedicated to neurologic patients is substantial and projected to rise with a particularly high burden of care for dementias [2, 7]. In younger populations, neurologic diseases such as traumatic brain injury (TBI) and spinal cord injury, multiple sclerosis (MS) and neurometabolic syndromes are among the leading causes of disability, and thus also carry high caregiver demand. For example, 30% of persons with MS require caregivers and 80% of this care is from informal caregivers [8].

The physical, social and psychological support given by informal caregivers occurs over years to decades [5] and this care is associated with improved patient morbidity, mortality and quality of life compared to patients who are alone [9, 10]. Informal caregivers also allow patients to achieve goals of care that would not otherwise be possible such as staying in their own home, spending increased time with friends and family, and participating in activities central to their sense of personhood [11]. From a financial perspective, studies estimate the contribution of informal caregivers to the United States health care system is approximately $470 billion per

[1]We will use the term "caregiver" hereafter to refer specifically to informal caregivers (that is, those that are not health care professionals and remain unpaid). The term "caregiver" may, in some sense, be denigrating to the close bond that informal carers and their loved ones' share. The term "care-partner" is a newer term favored by some advocates that may be more respectful of the carer's experience and journey (Olson [1]).

year in unreimbursed services [12] of which caregivers for Alzheimer's and other dementias contribute 17.9 billion hours of care with an estimated value of $217 billion [13]. A large review on the impact of caregiving on the workforce concluded that while caregivers are just as likely as non-caregivers to work, they are more likely to work fewer hours and withdraw from the labor market which may add hidden costs [14].

Timeline and Nature of Caregiver Involvement in Neurologic Disease

Caregiver involvement, and thus risk for caregiver strain, depends on the trajectory of a patient's illness which may be categorized as (1) *acute decline* such as ALS or glioblastoma; (2) *decline with exacerbations* such as MS; (3) *prolonged dwindling* such as neurodegenerative diseases; and (4) *severe acute brain injury* (SABI) as in stroke or TBI (see Chap. 1, "Neuropalliative Care – Introduction") [15]. For patients in all but the SABI categories, the impact on caregivers may precede the time of diagnosis as patients often experience a delay between symptom onset and diagnosis, and many illnesses are characterized by a period of nonspecific but disabling symptoms and changes in function and personality [16–18]. In dementia syndromes, for example, the disease process – and associated symptoms – may be present years before an official diagnosis is given and require shifts in the responsibilities and relationships of the caregiver and patient. The timeline of caregiver involvement tends to parallel the palliative care needs of the patients with the time of diagnosis, onset of new symptoms, loss of functional abilities and need for end of life care marking milestones where the need for caregiver support may increase either acutely or chronically. Events in the caregiver's life outside of the patient may produce additional sources of strain for the caregiver such as their own health issues, difficulties with their children, stress at work, etc. The duration of caregiving, particularly when associated with high physical or emotional strain, may also have a cumulative impact on caregivers [19]. However, it should be noted that there are individuals who seem immune to the this strain. Duration alone is not predictive of caregiver burden in many studies and is often overshadowed by other factors such as cognitive and physical disability and psychiatric symptoms [20, 21]. Caregiver strain also tends to increase toward the end-of-life [22].

Caregiver Roles

Caregivers take on several roles in patient support including serving as a proxy source of information for clinicians, gathering information and educational materials, helping with medications, assisting in navigating the healthcare system (e.g. insurance), transportation, providing emotional and spiritual support and assisting in difficult decisions [23, 24]. Depending on the age and socioeconomic situation of the patient and caregiver, the caregiver may be required to take on additional responsibilities at work or at home to meet financial and home maintenance needs. The multitude of significant life changes often come at an enormous cost to the caregiver, who find themselves having to make important changes in family life, routine/schedule, and employment status in order to fulfill their caregiving responsibilities [17].

The nature of caregiver involvement also depends on the symptoms and signs the patient is experiencing. For patients who are physically disabled, caregivers may be called upon to provide physical assistance with transfers and activities of daily living. For patients with impaired cognitive or communication abilities, this care may consist of guidance and organization of these same activities. Given the progressive nature of many neurological disease processes, caregivers can expect to progressively take on more and more instrumental tasks that may eventually include bathing the patient, helping with toileting, feeding, and other intimate self-care that the patient is no longer able to complete for themselves.

Alongside this increased need for basic daily care, the number and intensity of medical care decisions increases with disease progression

[23]. An important and especially pertinent example of this involves decisions regarding nursing home placement. Often, this process requires balancing choices that significantly limit the patient's autonomy with choices that place the caregiver at risk for physical, psychological and financial distress. Caregivers of cognitively impaired patients frequently find themselves in a position of having to relinquish their loved one's right to make crucial life decisions, including invasive medical care. This places the burden of these complex medical, and often, legal and family decisions onto the caregiver. For most patients with neurological illness, the cognitive decline is gradual, and ideally the patient and caregiver may prepare for the occurrence of incapacity. Much more dramatic is the sudden neurologic devastation seen in SABI that turns families acutely into surrogate decision-makers; representing a broader challenge of the interface between critical care and palliative approaches (see Chap. 2, "Severe Acute Brain Injury") [25]. These important decisions often have huge consequences for a patient's well-being, create distress for both the patient and the caregiver, and cause significant interpersonal discord [20]. Supporting caregivers as they navigate the trajectory of their patient's illness and the different decision points along the disease course is critical to a palliative approach.

Impact on Caregivers

With the various roles that caregivers balance, it is no surprise that their emotional, social, financial and physical well-being is often compromised [24, 26]. Neurologic illnesses present unique challenges to caregivers including high levels of needs over long periods (e.g. stroke), severe physical disability (e.g. amyotrophic lateral sclerosis), behavioral and psychiatric issues (e.g. Huntington's disease), unpredictable relapses and remissions (e.g. multiple sclerosis), and gradual loss of cognition and identity (e.g. dementia). Indeed, studies have found that caregivers of patients with SABI demonstrate higher levels of burden than caregivers of patients with advanced cancer [27]. High levels of caregiver burden are observed in care of patients with greater need for assistance, such as those with Huntington's disease, [28] but may also be seen in those caring for less severe neurological impairment, such as spouses of those with mild cognitive impairment [29]. Similar results, in which caregivers' experience decrements in mood, are also seen in small studies of caregivers of late-stage Parkinson's Disease and Progressive Supranuclear Palsy (PSP) [30]. Interestingly, studies suggest that the emotional health of a caregiver is intimately interrelated with the emotional health of the patient in both stroke survivors [31] and dementia patients [32] and that caregivers' mental health status is associated with dementia patient mortality [33].

Across all illnesses, when caregivers are under strain they are at increased risk for several adverse health outcomes. Depression is nearly six times more common in caregivers of those with dementia compared to non-caregivers [34]. Depression also worsens as a caregiver's care-recipient's cognitive symptoms worsen [35, 36]. Anxiety disorders are markedly higher in caregivers of dementia patients as compared to stroke [37]. The place of a loved one's death can also impact caregiver well-being, with the intensive care unit significantly worsening caregivers' risk for anxiety, depression, post-traumatic stress disorder or complicated grief [38, 39]. This constellation of symptoms is now recognized as postintensive care syndrome - family should be routinely screened for in both adult and pediatric contexts [40]. The caregiving role confers risks not only for psychiatric morbidity, but also for poorer health outcomes, such as increased heart disease and mortality [41]. This relationship between the caregiving role and poor health outcomes is stronger for women and with physiologic markers of strain, such as elevation of stress hormones [41]. Mechanisms of adverse health outcomes may include poor self-care, reduced utilization of healthcare by caregiver, social isolation, disrupted sleep and physiologic consequences of chronic stress including inflammation and immunological changes [42, 43].

A number of overlapping themes define the caregiving experience for this population of patients including loss, burden, and the need for additional support. The qualitative literature describes different aspects of ongoing loss including: acknowledging change, being in crisis, adapting and adjusting, accepting and moving forward [44]. Other qualitative approaches have grouped caregivers into positive, negative and ambivalent reactions to their caregiving role [32]. The multiple losses associated with caregiving, such as companionship, personal freedom and control, often result in anticipatory grief, a term which encompasses both current and ongoing losses in their lives and of their partner, as well as the loss of what they hoped and expected their future to be like (see Chap. 18, "Spiritual Care"). This anticipatory grief is particularly heightened in spouses of patients with late stage dementia, and especially when making institutional placement decisions [45]. Further, as patients approach the end of life, caregivers may experience greater anticipation of loss. However, this has the opportunity to be mitigated by a caregivers' level of preparedness for this loss [46]. In addition to anticipatory grief in these more severe stages of neurodegenerative states, caregivers of patients with newly diagnosed mild cognitive impairment show similar levels of anticipatory grief in relation to expectations of future decline [47]. These anticipatory grief reactions are independently associated with greater caregiver burden, after controlling for other known risk factors, such as economic status, depression and behavior problems in the patient [48]. Early diagnosis carries the potential risk of prolonging anticipatory grief but represents an opportunity to better prepare caregivers for what lies ahead if properly utilized [49]. For families of SABI patients, there is no time to prepare. In this context, it is particularly important to engage families through the language of hope and acknowledging the personhood of their loved one [50].

Over time, the strains of caregiving may lead to burnout, a state of emotional, physical and mental exhaustion characterized by emotional distress [51]. When burnout occurs, caregiving may no longer be viable or healthy for the caregiver or patient [52]. It is very difficult to restore compassion and emotional wellbeing once burnout has set in, making early and ongoing caregiver assessment and support critical. Risk factors for burnout in dementia caregivers include female sex, low education, cohabitating with the care recipient, greater time spent caregiving, depression, social isolation, financial stress, and lack of choice in being a caregiver [42]. Hospitalizations may also add to caregiver distress [35] and institutionalization, which while relieving caregivers of many physical tasks and safety concerns, does not eliminate emotional concerns or distress [53]. For patients following stroke, support may be focused on the acute phase of treatment, often ignoring the substantial chronic needs of patients and their families [54]. Certain diagnoses, such as glioblastoma, and specific symptoms, such as greater spasticity in stroke survivors or behavioral issues in dementia and ALS patients, can increase caregiver burden and may be better predictors of caregiver distress than disease duration or physical disability [9, 11, 55–57].

Given the high prevalence of functional impairment in neurological diseases, physical challenges may arise with transfers, bathing, toileting and dressing, and caregivers have often reported physical strain and injury as a result of attempting to move/transport their loved one [58]. Behavioral and cognitive issues also risk caregivers' physical safety, and physical, verbal and sexual abuse perpetuated by patients may be more common than previously believed [59]. Physical and emotional challenges are compounded by the impact of caregiving on social connections and finances. Social isolation is common in caregivers who often feel like they are living just to provide care [60]. Financial consequences may result from reduced employment and increased expenses [61]. Caregivers feel financially and socially vulnerable and may be afraid to reach out for help or utilize current finances or even long-term care insurance for fear of burning through these resources and being left bereft at a time when they may really need them [23].

The death of the patient is obviously an impactful event for caregivers and the acuity of their needs during this period are recognized by

12-months of psychosocial bereavement support under the Medicare hospice benefit [62]. Normal grief and bereavement may vary greatly across individuals and cultures [63]. For caregivers who were well prepared and supported, death may be accompanied not only by grieving but a sense of connection, accomplishment or relief [64]. For others, death may mark the beginning of a new and intense period of personal suffering. Prolonged grief disorder, or complicated bereavement, is marked by disabling distress around separation from their loved one and other cognitive, emotional or behavioral symptoms such as confusion, numbness, insecurity and suicidality [65, 66]. Risk factors for this disorder include premorbid depression, having a patient with dementia, and being the spouse of the patient [45, 66].

Despite the immense impact of caregiving for a loved one with a neurological disease, many individuals placed in the caregiving role find reward, positive growth, and personal and cultural meaning in the experience. For instance, in caregivers of dementia patients, personal mastery and self-efficacy appear to be protective factors against the negative health and psychological outcomes associated with caregiving [67] and caregivers' motivation and ability to find meaning protects their emotional well-being [68]. Therefore caregivers' ability to "reframe" their caregiving into a positive experience, may buffer the negative outcomes of caregiving (see Chap. 18, "Spiritual Care").

Caregiver Needs

While the range of caregiving demands associated with different diagnoses and stages of disease are highly varied, there are some basic needs shared across caregivers that of which clinicians of patients with neurological disease should be aware. These include: (1) physical, emotional, and psychological needs; (2) information and decisional support needs; and (3) instrumental support needs [69].

First and foremost, caregivers desire and appreciate attention to their person, identity and needs outside of their role as caregiver [23] including physical safety, healthcare, emotional and spiritual support, social connections and support of self-care efforts such as physical exercise. Emotional support may be particularly acute around the time of diagnosis, with significant changes in disease status, around difficult decisions and at the end-of-life [22]. Respite care and adult daycare may provide a much-needed break for caregivers but studies suggest that these interventions may not improve long-term caregiver outcomes and are associated with shorter time to nursing home admission [70].

Caregivers desire information about the patient's diagnosis, treatment and prognosis as a means of supporting their loved one, promoting feelings of competency and control, and in planning for the future [5, 23, 71]. Caregivers need assistance processing and making difficult decisions including early decisions around life-sustaining treatment after SABI, [15] dementia care, [72] and brain tumors [73]. In turn, satisfaction with such decisions is associated with reduced caregiver depression [72]. Studies in the critical care setting suggest that poor clinician-family communication results in worse psychological outcomes for both patients and caregivers [74, 75]. Families in the ICU benefit from simple gestures of personal support such as providing a place to sleep or using personal names to engage the family [50].

Caregivers' needs for information changes over time, from diagnosis (more information) to later stages where they express more interest in supportive services [76]. In the case of SABI there is a need for acute crisis support, possibly with the assistance of a social worker or chaplain, a need to recognize emotional distress and components of the post-intensive care syndrome-family, and a need to ensure follow through across transitions of care [39, 40, 77]. Some progressive neurologic conditions, such as frontotemporal dementia, may require preparing the caregiver to consider placing their loved one in a memory care facility [78]. Other decisions that limit patients' independence, such as driving, can also significantly burden caregivers [79]. Such decisions underscore the importance of addressing goals of care early on and with the involve-

ment of the patient when possible. During these discussions we recommend emphasizing safety as the clinician's highest duty (for the patient, caregiver and society) and for the clinician to assume responsibility for these decisions (to play the role of "the bad guy") so as to minimize strain and blame within the family unit.

Caregivers generally have high expectations for themselves and often feel guilty for perceived deficits in the care they provide, regardless of its actual quality [80]. Yet over half of caregivers of those with Alzheimer's disease and other dementias report no prior experience with medical tasks, and frequently lack resources to juggle these complex regimens [81, 82]. Caregivers thus have a need for both competence in caregiving, as well as self-efficacy, the belief in their ability to succeed and rise to meet future challenges [83]. Other resources that may prove helpful to caregivers include skilled medical and nonmedical home health care, patient assist devices (e.g. hoyer lift), financial support (e.g. reimbursement for caregiving activities) and transportation for themselves or the patient.

Assessing Caregiver Needs

Table 20.1 presents the recommended domains and constructs of caregiver assessment created by the Family Caregiver Alliance as well as sample questions which may be useful for clinicians in triaging caregiver issues [84]. Although this may appear intimidating and time consuming to physicians not used to formal caregiver assessment, the core aspects of caregiver assessment can be easily incorporated into the flow of both outpatient and inpatient care of patients with neurological illness and encompass questions and skills that many physicians already use outside of the context of a systematic assessment. The core aspects of this assessment include:

1. Establishing the Support Network for Patient's Care**:** This assessment can be easily added to a patient's social history and includes establishing the primary and any secondary caregivers, their relationship to the patient, their living situation, and whether there is a back-up plan should anything happen to the caregiver, especially if the primary caregiver is elderly or frail.
2. Caregiver's Perception of Patient's Health**:** Most neurologists who work with patients with cognitive or communication deficits are already used to eliciting proxy reports from patients and family on the patient's condition.
3. Assessment of Caregiver Values**:** As neurologic illnesses and treatment decisions do not just affect the patient, we recommend going beyond mere inclusion of the family in goals of care discussions to actively eliciting their values and preferences for care.
4. Assessment of Caregiver Health**:** This may be a new skill for many physicians. It can be quickly accomplished with a few choice questions directed to the caregiver such as: "Are you finding time to take care of yourself?" "Are you getting any outside help or support?" "Are you feeling overwhelmed?" and "Do you have any of your own health issues or concerns we should be aware of?" Regardless of the state of the caregiver, these questions can be addressed in just a few minutes and caregivers greatly appreciate the individual attention.
5. Assessment of Caregiver Knowledge and Skills**:** This assessment is dependent on the diagnosis and needs of the patient. For patients with significant disability living at home, home health assessments by physical or occupational therapists and/or a nurse may be needed to fully understand the needs of the patient and requisite skills and resources for the caregiver.
6. Assessment of Caregiver Resources**:** For this domain, the neurologist will generally serve to triage caregivers with a few focused questions. Resources needed beyond basic guidance may best be served by a referral to a hospital or community social worker. For physicians in private practice, creating an alliance with local support organizations (e.g. Parkinson's or Alzheimer's Association) or hospital can be invaluable in accessing a social worker.

Table 20.1 Categories of caregivers' needs and potential responses

Category	Clinical approach/question	Potential intervention/clinical response
Context of care		
Caregiver/patient relationship	What is the relationship between the caregiver and patient?	Validating potential conflict and changing roles. Social work counseling if available
	How long have they know each other and/or served in the caregiving role?	
Additional caregivers	Are other family members involved in providing care?	Suggesting respite for the caregiver most burdened. Problem-solve breaks from caregiving responsibilities
	Are formal/paid caregivers involved?	
Living arrangements	Do they share their household?	Encourage caregivers' self-care. Problem-solve respite as above
Caregiver's perception of care recipient's health		
Cognitive status	How cognitively impaired is the patient and how does this impact the level of care needed?	Preparing caregiver for additional responsibilities if patient is declining. Support around challenging decision point (e.g., driving priveleges; skilled nursing)
Caregiving needs	What level of care is required?	Training around medical tasks. Attempt to increase caregivers' self-efficacy and confidence
	Is there evidence that adequate care is being provided?	
Assessment of caregiver values		
Willingness to provide care	Is the caregiver willing to undertake the caregiver role?	Validate resistance to caregiving. Potentially explore ambivalence and barriers to providing care
	Is the caregiver recipient willing to accept care provision?	
Cultural norms	What care arrangements are culturally acceptable for this family?	Explore cultural norms and validate views of receiving/providing help with the family context
Assessment of caregiver health		
Self-rated health	How does the caregiver assess his or her own health?	Normalize that caregiving often impacts carers' health. Address self-care
Mental health	Does the caregiver feel she is under significant stress?	Refer to social work or community mental health if available
	Is there evidence of anxiety, depression, suicidal ideation?	
Impact of caregiving	Is the caregiver socially isolated? Does the caregiver feel his or health has suffered because of caregiving?	Address caregiver's self-care. Explore social outlets that caregiver may pursue outside of caregiving role
Assessment of caregiver knowledge and skills		
Caregiver confidence	How knowledgeable does the caregiver feel about the care recipient's condition?	Ask open-ended questions around tasks and troubleshoot topics where caregiver is less knowledgeable. Encourage self-efficacy
Caregiver competence	Does the caregiver have appropriate knowledge of medical tasks required to provide care?	Provide education around neurologic disease
Assessment of caregiver resources		
Social support	Do friends and family help the care recipient so that the caregiver may seek respite?	Explore opportunities for respite and pleasurable social activities outside of caregiving
Coping strategies	What does the caregiver do to relieve stress and tension?	Suggest alternative coping strategies if these are not effective. Refer to mental health/social work if available
Financial resources	Does the caregiver have access to all the financial benefits and entitlements for which the care recipient is eligible?	Put in contact with social work and verify that caregiver is pursuing benefits through insurance
Community resources and services?	Is the caregiver aware of available community resources and services?	Refer to social worker, caregiver support if available. Encourage engagement with online community if not

Adapted from [42, 86]

Other comprehensive assessment systems have been developed for specific illnesses, such as stroke, and may offer prompts to assess and support caregivers through unique aspects of the illness, such as the initial crisis of an acute stroke [71].

At times, assessing the caregiver separate from the patient may be particularly important. First, the caregiver may be a more reliable informant of a patient's status and details of care than the patient themselves. For instance, patients with neurodegenerative disease may progress to a point of anosognosia in which they cannot recognize their own limitations, increasing the need for caregiver perspectives during comprehensive evaluations. The caregiver may also feel more comfortable discussing medical decisions for their patient in the absence of their loved one, particularly if the patient's mental and cognitive capacity is in question or the patient holds delusions concerning the caregiver. Second, a caregiver may be more willing to admit their emotional concerns in a more private setting. The caregiver may shelter feelings of guilt, views of their changing relationship, or their desire (or guilt) for wanting their own support.

Several tools have emerged to more formally assess caregivers' needs and the potential burden associated with this role. Although there are a number of validated tools, the empirical reviews of this literature acknowledges the lack of consensus regarding best methods [85]. While these scales are generally used in a research setting, clinicians may find some of these surveys helpful or may even consider adding only a few items from these surveys, in their prescreening questionnaires for patients and caregivers. Table 20.2 outlines issues that should prompt consideration for more in-depth caregiver assessment and potential referral to a social worker, counselor or other healthcare professional with specialized skills in caregiver assessment, support or resources.

Table 20.2 Triggers for more intensive caregiver support or referral

Caregiver reports feeling overwhelmed or burnout
Caregiver showing signs or symptoms of anxiety or depression
Caregiver is socially isolated
Caregiver has significant health issues or is frail
Caregiver has low level of education or financial resources
There are safety concerns for patient or caregiver (e.g. physical abuse, frequent falls, wandering)
Patient has rapidly progressive disease or is nearing end-of-life phase
Patient has significant behavioral, psychiatric or cognitive issues

Providing Support to Caregivers

Caregiver support should follow the domains of assessment outlined in Table 20.1 or the three main domains of needs outlined above: (1) physical, emotional, and psychological needs; (2) information and decisional support needs; and (3) instrumental support needs [69]. Primary palliative care support for caregivers includes actively engaging caregivers in primary disease and treatment education, recommendations of the importance of caregiver self-care for both the patient and caregiver, referrals to support groups or counseling services, and suggestions to build coping skills and resiliency (see Chap. 18, "Spiritual Care") [86]. For appropriate patients, hospice may provide additional resources for the caregiver (see Chap. 16, "Hospice and End of Life Care in Neurologic Disease"). Home palliative care is another option that can provide closer patient monitoring, decrease medical travel and provide additional resources for caregivers.

For patients with significant physical limitations and risk of falls, home safety evaluations and rehabilitation therapy can provide caregivers training in specialized techniques to safely move and transport the patient. While medical services (e.g. physical therapy, visiting nurse) are consistently covered by insurance, nonmedical services (often derogatorily called "unskilled" or "non-skilled" home care) are typically covered only by long-term care insurance or Medicaid, may be difficult to access in many parts of the country and may be unaffordable for many families. As noted above, decisions that remove the patient from the home, including respite care, adult day-care and institutionalization, should be considered carefully. These interventions may be necessary due to overwhelming care needs or safety concerns and can lead to positive outcomes

if aligned with patient and family's goals of care. However, as noted above, they do not always lead to improved caregiver outcomes and should be carefully considered if pursued primarily for caregiver wellbeing [70].

The emerging research literature suggests several interventions to support caregivers emotionally. These services vary widely and include interventions such as caregiver support groups, [87] cognitive behavioral therapy approaches (targeting negative thought patterns around reaction to caregiving), [88] psychoeducation (educating caregivers around their changing needs), [89, 90] and interventions that target both the patient and caregiver as a dyad [67, 91]. Mindfulness-based approaches (cultivating a non-judgmental present moment awareness) also show promise in reducing caregiver distress, [92, 93] as do interventions aimed at increasing caregivers' self-efficacy in assisting in patients' daily activities, [94] acceptance and commitment therapy based approaches (where the focus is on committing to one's values and not working to change the current situation), [95] and complementary therapies, such as meditation [96, 97] and yoga [98]. Leveraging technology to increase the reach of supportive interventions also holds promise, such as using video chat technologies [99] and web-based supportive interventions [100]. Importantly, by improving caregiver wellbeing, these interventions may also improve patient outcomes such as delaying patients' placement into nursing homes [101].

Several significant barriers exist for caregivers receiving additional support. Many of these barriers stem from caregivers prioritizing their patients' health over their own, and may be particularly pronounced for home-based caregivers taking care of a terminally ill loved one [102]. Caregivers often need increased education regarding the utility of support services or remain unaware of their existence [103]. As highlighted in the case example at the beginning of this chapter, these barriers often influence a caregiver's ability or willingness to follow through on recommendations to receive additional support. Insurance coverage for mental health services, for example, poses a significant barrier to caregivers receiving the support they require [104]. Acknowledging these barriers and creating solutions to these issues may increase the likelihood of a caregiver seeking help and, at the very least, validate their experience. Indeed, identifying caregivers' concern may promote therapeutic alliance, [105] thereby increasing the likelihood of follow through on recommendations for additional support. Motivational interviewing, in which values are reflected and there is a mutual respect for autonomy, is another helpful approach that shows promise in facilitating discussion of palliative care treatment options [106] and may increase caregivers' likelihood of following through with treatment/care plans. This approach identifies patient and family members' goals, explores ambivalence in decisions and meets individuals where they currently are in the decision-making process [107]. Such approaches acknowledge the existing barriers to caregivers receiving support and are individually tailored to the supportive needs of patients and families.

Education and Research Agenda

Many clinicians are uncomfortable assessing or supporting caregivers and may ignore or purposefully redirect calls for assistance from caregivers as they consider them outside of their purview. As outlined in this chapter, it is essential for clinicians to recognize the multiple benefits caregivers have to patients and the healthcare system in general, as well as the risks taken on by these individuals, to motivate them to provide not just patient-centered, but also family-centered care. Training in caregiver assessment and management is an essential part of the primary neuropalliative skillset, and more specialized training may be required for individuals specializing in neuropalliative care or subspecializing in an area with unique family needs (e.g. neurointensivist).

The needs of informal caregivers are being increasingly recognized by researchers involved with many, but not all, neurologic illnesses and some are particularly well-documented (e.g. dementia). More work is needed on the optimal means to assess these needs within the context of

clinical care and this field could benefit from consensus standards for outcome measures to allow more direct comparisons across studies. Caregiver interventions need to be developed and validated for many challenging illnesses (e.g. Huntington's disease) and situations (e.g. the intensive care unit). Finally, dissemination and implementation studies are needed to translate these findings into clinical practice and to test the effectiveness of various models of caregiver support, including models of cost-effectiveness and how to integrate caregiver support into both inpatient and outpatient care.

Take Home Messages

- Caregivers often feel isolated and burdened by their caregiving role.
- Caregivers' needs can change over the trajectory of their patient's illness.
- Assessing caregiver well-being is vital to a neuropalliative approach, to better support patients and families.
- Many efficacious interventions exist for caregivers yet barriers, including access, may prohibit caregivers from receiving such services.
- Basic training in caregiver assessment can empower neurologists to address caregivers' concerns.
- Caregiving has the potential to provide meaning and positive growth and interventions around meaning and self-efficacy can build caregiver resilience.

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Practical Implementation Strategies for Outpatient Neurology Palliative Care

21

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Once clinicians have established an interest and knowledge base in primary neuropalliative care the question arises of how to put these new skills into practice. Current models of care that emphasize efficiency, uniformity, and attention to billing requirements do not naturally foster a palliative care approach [1]. Similarly clinical habits and mental checklists developed in residency and subspecialty fellowships, while important to providing detailed neurologic assessments and treatment plans, may need to be modified to allow room to understand other aspects of your patients as people and engage in important conversations.

Practicing Primary Palliative Care in an Outpatient Setting

Self-Training in Primary Palliative Care Skills

In any model of palliative care, self-training is a critical step. In the current "primary palliative care" model (see Chap. 1 "Neuropalliative Care: Introduction"), a highly motivated individual seeks self-education and other training to develop knowledge and skills which they incorporate into their practice. In the future, we hope that palliative care training will be a standard part of the curriculum of medical schools and neurology residency programs. In fact, providing a self-education resource for primary neuropalliative care skills is the major goal of this book. Identifying local palliative care mentors can also help greatly for clinical guidance, learning the local landscape of resources, connecting to other clinicians interested in palliative care and offering suggestions for readings, online education, workshops, and conferences. The Education in Palliative and End-of-life Care (EPEC) program provides in-person workshops, online modules and train-the-trainer courses for persons interested in teaching palliative care (https://www.nhpco.org/link/education-palliative-and-end-life-care-epec-project). A new Neurology module (EPEC-N) linked to this book is now available http://bioethics.northwestern.edu/programs/

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epec. The American Academy of Hospice and Palliative Medicine (AAHPM) provides several options for self-study in addition to meetings and workshops for non-specialists (http://aahpm.org/education/self-study). VitalTalk is an evidenced-based interactive education program to improve communication surrounding serious illness (http://vitaltalk.org/).

Integrating Palliative Care into Neurology Clinics

As noted throughout this book, there are many situations in neurology in which a palliative care approach may improve the patient or caregiver experience including the time of diagnosis, nearing end-of-life care, and other triggers for important conversations. In these situations, it may be helpful to schedule a dedicated visit to allow the patient and family time to process new information and to ensure adequate time is available for the conversation. Regarding concerns for reimbursement for the time needed to provide this care, there are now billing codes for Prolonged Services (e.g. 99354), Encounters for Palliative Care (Z51.5) and Advanced Care Planning (99497, 99498). Clinicians in the primary palliative care model should also feel comfortable referring patients to specialized palliative care services when needed including hospice (see Chap. 16 "Hospice and End of Life Care in Neurologic Disease").

Becoming a Palliative Care Champion

Many institutions and hospitals promote the idea of "palliative care champions"; clinicians who not only pursue self-training in primary palliative skills, but also seek out like-minded clinicians to champion care based on palliative care principles for their population of interest [2]. In the field of neurology, this may include sitting in on ethics and palliative care rounds, promoting palliative care related educational programs (e.g. curriculum integration, grand rounds) and quality improvement projects (e.g. advance care planning documentation), and working to ensure neurology patient and family needs are met by available palliative care services. As a palliative care champion, one is able to learn of new ideas at their institution, to network and to bring innovations to neurology patients.

Developing a Palliative Care Clinic

Two important aspects of developing a palliative care outpatient neurology clinic are the ***purpose*** and the ***setting*** of the clinic. On a personal level, finding purpose and meaning in one's practice and providing more comprehensive care for patients with advanced serious illnesses are common motivations for acquiring palliative care skills and developing a palliative clinic. There are other questions to consider. What gaps will this clinic attempt to address? Is there stated interest or need from patients and the community, or from one's medical group or health system? In other words, a certain amount of introspection and assessment of one's self, local community, and medical culture is required before embarking on this endeavor. Included in this clarification of purpose is making the definition and goals of palliative care clear to all stakeholders.

The setting of your clinic is the primary determinant of which care model options are feasible. The choice of care model should also reflect the purpose of your clinic, the needs and goals of your patient population, the referral base, and the availability of resources including financial, logistical, and institutional support. There will be different needs and challenges to address depending on whether one is planning to set up an outpatient neurology clinic as part of a community neurology practice, multi-specialty group, managed care or other large health system, or a university academic clinic.

Models of Outpatient Neuropalliative Care Delivery

In the "primary palliative care" model, primary care and disease-specific clinicians (e.g.

neurologists) incorporate a palliative care approach into their work using event and symptom-based triggers and refer to other clinicians (e.g. social work) and specialist palliative care when needed [3, 4]. An emerging approach to outpatient palliative care is the "embedded palliative care" model in which specialized palliative care services are integrated into comprehensive care for a chronic or progressive illness [5, 6]. In neurology, palliative care may be embedded into disease specific palliative care such as Parkinson's disease (PD) or Amyotrophic Lateral sclerosis (ALS) [7, 8]. This type of clinic most often arises from a subspecialty neurologist who becomes a palliative care champion, pursues informal training and collaborates with a palliative medicine specialist to create a dedicated outpatient neuropalliative care clinic. A third model is the "specialist neuropalliative care" model which provides expert neuropalliative care to all neurologic conditions. This model most often arises from a neurologist who has pursued a formal palliative care fellowship.

As discussed below, specialized palliative care benefits from a team approach and may be difficult for persons outside of an academic center or large hospital group to replicate. Trials of alternative models to allow greater dissemination of outpatient palliative care in the community are underway [9]. These include a spoke-and-hub model, in which community neurologists receive training and individual coaching in neuropalliative care and have access to team-based resources for their patients via telemedicine virtual house calls (R01NR016037).

Building the Interdisciplinary Palliative Team

At this point in the development of a clinic, a thorough needs assessment for your patient population is essential to identify which skills are most critical to your team. This will depend greatly on the scope of your clinic (e.g. ALS vs. General Neuropalliative Care). It is also important to decide how the team will be run, whether led by a neurologist or palliative specialist or co-managed by other members of the care team.

Some authors have suggested the concept of a "core" neuropalliative care team central to the running of any palliative clinic [10]. A common neuropalliative core team includes a palliative neurologist, nurse, chaplain, and social worker. It is important that everyone on the team has a well-defined role, and we recommend the use of checklists to ensure coverage of important issues and avoid redundancies in care (see Table 21.1).

Common roles include:

- The **neurologist** may serve as a team leader who performs clinical assessments to confirm diagnosis and determine prognosis, and is the clinician who is responsible for intensive symptom management, placing all required orders and referrals, and overseeing the plan of care.
- In some clinics, **nursing** or other **advanced practice providers** may also be a part of the team leadership. Nurses bring a unique background with expertise in clinical care, caregiver support, and clinic coordination. Therefore, in many clinics, the nurse is the key point person for welcoming the patient and completing the initial assessment; screening of symptoms and issues relevant to both the patient and caregiver; medication reconciliation; and after-visit planning and telephone follow-up.
- **Medical social workers** are well-equipped to help the patient and caregivers navigate the medical system, apply for disability, work with insurance companies, and attain resources. Their knowledge of the local landscape of available services for both patient and family are indispensable, such as elder law consultations, home health services, and housing services. Furthermore, medical social workers frequently have training in counseling.
- A **chaplain** is perhaps the role most misunderstood in the setting of a neurological clinic. When offered a choice, many patients decline to see a chaplain because they associate chaplains with specific religious (as opposed to spiritual) support and end of life. If on the team, we recommend that all patients and families meet with the chaplain at least once and specifically for issues related to building

Table 21.1 Clinical team checklists

NEUROLOGIST Checklist
Complete Medical History

- ☐ History of Neurologic Illness
  - ☐ Recent hospitalizations or other complications
  - ☐ Functional Status (e.g. independence or assistance with ADLs)
- ☐ Patient and Caregiver Goals of Care
  - ☐ How define quality of life (sources of suffering; sources of joy)
  - ☐ Worries about the future/Fears
  - ☐ Sources of support and meaning
  - ☐ If caregiver present – any issues of safety, overwhelmed, burnt-out, own health concerns
  - ☐ Educational needs
  - ☐ Status of Advance Care Plans/Documentation
  - ☐ Specific Goals of Care
- ☐ Review of Systems (specific focus on the following)
  - ☐ Psychiatric and Behavioral Symptoms
  - ☐ Pain Issues
  - ☐ Falls, balance and mobility
  - ☐ Swallowing, sialorrhea and nutrition (weight changes)
- ☐ Review Medications
- ☐ Allergies and medication side effects
- ☐ Past Medical and Surgical History
- ☐ Social History, including Current Living Situation
- ☐ Family History

☐ **Physical Examination**

- ☐ Review orthostatic vital signs and weight
- ☐ Neurologic Exam

☐ **Assessment**

- ☐ Review Prognosis and Disease Stage
- ☐ Reflect Goals

☐ **Plan**

- ☐ Safety issues (e.g. home safety, abuse, driving)
- ☐ Medication changes
- ☐ Referrals for other services
- ☐ Heads up to other team members
- ☐ Need for Palliative Care Referral (in clinic or outside): Complex symptom management (e.g., pain)
- ☐ Follow-up plan including issues for phone call

hope and resilience, coping with difficult emotions, dealing with existential suffering and promoting spiritual wellbeing (see Chap. 18 “Spiritual Care”).

– A **palliative care specialist** who is available for case review and consultations can also prove invaluable, particularly for neurologists who lack palliative care fellowship training, to

assist with difficult symptom management or complex goals of care discussions.

Other team members to consider would include rehabilitation specialists (e.g. physical therapists, occupational therapists, speech language pathologists), mental health specialists (psychologists, psychiatrists, counselors), nutrition, and respiratory therapists. Team membership will vary according to the specific care needs of your patient population and resources available. For instance, respiratory therapists will likely be central to any clinic with an ALS focus but would only occasionally be needed for a PD clinic.

Overcoming Barriers/Challenges

Funding

Team-based palliative care clinic appointments for new or complex patients may be over 2 h long, which leads to concerns regarding low reimbursements for prolonged evaluation and management (E&M) clinical visits. In addition, many of the clinical team members are not able to independently bill for services provided (e.g. social worker, nurse, or chaplain). Sources of support for the clinic may include:

- Physician Billing: There are billing codes for Prolonged Services (e.g. 99354), Encounters for Palliative Care (Z51.5) and Advanced Care Planning (99497, 99498).
- Cost Saving: While interdisciplinary palliative care is time and staff-intensive, it may result in cost savings for health care systems by reducing aggressive medical/surgical interventions, intensive care unit services and hospitalizations, particularly near end of life [11]. This is particularly true for closed systems such as Health Management Organizations (HMO), Accountable Care Organizations (ACO) and certain government health care (e.g. the U.S. Veterans Affairs health system). Unfortunately, the long-term financial benefit of palliative care services is not often seen by health insurance companies or integrated health systems, including academic medical centers who see the upfront costs of care in a palliative clinic setting as prohibitive. Clinicians who are part of a larger group or academic department, can argue that neuropalliative care may have advantages on a group level; by effectively taking on and caring for high needs and time-intensive patients other clinicians are free to pursue more high revenue procedures or patients. Hopefully, with similar "business case" planning efforts, the long-term medical and financial benefits of outpatient palliative program will be appreciated, much like has occurred in the inpatient setting.
- Research: There is a growing interest in establishing an evidence base for palliative care models in general, and a great need to expand this research to neurologic illness. Sources of funding that should be considered include the National Institutes of Health (institutes of Neurologic Disease and Stroke (NINDS), Aging (NIA), and Nursing (NINR)), the Patient Centered Outcomes Research Institute (PCORI), the Agency for Healthcare Research and Quality (AHRQ), and disease specific organizations.
- Other Sources of Funding: Other sources of funding may include departmental support, institutional support, and research grants.

Cultural Barriers

Patients and clinicians may not be familiar with palliative care, and those who have heard of the term frequently carry significant misperceptions of the goals and practice of palliative care including conflating palliative care with hospice, believing it is incompatible with disease modifying treatments, that it is giving up on patients or only for the imminently dying [12, 13]. As palliative care is relatively new to the field of neurology and most neurologists have minimal exposure to palliative care during their training [14]. It remains to be seen how rapidly and fully palliative care will be embraced in neurology and this process may differ across nations, regions, institutions, subspecialties and individuals. Even within oncology, where palliative care originated, this evolution has proceeded over decades and is far from complete [15].

To overcome these misperceptions, the field has taken two complementary approaches. First is to provide education on palliative care to colleagues and patients who are more likely to embrace palliative care when they understand how it can complement current models of care [16]. Second is to rebrand palliative care. To this end, the majority of neuropalliative care clinics have chosen names underplaying the term palliative such as "Supportive Care Clinic", "Complex Symptom Management Clinic" and "Next Step Clinic" or incorporating palliative care principles in the design of multidisciplinary subspecialty clinics (e.g. for ALS). Even in the setting of metastatic cancer, significantly fewer patients accepted a referral to a "palliative clinic" compared to the same clinic when it was relabeled "supportive care clinic". The same findings were seen among oncologists, where significantly more physicians were willing to refer patients with metastatic cancer to a "supportive care clinic", than when the same clinic was called a "palliative clinic" [17, 18].

Running a Palliative Care Clinic

Before the Clinic Visit: Gathering Information

As with most clinical services, the beginning of the clinical encounter usually starts at the time of the referral. Therefore, the referral plan should be very well organized. Colleagues and other referring clinicians will need some level of education about what is an appropriate referral to the clinic. If possible, specific needs assessment tools can be provided, such as the Brief Needs Assessment Tool (BNAT – See Table 21.2). Referral forms should indicate common reasons for referral (e.g. goals of care, caregiver support) and whether the referral is for help with a specific issue (e.g. pain), co-management or transfer of care. Referring clinicians should be educated about the importance of palliative care across the disease spectrum and that proactive support, rather than waiting for the "right time", is especially important when dealing with neurological conditions that lead to cognitive impairment.

Table 21.2 Brief palliative care needs assessment tool (B-NAT)

1. Would you be surprised if this patient passed away within the next year?	**Yes**	**No**
2. Does the patient or caregiver have a severely reduced quality of life because of the diagnosis listed above?	**Yes**	**No**
3. Does the patient have motor or non-motor symptoms that are resistant to treatment, such as postural instability, pain, fatigue, constipation, or dysphagia?	**Yes**	**No**
4. Is the patient experiencing mood problems (e.g. depression, anxiety, apathy) or behavioral issues (e.g. hallucinations, delusions, agitation)?	**Yes**	**No**
5. Is the caregiver struggling with feeling overwhelmed?	**Yes**	**No**
6. Is the patient or caregiver struggling with difficult emotions such as guilt, grief or anger?	**Yes**	**No**
7. Is the relationship between the patient and caregiver strained due to illness?	**Yes**	**No**
8. Does the patient or caregiver have spiritual or existential concerns such as loss of hope or feeling demoralized?	**Yes**	**No**
9. Does the patient or caregiver have significant concerns or worries about the future?	**Yes**	**No**

A "NO" for question #1, and/or "YES" for any of the questions #2 through #9 is considered a trigger

Patients will have many questions about why they're being referred to a separate clinic, how this clinic is different from their usual chronic care, and what they should expect. The purpose and expectations of the clinic should be communicated to patient and caregivers including the duration of visits and the importance of family/caregivers being present. We have found that a call from the clinic nurse to reconcile medications, remind patients to bring-in advance directives, and to summarize patient and caregiver issues a week prior to their palliative care clinic appointment greatly improves clinic efficiency. Educational materials, such as pamphlets, letters or online materials, can help prepare patients and ease discussions for referring clinicians. You should be prepared to address concerns associated with the stigma that palliative care has and may want to consider leaving the word "palliative" out of the title of the clinic.

Clinic Flow: Avoiding Patient Fatigue and Maximizing Time for Person-Centered Conversation

Perhaps the most important organizing principle of how to run your clinic visit with the patient is to keep in mind the goal of minimizing fatigue and redundancy. This can be accomplished through clear team member roles, checklists (Table 21.1), and brief planned sign-outs between team members.

There are two general models for clinic flow. In the first model, each member of the clinical team sees the patient separately. When possible, the patient and caregivers should be able to remain in one clinic room, with the team members rotating according to a predetermined schedule. The exception is that we frequently separate the patient and caregiver to meet with the social worker and chaplain individually, since this can be the first time that each person can freely express their concerns without their partner present. In this model, the clinic nurse takes 15 min at the start of the visit to confirm the main issues to be discussed, and review skin integrity, nutrition, and other clinical care aspects specifically assigned to the clinic nurse. The primary palliative neurologist sees the patient last and is responsible for summarizing all of the recommendations into a verbal and written plan provided to the patient. In the second model, all members of the clinical team see the patient together. The primary palliative neurologist in this model is also responsible for summarizing the final plan to the patient and caregiver. Some clinics have created hybrid models in which members of the team pair up (e.g. chaplain and social worker) and all members of the team may be present for certain portions of the visit (e.g. wrap-up) [19].

For the neurologist developing primary palliative skills, it can be easy to slip back into a mindset focused on "treating the disease". While advanced symptom management is an important aspect of any palliative clinic, one should remain mindful that a generous portion of the visit should emphasize what makes palliative care different from chronic care; providing person-centered care to reduce suffering, improve quality of life, and provide caregiver support, as well as spiritual and emotional support. When needed, time for discussing goals of care, prognosis, and other critical conversations, is essential. Another advantage of checklists is to ensure that the conversation will get to things not covered in usual clinic visits such as universal assessment, screening for incidents, psychosocial stressors, caregiver screening, and goals of care discussions. The physical examination may also shift in a neuropalliative clinic, with more emphasis placed on weight and nutrition, mental status, mobility, and potential sources of pain.

When present, we consider the patient AND caregiver or family dyad as the unit of care. We emphasize the importance of caregivers and family being present at the in-person clinic visit as caregiver assessment and support is a central aspect of palliative care (see Chap. 20 "Caregiver Assessment and Support"). Furthermore, caregivers are essential sources of collateral history and extremely helpful in carrying out the plan of care after the visit. The absence of a caregiver may in fact serve as a trigger for important conversations or referral as such patients may have a greater need for mobilization of psychosocial support and other resources.

We begin each clinic day with a 30-min review of all scheduled patients and notes from clinic nurse summarizing key clinical issues and end each day with a brief synopsis of important findings, recommendations and follow-up plans. Plans typically involve symptom management, referrals to ancillary services, addressing caregiver needs, providing needed resources, discussing next steps for advanced care planning, and ongoing communication. A clinic or note template based on the checklist helps to ensure all necessary domains are considered.

After Visit Communication

There is a need for very close follow-up of patients and their caregivers. First, families are frequently overwhelmed, and the plans developed in clinic are very often complex. A clear communication plan should be discussed including when and how

to reach the clinical team. We provide written summaries to patients and our nurse plans for a check-in call 2 weeks and then 6 weeks after each appointment. Patients may need follow-up calls with the social worker, chaplain or other team members depending on their primary issues.

Other Considerations

Telemedicine

It is an unfortunate fact that those who stand to benefit the most from palliative care services often have significant travel burden. Thankfully, due to rapidly changing technology (i.e. faster internet speeds, more user-friendly software), telemedicine video conferencing is now a feasible means of delivering subspecialty neurological care. "Virtual house calls" can improve access to multidisciplinary clinics, decrease travel burden, reduce patient fatigue and allow patients to receive health care in the comfort of their home. Furthermore, seeing a patient in their home environment frequently provides surprising insights into a family's situation. Many aspects of palliative care are amenable to telemedicine visits but it is important to identify impediments to good telemedicine communication such as poor vision, hearing loss, and low internet speeds. We have found that once patients have less than 1 year of life expectancy, they are frequently unable to come to clinic in-person and have been able to follow these end-stage patients intensively with virtual house visits, even acting as their main hospice providers, to intensively manage symptoms and continue providing support even in their last days of life. We envision that telemedicine will be a growing part of any substantial model of palliative care delivery, especially in larger medical centers and academic practices as billing and logistic issues are overcome [20].

Resource Lists

Providing care based on palliative principles often involves bringing multiple clinical services into the care map of the patient. Large health systems will frequently have a built-in, integrated network of provides to refer patients to. However, for clinicians developing a primary palliative care practice, or those in tertiary academic centers with large referral areas and multiple payers, it can be overwhelming to find reliable, quality resources for patients spread out over a several-hundred-mile radius.

We recommend creating lists of known and trusted resources, clinicians, and care services incorporating your own experiences, recommendations from colleagues, and positive patient feedback. Lists of different clinicians (e.g. physical and occupational therapists, speech language pathologists, personal trainers, psychiatrists, psychotherapists, etc.) organized by location, accepted insurance, and availability is essential to our practice. Resource lists may be on paper or online but should be readily accessible by all team members and easily provided to patients in clinic.

Quality Improvement, Education and Research

Quality improvement approaches should be multi-faceted. Continually soliciting patient and caregiver feedback is important in assessing the benefits of the palliative clinical intervention. This can be done through anonymous surveys as well as qualitative interviews, and impromptu feedback obtained during visits. Basic data on outcomes can be collected to track quality. Continued education in this evolving field can include regular journal clubs and case conferences among the clinical staff. We also strongly recommend developing self-care practices both as individuals and as a team (see Chap. 19 "Self-Care"). This may include rituals to start the day (e.g. intention setting), end the day (e.g. gratitude, discussing difficult situations), and regular meetings (e.g. monthly meeting to check in with team members on difficult cases or issues as a team).

As a field, there is a need for pragmatic research to: (1) Determine the efficacy of novel models of care; (2) Compare the effectiveness of existing models of care; (3) Understand the costs

and savings of neuropalliative care models; and (4) Develop and test models to implement and disseminate palliative care in a community setting. Palliative care may also serve as an organizing framework for improving the patient and family-centeredness of multidisciplinary subspecialty team-based care as well as standardizing procedures across institutions. Implementation strategies should be included in palliative care education for both palliative care specialists, who will need guidance in establishing new clinics, as well as for primary palliative care providers who will need guidance in incorporating these skills into their routine clinic flow.

Take Home Messages

- Primary neuropalliative care may be facilitated by self-education, connecting with other interested clinicians, and knowing appropriate billing codes for prolonged services and advance care planning.
- Developing a successful outpatient neuropalliative care clinic requires an assessment of the needs of your colleagues and patients and the resources available at your institution.
- Specialist neuropalliative care clinics benefit from an interdisciplinary approach including chaplain, social work and nursing expertise.
- Clear team member roles, checklists and rules for team communication are essential to the efficiency and effectiveness of team-based care.

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The Future of Neuropalliative Care

22

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As remarkable advances in the prevention, diagnosis and treatment of neurological illness continue to revolutionize our field, we will also face an increasing need to support and guide patients and families through complex choices involving immense uncertainty and intensely important outcomes of mind, body and spirit. To improve the lives for all patients with neurological illness and their families will require a broad range of clinical, educational and investigative efforts in this nascent field of neuropalliative care.

Clinical efforts should focus on improving access to skilled neuropalliative care to all patients with serious neurological disease and their families. This will require that we develop effective and appropriate **models of care** for integrating palliative care into neurology in different settings, and implement meaningful companion **quality measures** to encourage high quality practice across sites. In addition, we need to develop trigger systems for clinicians to recognize specific palliative care and communication needs; and implement triage systems to facilitate timely specialist palliative care consultation.

We need to find ways to better **align incentives** to promote patient-centered care by advocating for payment reform and use of appropriate evaluation and management codes that recognize key elements of effective palliative care including advance care planning, goals of care and other important conversations, caregiver and family support, reimbursement for team-based services, and coordination of care. Finally, we need to re-evaluate eligibility **criteria for hospice** in patients with neurological disorders and establish a neuro-specific toolkit for hospice nurses and facilities.

Educational efforts need to focus on establishing a core neuro palliative care skill set for all neurologists, and more specialized training for persons subspecializing in certain diseases. Formal collaboration between palliative care and neurology training programs need to be established to promote a reciprocal understanding of the two fields, and more neuro-specific educational tools need to be available to palliative medicine specialists and other clinicians. There are situations where patients have needs that go beyond primary palliative care, and neuropalliative care is an emerging subspecialty for persons interested in making this their career focus. Finally, ongoing education is required to help clinicians, patients, families, and other stakeholders as well as the public understand the advantages

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of palliative care to promote informed choices and improve quality of life.

Research needs in the field of neuropalliative care include a better understanding of the natural history of neurological disease, not only as it relates to mortality but also as it relates to other outcomes important to patients and to their families such as quality of life. Investigations should focus on processes that optimize the delivery of "goal-concordant care", such as best communication practices and treatment decision aids. More evidence is needed regarding methods to help identify the palliative care needs of an individual patient, family, and situation and prompt certain conversations (including goals of care discussions), specialist consultations or hospice referral. This includes improving the tools to prognosticate neurological illness and communicate the information to loved ones and decision-makers. We need to better understand how people make decisions, how we can support them in finding the right decision and how we can measure decision quality. Finally, drugs, devices, service delivery strategies, and behavioral interventions need to be tested to improve complex symptom management and meet other needs of our patients and their families and to improve care while reducing unwanted burden and costs.

Conclusions

Neurology in 50 years will look very different than it does today. Our concept of disease will change, our ability to diagnose will become much more precise, and the impact of our therapies more profound and meaningful to patients. Almost everything will change. The way we measure outcomes, the way we organize our subspecialties, how we conduct research, what we teach our trainees, how we round on patients, where they are principally cared for, how we are valued and the way we get paid. But some things will not change. The patient will remain at the center of all we do guiding our way, because the most important things we do in our lives, we do for others. We hope this book lays the foundation for neurologists to learn more palliative care and for palliative care specialists to learn more neurology, such that the optimal "neuropalliative care approach" will always be provided to patients and families as we usher in this most exciting era in medicine.

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